Bailey & Love
REVISION GUIDES

SBAs & EMQs for the MRCS PART A

Vivian A Elwell, Jonathan M Fishman, Rajat Chowdhury

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Contents

All things are possible until they are proved impossible –
and even the impossible may only be so, as of now.
Pearl Buck, A Bridge for Passing (1962)

About the authors

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Currently working as a Specialist Registrar in Neurosurgery, Vivian held posts in Accident and Emergency, Orthopaedics, Neurosurgery, and General Surgery with the Surgical Rotation at St Mary's Hospital, Imperial College NHS Trust, London.

Vivian is an author of undergraduate and post-graduate medical textbooks: *Essential OSCE Topics for Medical and Surgical Finals* (Radcliffe 2008), *The Insider's Guide to the MRCS Clinical Examination* (Radcliffe 2009), and *OSCEs for the MRCS Part B: A Bailey and Love Revision Guide* (Hodder Arnold 2009).

She taught clinical skills to medical students and doctors, and was an anatomy demonstrator at the Imperial College School of Medicine, London. She served on the Imperial College School of Medicine Curriculum Development Committee.

Vivian's awards include: the Swinford Edward Silver Medal Prize for her OSCE Examination, the Columbia University Research Fellowship at Columbia College of Physicians and Surgeons in New York City, the Columbia University King's Crown Gold and Silver Medal Awards, the Kathrine Dulin Folger Cancer Research Fellowship and the "Who's Who of Young Scientists Prize." In 2010, Vivian was a finalist for the BMA's Junior Doctor of the Year Award.

Vivian earned a Bachelor's Degree in Biological Sciences at Columbia College, Columbia University, and a MA from the University of Cambridge. She earned a Bachelor of Medicine and Bachelor of Surgery from the Imperial College School of Medicine. She is a member of the Royal College of Surgeons and is a College Instructor on the "Care of the Critically Ill Surgical Patient (CCrISP)" course.

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Jonathan is an Oxford Specialist Registrar in ENT and a member of the Royal College of Surgeons. He graduated with a First Class Honours Degree in Natural Sciences from Sidney Sussex College, University of Cambridge, and completed his clinical training at St John's College, University of Oxford. He has held posts in Accident and Emergency, ENT, General Surgery and Neurosurgery, as part of the surgical rotation at St Mary's Hospital, Imperial College, London.

Jonathan has extensive teaching experience and is the primary author of three undergraduate and three postgraduate medical textbooks, including the highly successful *History Taking in Medicine and Surgery* (Pastest Publishing, 2005; 2nd Edition, 2010). He spent part of his medical training at both Harvard University and the NASA Space Center.

Jonathan was awarded Taylor and Howard-Agg Scholarships at Sidney Sussex College, Cambridge, and has been awarded the highly prestigious title of 'Lifelong Honorary Scholar' by the University of Cambridge, for academic excellence. He has been awarded a fellowship from the British Association of Plastic Surgeons for research at NASA, and from Cambridge University for research at Harvard University.

Jonathan is committed to a career in academic ENT, with a strong emphasis on research and teaching. In 2009, he was awarded a Royal Society of Medicine GlaxoSmithKline Fellowship Award for his academic achievements to date. In 2010, he was awarded a Foreign and Commonwealth Office UK-USA Stem Cell Collaboration Fellowship, in addition to a Royal College of Surgeons of England Surgical Research Fellowship.

In 2011, he was awarded a prestigious Medical Research Council Clinical Research Training Fellowship.

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Rajat is a Specialist Registrar in Radiology and has held posts in Accident and Emergency, Orthopaedics & Trauma, Cardiothoracic Surgery, General Surgery, and Plastic Surgery with the Surgical Rotation at St Mary's Hospital, Imperial College NHS Trust, London. He completed his medical studies at Oxford University, May Clinic and Harvard University. He is a member of the Royal College of Surgeons.

He taught clinical skills to medical students and doctors in Oxford and London, and tutored Biochemistry and Genetics students at Oxford University. He was an anatomy demonstrator at the Imperial College School of Medicine, London, and was President of Oxford's Hugh Cairns Surgical Society. He is currently pursuing a Postgraduate Certificate in Medical Education.

Rajat's academic awards include: Oxford University's Bristol Myers Squibb Prize in Cardiology; The Radcliffe Infirmary Prize in Surgery; GlaxoSmithKline Medical Fellowship; the Warren Scholarship for Paediatric Studies at the University of Toronto; Exhibition and Kennedy scholarships to Harvard University. Rajat was also awarded Bachelors and Masters Degrees from University College London. In 2009, Rajat won the prestigious British Society of Interventional Radiology Specialist Registrar Prize. In 2010, he was elected to the chair of the National Trainee Committee of the British Institute of Radiology. Rajat has been awarded a NICE Scholarship and plans to become a future NHS leader. He is also the lead author of *Radiology at a Glance* (Wiley-Blackwell 2010) and *Consent in Surgery* (Radcliffe 2010).

Preface

This book has been written as an accompaniment to *Bailey and Love's Short Practice of Surgery* with the MRCS examination in mind. It is dedicated to the Intercollegiate MRCS Part A Examination, which is the first part of the Intercollegiate MRCS Examination. This new examination was introduced in the Autumn of 2008 and replaced the MRCS Parts 1 and 2 examinations, in line with the new pattern of surgical training in the UK. The examination syllabus, format and content are common to The Royal College of Surgeons of Edinburgh, The Royal College of Surgeons of England and The Royal College of Physicians and Surgeons of Glasgow. This examination is designed and set by the Royal Colleges of Surgeons to test the knowledge, skills and attributes acquired during core surgical training.

The Intercollegiate MRCS Part A examination comprises of two MCQ papers taken on the same day. Each paper is 2 hours in duration. The first paper covers 'Applied Basic Sciences' (single best answer (SBA) format) and the second paper covers 'Principles of Surgery-in-General' (extended matching questions (EMQ) format). A minimum mark must be obtained in both papers, in addition to attaining the total pass mark to obtain an overall pass in the Intercollegiate Part A Examination. Successful completion of the Intercollegiate Part A Examination qualifies the trainee surgeon to enter the Intercollegiate Part B Objective Structured Clinical Examination.

This book is based on our highly successful *Insider Medical MRCS Courses,* and the feedback obtained from candidates who sat the examination. We have, therefore, written this book with the aim of targeting high-yield topics that are likely to be faced and offer methods to tackle the challenges that may be posed in the examination. We have drawn from our breadth of experience of teaching at both the undergraduate and postgraduate levels and have identified common pitfalls.

A thorough understanding of applied basic science and the ability to problem-solve underpins surgical science and sets the foundation for future surgical practice. Whilst it is not feasible to cover the complete syllabus within the remit of this book, we have selected the most important and high-yield topics to facilitate examination study and revision. The style of questions mimics those found in the real examination and these will therefore serve well as mock papers. We are confident that this book will assist any trainee surgeon in their revision for the MRCS Part A Examination and, in doing so, refine their analytical approach to all areas of their surgical practice.

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Rajat Chowdhury

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Introduction: The Insider's Guide to the MRCS Part A

So you want to be a surgeon? Fantastic choice! The road to enlightenment begins with the first test – the *Intercollegiate MRCS Part A Examination*.

Studying for examinations is often not the most pleasant experience. However, this examination is not peppered with esoteric topics but ones that you will find genuinely useful in your daily practice, even at your junior stage.

The Part A examination consists of two MCQ papers of multiple-choice questions, each of two hours' duration taken on the same day. The papers cover generic surgical sciences and applied knowledge.

- Paper 1 covers **applied basic science** and consists of 135 single best answer questions (SBAs). Each question contains five possible answers, of which there is only one single best answer.
- Paper 2 covers **principles of surgery-in-general** and consists of 135 extended matching answer questions (EMQs). Each theme contains a variable number of options and clinical situations. Only one option, however, will be the most appropriate response to each clinical situation. It is possible for one option to be the answer to more than one of the clinical situations.

To achieve a 'pass', a minimum level of competence in each of the two papers will be required in addition to achieving or exceeding the pass mark set for the combined total mark for the whole of Part A. There are equal marks for each question and there is no negative marking. In other words, marks will not be deducted for a wrong answer.

Preparing for an examination is never straightforward and you are often faced with a vast range of revision sources, from traditional textbooks to scientific journals. The secret to passing any kind of MCQ exam is to practice as many questions as possible. Sitting in front of large textbooks will help to a degree, but it is important to get a feel for the type of questions that may appear in the exam and then to focus revision on reading around the questions. Inevitably, at some stage during the revision process you will want to test yourself on exam-style questions, so this book aims to fulfil that need. The questions are grouped into single best answers and extended matching questions as in the real examination, and the explanations have been divided into separate chapters so that you can attempt the questions under mock examination conditions, or use each question as a syllabus guide.

Most questions will require you to read a **clinical vignette** and will therefore test both your knowledge and correct application. There may be more than one answer that could fit each question, but there will always be one answer that is considered *the best answer*. Beware of absolute terms such as 'always' and 'never': these are rarely ever the best answer!

One of the first techniques in approaching these types of questions is to cover up the answers initially, read the question and suggest an answer. Then look for the answer in the options available. If the answer appears, you have a very high chance of being correct. You should check that the other answers are in fact incorrect, before selecting your final answer. If you are unable to answer the question initially, work your way down the list and start by eliminating those answers that you definitely feel are incorrect.

These new questions take time to read as they can be several lines long, so you must keep a careful eye on the time you spend on each. There is no obligation to answer the questions in the order they appear, but you must keep a close check on those that you wish to revisit later. If there are any questions you are unsure of, we recommend that you asterisk that particular question so that if you have time, you can come back to it at the end. If you run out of time, it is well worth guessing any answer for the outstanding questions – you have nothing to lose and may well get lucky.

Research has shown that changing your answer in the exam is neither good nor bad: if you

have a good reason for changing your answer, then change it. It is a myth that people always change from 'right' to 'wrong', in that it is those questions that you will remember and review after the exam. You will not remember the questions you changed from wrong to right!

Although everyone may tell you before the exam **'read the question'**, it is imperative to do so in the MCQ exam. Underline the key words, and do not be caught out, as so often people are, when the question says which of the following is false as opposed to being true! When you have finished the exam, make a final check that you have answered **all** the questions.

Finally, remember that common things are common. The examination is testing your ability to diagnose and manage common and important conditions to be a safe and competent surgeon.

Turn your passion into perfection. Happy studying, and good luck!

Section 1
Applied Basic Sciences

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Single best answer questions

1. **A 21-year-old footballer presents to A&E with a stabbing pain above his right knee joint. He states the pain came on suddenly while he was sprinting. On examination he is unable to extend the leg and he walks with a limp. There is suprapatellar swelling and an absent knee jerk. What is the likely diagnosis?**
   - A Fracture of patella
   - B Injury to posterior cruciate ligament
   - C Tear of adductor magnus muscle
   - D Tear of biceps femoris muscle
   - E Tear of quadriceps tendon

2. **During strenuous exercise, what else occurs besides tachycardia?**
   - A Rise in $Paco_2$
   - B Increased stroke volume
   - C Rise in mixed venous blood O_2 saturation
   - D No change to blood pressure
   - E Increased renal blood flow

3. **A patient is found to have thrombophlebitis migrans. What other condition must be considered?**
   - A Venous insufficiency
   - B Diabetes mellitus
   - C Bronchial carcinoma
   - D Lyme disease
   - E Beckwith–Wiedemann syndrome

4. **A 42-year-old lady is involved in a road traffic accident. She presents with a dislocated shoulder. The shoulder is relocated by you in A&E but afterwards you notice there is winging of the scapula. Which nerve or muscle is likely to be damaged?**
   - A Axillary nerve
   - B Teres major
   - C Radial nerve
   - D Long thoracic nerve of Bell
   - E Deltoid

5. **Which cells cannot regenerate?**
   - A Peripheral nerve cells
   - B Schwann cells
   - C Renal tubular cells
   - D Mucosal cells
   - E Liver cells

6. **Which of the following is a feature of metastatic spread?**
   - A Commonly occurs transluminally
   - B Basal cell carcinomas commonly spread via lymphatics
   - C Osteosarcomas commonly spread via lymphatics
   - D Prostatic carcinoma commonly spreads via the blood
   - E Spread follows the pattern of venous drainage

7. **A 35-year-old man is knocked off his cycle and hits his head on a kerb. He is brought into hospital with a fluctuating score on the Glasgow Coma Scale. He underwent a CT head scan which shows a biconvex-shaped haematoma. What other finding is he most likely to have?**
   - A Midline shift
   - B Subdural haemorrhage
   - C Skull fracture
   - D Subarachnoid haemorrhage
   - E Papilloedema

8. **In wound healing, which cells are responsible for wound contraction?**
   - A Fibroblasts
   - B Macrophages
   - C Reticulocytes
   - D Giant cells
   - E Lymphocytes

9. Which is a feature of an adenoma?
   A Typically encapsulated
   B Can arise in transitional epithelial cells
   C Typically invades the basement membrane
   D Typically annular lesions
   E Does not contain dysplastic cells

10. A singer complains of not being able to sing high notes following her thyroidectomy. What is the likely cause?
   A Damage to the recurrent laryngeal nerve
   B Damage to the external laryngeal nerve
   C Damage to the vagus nerve
   D Tracheal stenosis
   E Vocal cord hemiparalysis

11. During fracture healing, what type of bone makes up the provisional callus?
   A Cortical bone
   B Cancellous bone
   C Cartilage
   D Woven bone
   E Lamellar bone

12. Radiotherapy can be the sole treatment for which of the following cancers?
   A Adenocarcinoma of the oesophagus
   B Rectal carcinoma
   C Anal cancer
   D Gastric carcinoma
   E Phylloides breast tumour

13. A woman has a pleomorphic adenoma. She is undergoing a total parotidectomy. Which important vascular structure should the surgeon be most aware of?
   A Facial artery
   B Facial vein
   C External carotid artery
   D Retromandibular vein
   E Internal jugular vein

14. What is the cardiac index?
   A Stroke volume × heart rate
   B Mean arterial pressure × systemic vascular resistance
   C Cardiac output divided by body weight
   D Cardiac output divided by heart rate
   E Cardiac output divided by body surface area

15. A patient is known to have exposure to beta-naphthylamine. What is he/she at increased risk of developing?
   A Small-cell lung carcinoma
   B Bladder cancer
   C Breast cancer
   D Chemical pneumonitis
   E Lymphoma

16. A 70-year-old man suffers an ischaemic stroke and develops a left homonymous hemianopia. Where is the likely infarct?
   A Left frontal lobe
   B Right frontal lobe
   C Left occipital lobe
   D Right occipital lobe
   E Left temporal lobe

17. When does the heart rate decrease?
   A After a meal
   B On inspiration
   C Pressure on the eyeball
   D Pressure on the sinoatrial node
   E Exercise

18. Which of the following suggests that respiratory failure is chronic rather than acute?
   A Plasma bicarbonate of 39 mmol/L
   B Pao_2 of 9 kPa
   C Pao_2 of 7 kPa
   D Arterial pH of 7.2
   E Hypoventilation

19. A 12-year-old boy develops acute tonsillitis. He starts to complain of pain in the ear. What nerve is likely to be involved?
   A Superior laryngeal
   B Glossopharyngeal
   C Facial
   D Hypoglossal
   E Lesser palatine

20. A man undergoes an open inguinal hernia repair. During the procedure the spermatic cord is visualized. What structures does this contain?
   A Dartos muscle
   B Femoral branch of the genitofemoral nerve
   C Ilioinguinal nerve
   D Inferior epigastric artery
   E Pampiniform plexus

21. When performing a left nephrectomy from a posterior approach, which of the following structures are encountered before reaching the kidney?
    A Peritoneum
    B Suprarenal gland
    C Subcostal nerve
    D Tail of pancreas
    E Right hemidiaphragm

22. When performing a right hemicolectomy, which of the following structures is encountered during dissection?
    A Caudate lobe of liver
    B Inferior vena cava
    C Third part of duodenum
    D Right ureter
    E First part of duodenum

23. What structure does the pancreas overly?
    A Right kidney
    B Left kidney
    C Right adrenal gland
    D Left adrenal gland
    E Gall bladder

24. What causes a reduction in pulmonary functional residual capacity?
    A Asthma
    B Pulmonary fibrosis
    C Emphysema
    D Pneumonia
    E Pulmonary oedema

25. Which is a feature of the physiology of angiotensin II?
    A Stimulates renin release
    B Inhibits aldosterone release
    C Weak arteriolar vasoconstriction
    D Converted from angiotensin I in the liver
    E Released in hypovolaemia

26. Which displaces the oxygen–haemoglobin curve to the left?
    A A decrease in pH
    B Anaemia
    C A rise in Pco_2
    D A fall in Pco_2
    E Pyrexia

27. What factor decreases coronary perfusion?
    A Hypoxia
    B Antidiuretic hormone (ADH)
    C Alpha stimulation
    D Beta stimulation
    E Glyceryl trinitrate (GTN) spray

28. Resection of the terminal ileum is associated with malabsorption of which of the following substances?
    A Calcium
    B Folic acid
    C Cholesterol
    D Bile salts
    E Potassium

29. Which is a feature of the action of insulin?
    A Promotes protein synthesis
    B Promotes gluconeogenesis
    C Inhibits potassium entry into cells
    D Promotes calcium release from bone
    E Promotes phosphate release from bone

30. Which causes prolonged vomiting due to pyloric stenosis?
    A A drop in serum urea
    B A drop in bicarbonate
    C A rise in serum potassium
    D A rise in serum chloride
    E A rise in arterial Pco_2

31. Extracellular fluid differs from intracellular fluid by which of the following?
    A Lower chloride concentration
    B Higher potassium concentration
    C Greater volume
    D Lower protein concentration
    E Lower pH

32. Which is a feature of raised intracranial pressure?
    A Caused by shearing injury to the scalp
    B Occurs immediately after an acute subdural haematoma
    C Leads to a rise in cerebral perfusion pressure
    D Causes constriction of the ipsilateral pupil
    E Can lead to a rise in blood pressure and bradycardia

33. Which is a feature of metabolic acidosis?
    A There is negative base excess
    B Bicarbonate is the main intracellular buffer
    C Proteins and phosphates are the main extracellular buffer
    D Compensation occurs by a decrease in alveolar ventilation
    E Bicarbonate infusion is the mainstay of treatment

34. **Which is a feature of the posterior third of the tongue?**
    - A Filiform papillae
    - B Fungiform papillae
    - C Sensory innervations from the internal laryngeal nerve
    - D Sensory innervations from the chordae tympani
    - E Villiform papillae

35. **Which is a feature of the knee joint?**
    - A The popliteus tendon is extracapsular
    - B The suprapatellar bursa does not communicate with the joint
    - C The anterior cruciate ligament is supplied by the middle geniculate artery
    - D The iliotibial tract inserts into the fibula
    - E Rotation occurs above the meniscus

36. **Which is a feature of the hepatic artery?**
    - A Supplies the same amount of blood to the liver as the portal vein
    - B Provides the same amount of oxygen to the liver as the portal vein
    - C Contains blood with the same oxygenation as the portal vein
    - D Does not supply blood to hepatic metastases
    - E Divides the liver into anatomical segments

37. **Metabolic alkalosis is commonly seen in patients with which of the following?**
    - A Pancreatic fistula
    - B Aspirin poisoning
    - C Protracted vomiting
    - D Hypoglycaemia
    - E Hyperventilation

38. **Osteomyelitis is most commonly caused by which microbe in adults?**
    - A *Staphylococcus aureus*
    - B *Escherichia coli*
    - C *Staphylococcus epidermidis*
    - D *Pseudomonas* sp.
    - E *Streptococcus viridans*

39. **Which is a feature of a keloid scar?**
    - A May respond to pressure dressing
    - B Occurs within the limits of the surgical wound
    - C Is most common on flexure surfaces of the limbs
    - D Can be prevented by subcuticular sutures
    - E May be re-excised with good results

40. **Splenectomy patients are at particular risk of overwhelming sepsis from which organisms?**
    - A Anaerobic bacteria
    - B *Bacteroides fragilis*
    - C *Haemophilus influenzae*
    - D Fungi
    - E *Staphylococcus aureus*

41. **A boy is found to have haemophilia B. What pathological problem does he have?**
    - A Deficiency of platelets
    - B Deficiency of factor VIII
    - C Deficiency of factor IX
    - D Deficiency of factor X
    - E Deficiency of factor XI

42. **A patient is found to have chronic iron deficiency anaemia. What symptom might he also describe?**
    - A Dysphagia
    - B Vomiting
    - C Diarrhoea
    - D Dysuria
    - E Nausea

43. **What features would you expect to find in a patient with haemorrhagic shock?**
    - A Decrease in catecholamine secretion
    - B Oxygen–haemoglobin dissociation curve shifted to the right
    - C Stimulation of aortic chemoreceptors
    - D Increase in tidal ventilation
    - E Decrease in antidiuretic hormone (ADH) secretion

44. **Gastrointestinal consequences of major burns include which of the following?**
    - A Splanchnic vasodilation
    - B Acute gastric dilatation
    - C Cushing's ulcers
    - D Terminal ileal hyperplasia
    - E Mechanical bowel obstruction

45. **When is nitrogen balance positive?**
    - A In sepsis
    - B During the first 3 days following surgery
    - C During growth
    - D While adrenocorticotropic hormone (ACTH) levels are high
    - E Following bone fractures

46. **Hormones of the anterior pituitary include which of the following?**
    - A Prolactin
    - B Oxytocin
    - C Thyroxin
    - D Antidiuretic hormone (ADH)
    - E Vasopressin

47. **Which is a feature of the scalenus anterior muscle?**
    - A Attaches into the anterior tubercles of the transverse processes of C1–C7 vertebrae
    - B Attaches to the scalene tubercle of the 2nd rib
    - C Has the subclavian vein passing posterior to it
    - D Has the subclavian artery passing anterior to it
    - E Lies deep to the prevertebral layer of the deep cervical fascia

48. **What is the normal glomerular filtration rate?**
    - A 50 mL/min
    - B 75 mL/min
    - C 100 mL/min
    - D 125 mL/min
    - E 150 mL/min

49. **What is the commonest cancer in the UK?**
    - A Colorectal cancer
    - B Lung cancer
    - C Breast cancer
    - D Melanoma
    - E Leukaemia

50. **What is the 5-year survival rate of carcinoma of the pancreas?**
    - A 5 per cent
    - B 15 per cent
    - C 30 per cent
    - D 50 per cent
    - E 60 per cent

51. **Regarding enteral tube feeding, which statement is true?**
    - A Requires just as much monitoring as parental feeding
    - B Continuous feeding with iso-osmolar fluids may cause diarrhoea
    - C Elemental fluids require minimal digestion by the patient
    - D Maintains the structural, but not the functional, integrity of the small bowel
    - E Fluids should contain glucose rather than sucrose to lower the osmolality

52. **Which statement applies to the original Dukes' classification for colorectal carcinoma?**
    - A Is a tumour grading scale
    - B Accurately defines the number of lymph nodes involved
    - C Distinguishes tumours that penetrate the muscularis mucosa from those that are confined by the mucosa
    - D Does not take into account the presence of metastases
    - E Highlights the improved prognosis in those patients with villous rather than tubular carcinoma

53. **In acute osteomyelitis of a long bone, which statement applies?**
    - A If blood-borne, is usually caused by streptococci
    - B Acute inflammation causes a rise in intraosseous pressure
    - C The involucrum is a focus of dead bone
    - D Early radiographs will demonstrate rarefaction and periosteal new bone formation
    - E *Pseudomonas* tends to occur in patients with sickle cell disease

54. **In intestinal anastomatic leaks, which statement applies?**
    - A Are apparent 10–14 days after surgery
    - B Abdominal pain, pyrexia and tachycardia are suggestive of a leak
    - C The appearance of bowel contents through the abdominal wound is proof of an anastomatic leak
    - D Early leaks are best tested by local surgical repair
    - E Late leaks are treated by urgent laparotomy, abdominal washout and repair

55. **Which of the following chemotherapeutic drugs is an alkylating agent?**
    - A Cyclophosphamide
    - B Doxorubicin (Adriamycin)
    - C 5-Fluorouracil (5-FU)
    - D Vincristine
    - E 6-Mercaptopurine

56. Which statement applies to metastatic calcification?
    - A Occurs in normal tissue
    - B Is characterized by psammoma bodies
    - C Has normal blood levels of calcium
    - D Characteristically occurs in osteoarthritis
    - E Is associated with degenerated foci in leiomyomas and has caseous nodules

57. Complications of an above-knee amputation include which of the following?
    - A Joint contractures affecting the hip joint
    - B Sudek's atrophy
    - C Myoglobinuria
    - D Neuroma formation
    - E Amyloid deposition

58. Which statement applies to the cephalic vein?
    - A Begins in the region of the anatomical snuffbox
    - B At the elbow is deep to the lateral cutaneous nerve of the forearm
    - C Ends by joining the brachial vein
    - D Is medial to the biceps muscle in the arm
    - E Has no valves

59. Thyrotoxicosis is characterized by which of the following?
    - A Weight gain
    - B Proximal myopathy
    - C Enopthalmos
    - D Hypertrophy of the vascular elastic lamina
    - E Nose bleeds

60. Which is a product of occlusion of the right posterior cerebral artery?
    - A Blindness in the right eye
    - B Left homonymous hemianopia
    - C Bilateral hemianopia
    - D An absent light reflex
    - E Extraocular muscle paralysis

61. The adductor (subsartorial) canal contains which of the following?
    - A Vastus lateralis muscle in its lateral aspect
    - B Profunda femoris vessels
    - C Femoral arterial branch, which takes part in the anastomosis around the knee joint
    - D Vastus medialis muscle
    - E Adductor longus muscle

62. Which is a feature of a cervical rib?
    - A A cause of brachial artery aneurysm
    - B Best diagnosed by posteroanterior (PA) chest radiograph
    - C Compresses the upper trunk of the brachial plexus
    - D A cause of thoracic outlet syndrome
    - E Most commonly symptomatic in the 50–60 years age group

63. Which statement applies to a 5 cm abdominal aortic aneurysm?
    - A Has an annual risk of rupture of 80 per cent
    - B Involves the renal artery origin in 15 per cent of cases
    - C If the aortic aneursym grows at a rate of more than 5 mm/year, elective surgery should be considered
    - D Is more common in builders
    - E Is a cause of toe gangrene

64. Which statement applies to the hepatic portal vein?
    - A Is formed by the union of the splenic and superior mesenteric veins
    - B Runs behind the epiploic foramen
    - C Lies anterior to the common hepatic artery
    - D Originates behind the body of the pancreas
    - E Approximately 25 per cent of hepatic blood flow is derived from the hepatic portal vein

65. Which statement applies to chronic lower limb ulceration?
    - A Affects 10 per cent of the elderly population
    - B Is most commonly caused by arterial disease
    - C Is linked to varices
    - D Predisposes to malignant change
    - E Should be treated by compression bandaging if the ankle–brachial pressure index (ABPI) is less than 0.5

66. Which statement applies to lymphoedema?
    - A Affects the lower limbs in 80 per cent of cases
    - B Presents with bilateral limb swelling
    - C Is diagnosed by ultrasound

D Is most commonly iatrogenic in aetiology
E Is best treated by graded compression stockings

67. Which statement regarding Hodgkin's disease is true?
A Typically seen in the gastrointestinal tract
B May be classified using the Rappaport classification
C Is characterized by Reed–Sternberg cells
D The lymphocyte-depleted type is associated with a more favourable prognosis
E Usually presents with painful lymphadenopathy

68. What is supplied by the facial nerve?
A Palatoglossus muscle
B Medial pterygoid muscle
C Masseter muscle
D Temporalis
E Parasympathetic fibres to the submandibular gland

69. Which is a feature of the submandibular duct?
A Lies between mylohyoid and hyoglossus muscle
B Is 10 cm long
C Develops from the endoderm
D Is closely related to the facial nerve
E Opens into the mouth at the side of the cheek

70. Which is a feature of the Eustachian tube in a child?
A Extends from the middle ear to the oropharynx
B Is at more of a horizontal angle than in an adult
C Is longer in length than in an adult
D Is cartilagenous
E Is derived from the second pharyngeal pouch

71. In intussusception in children, which statement applies?
A Occurs more commonly in girls
B The commonest form is ileo-ileal
C Is characterized by severe colicky abdominal pain with pain-free intervals
D There is an association with Henoch–Schönlein purpura
E Usually occurs in the 2–3 years age group

72. Which statement is true of Sjögren's syndrome?
A Is a condition in which the patient has wet eyes and mouth
B Is most commonly seen in young men
C Is characterized by beta-pleated sheets
D Is associated with autoimmune diseases
E Predisposes to adenocarcinoma

73. Which applies to rigid sigmoidoscopy?
A Is useful in the examination of haemorrhoids
B Will usually demonstrate the first 25 cm of sigmoid colon
C Allows the biopsy of rectal tumours without anaesthetic
D Is the best way of obtaining tissue to diagnose Hirschsprung's disease
E Causes perforation in about 5 per cent of patients

74. Which of the following is associated with hyperparathyroidism?
A Paravertebral ossification
B Peptic ulcer
C Retinal haemorrhages
D Aortic stenosis
E Hoarse voice

75. Which statement applies to the posterior triangle of the neck?
A Is bounded by the lateral third of the clavicle inferiorly
B Has a roof formed by the prevertebral fascia
C Has a roof pierced by the external jugular vein
D Is bounded by the anterior border of sternocleidomastoid
E Contains the carotid sheath

76. Which statement applies to the tongue?
A Develops from the first and third branchial arches
B Has taste buds supplied by the hypoglossal nerve
C Is supplied by the facial artery
D Has a profuse anastomosis of blood vessels across the midline
E Deviates to the left in lesions of the left glossopharyngeal nerve

77. **Which statement is true of postcricoid carcinoma?**
    - A Is more common in patients with Plummer–Vinson syndrome
    - B Is highly radiosensitive
    - C Is associated with workers exposed to iron
    - D Has a 5-year survival rate of more than 60 per cent
    - E Is more common in males

78. **In a 65-year-old women with a retrosternal goitre discovered on a routine chest X-ray, which of the following statements is appropriate?**
    - A Thyroid dysfunction is unlikely
    - B Stridor is likely if the trachea is deviated to one side
    - C Thyroid antibodies will be present
    - D Thyroid malignancy is common
    - E Recurrent laryngeal nerve palsy is common

79. **Which of the following statements is true of salivary gland carcinoma?**
    - A Typically occurs in the minor salivary glands
    - B Is related to smoking
    - C Occurring in the parotid gland results in Frey's syndrome
    - D In the parotid gland can be reliably diagnosed by fine-needle aspiration
    - E Is characteristically sensitive to radiotherapy

80. **Which of the following statements is true of Colles' fracture?**
    - A Is a cause of carpal tunnel syndrome
    - B Results in palmar displacement of the distal fractured fragment
    - C Extends into the wrist (radiocarpal) joint
    - D Is typically associated with compression of the ulnar nerve
    - E Involves the ulnar styloid process

81. **When a person lifts his right leg and stands unaided with only his left foot on the ground, the iliac crest on the right side does not descend (negative Trendelenburg sign) provided that one of the following applies. Which?**
    - A The right gluteus medius muscle is actively contracted
    - B The left hip joint is not congenitally dislocated
    - C The right superior gluteal nerve is intact
    - D The left psoas muscle is actively contracted
    - E The neck of the right femur is not been shortened by a healed fracture

82. **Which of the following describes laminar flow in a blood vessel?**
    - A Has maximum velocity in the centre
    - B Is a flow regime characterized by low momentum diffusion and high momentum convection
    - C Produces the highest concentration of cells at the periphery of the vessel
    - D Reynolds numbers of greater than 2300 are generally considered to be of a laminar type
    - E Is considered to be 'rough' whereas turbulent flow is considered to be 'smooth'

83. **The clinical features of a lumbar disc prolapse affecting root S1 may include which of the following?**
    - A Paraesthesia on the medial aspect of the foot
    - B A positive femoral stretch
    - C Weakness and wasting of the muscles that dorsiflex the foot
    - D Limitation of straight-leg raising
    - E An impaired knee jerk

84. **Which is true of umbilical hernias in children?**
    - A Are a rare problem (1 in 10 000)
    - B Are commonly associated with incarceration of the bowel
    - C Are most commonly found in Caucasian children
    - D Are typically associated with a patent vitello-intestinal duct
    - E Have small orifices and characteristically close spontaneously before the age of 5 years

85. **A patient is suspected of having a haemolytic transfusion reaction. How should the patient best be managed?**
    - A Removal of inessential foreign body irritants (nasogastric tube, Foley's catheter)
    - B Fluid restriction

C 0.1 M HCl infusion
D Steroids
E Fluids and mannitol

86. Which of the following statements concerning access to the abdomen is true?
A Muscle-splitting incisions are more painful than cutting incisions
B Failure to close the peritoneum increases the incidence of adhesions
C Collagenase dissolves sutures near wound edges
D The Veress needle in laparoscopic surgery is inserted under direct vision
E Burst abdomen is preceded by serosanguinous discharge

87. Which of the following is true of pseudomembranous colitis?
A Does not cause colonic bleeding
B Is caused by *Clostridium perfringes*
C Is the result of metronidazole administration
D Is a cause of toxic dilation of the stomach
E Responds to treatment with vancomycin

88. The diagnosis of acute cholecystitis can be reliably confirmed by which of the following?
A Ultrasound
B Plain radiograph
C Abdominal radiograph
D Oral cholecystography
E Liver function tests

89. According to the modified Glasgow scoring system, indices of poor prognosis in severe pancreatitis at 48 hours include which of the following?
A Albumin of 30 g/L
B Urea of 10 mmol/L
C Corrected serum calcium of 2.98 mmol/L
D Arterial Po_2 of 10 kPa
E Blood glucose of 6 mmol/L

90. Which statement is true of the rectum?
A Has a venous drainage into the superior mesenteric vein
B Has a lymphatic drainage to the superficial inguinal nodes
C Is supplied by the superior mesenteric ganglia
D Is anteriorly bounded by the seminal vesicles and prostate
E Receives its main arterial blood supply from the middle rectal artery

91. What is a characteristic feature of the liver?
A It weighs 750 g
B It receives 60 per cent of the body's total cardiac output
C It drains through hepatic veins into the superior vena cava
D It receives its nerve supply from the right vagus via the superior mesenteric ganglia
E It is attached to the diaphragm by the falciform ligament

92. Which statement regarding choledochal cysts is true?
A Rarely present beyond childhood
B Iron deficiency may develop
C Dumping syndrome may develop
D Incapacitating diarrhoea is not infrequent
E Recurrent duodenal ulcers usually follow an aggressive course

93. Which of the following is true of talipes equinovarus?
A Is a structural deformity of the midfoot and forefoot
B Is bilateral in fewer than 10 per cent of cases
C Is more common in females
D Is initially treated by correction of the equines deformity first
E Is treated by operative correction and may result in articular damage and foot stiffness

94. Concerning bone tumours, which is true?
A There is an association between osteosarcoma and Paget's disease of the bone
B Chondosarcomas most commonly occur in young children
C Chemotherapy has a limited role in overall management
D Metastasis usually occurs via lymphatics
E Pain is rarely a presenting feature

95. The posterior relations of the kidney include which structure?
A Rectus abdominis muscle

B Femoral nerve
C Long thoracic nerve of Bell
D Costodiaphragmatic recess of the pleura
E Lumbar sympathetic trunk

96. Which statement is true of Meckel's diverticulum?
A Is present in 20 per cent of the population
B Arises from the mesenteric border of the jejunum
C May contain heterotropic pancreas
D Is present only in males
E Is a diverticulum of the bladder

97. Which of the following is a recognized curative treatment option for localized carcinoma of the prostate?
A Radiotherapy
B Lithotripsy
C Hormonal treatment
D Cytotoxic therapy
E Tamsulosin

98. Which of the following statements is true for a patient who has been maintained on haemodialysis for 10 years?
A Will need a parathyroidectomy shortly after renal transplant
B Will have vascular calcification, which will resolve after parathyroidectomy
C Is no more likely to have secondary hyperparathyroidism than someone on continuous ambulatory peritoneal dialysis (CAPD) for the same period
D Could have osteoporosis if has taken aluminium hydroxide over this time
E Will need bisphosphonates after parathyroidectomy

99. In relation to breast carcinoma, which statement is true?
A Will affect 1 in 15 women
B Is more common in multiparous women
C Is more common in women with late menarche
D Is more common in women who breast-feed
E Has a 60 per cent chance of occurring in patients with a first-degree relative who had a premenopausal breast cancer

100. Concerning statistical analysis of a population with a normal (Gaussian) distribution, which is true?
A The population may be uniquely defined by its mean and its median values
B About 95 per cent of the population lies within one standard deviation of the mean
C It would be inappropriate to apply a chi-squared test because the distribution is not linear
D Non-parametric tests could be used
E Fewer than 5 out of 1000 of the population would be expected to be more than two standard deviations from the mode

101. Which of the following cells secrete intrinsic factor?
A Goblet cells
B Kupffer cells
C Peptic cells
D Chief (zymogenic) cells
E Parietal cells

102. Splenectomy increases susceptibility to which of the following organisms?
A *Streptococcus pyogenes*
B *Schistosoma haematobium*
C *Bacteroides fragilis*
D *Neisseria meningitidis*
E *Staphylococcus aureus*

103. Cardiac output is decreased under what circumstances?
A During stimulation of sympathetic nerves to the heart
B On cutting the vagus nerves to the heart
C By increasing the end-diastolic volume of the heart
D As a result of decreased pressure within the carotid sinus
E Upon assuming the upright position

104. Which statement is true for flow through a vessel or lumen?
A It is inversely proportional to the pressure head of flow
B It is inversely proportional to the radius
C It is directly proportional to the length of the tube
D It is directly proportional to the viscosity of blood passing through the tube
E It is directly proportional to the fourth power of the radius

105. **You request preoperative lung function tests on a patient with longstanding emphysema. What is true of the functional residual capacity?**
   - A It is the sum of the tidal volume and residual volume
   - B It is the sum of the inspiratory reserve volume, the expiratory reserve volume and the tidal volume
   - C It can be measured directly by spirometry
   - D It is the sum of the residual volume and the expiratory reserve volume
   - E It is the volume of air that remains in the lung after forced expiration

106. **Which statement is true of lung compliance?**
   - A Is defined as the change in pressure per unit volume
   - B Is synonymous with elastance
   - C Is increased in emphysema
   - D Is equal in inflation and deflation
   - E Is reduced by the presence of surfactant

107. **Which of the following hormones is secreted by the anterior pituitary gland?**
   - A Testosterone
   - B Oxytocin
   - C Thyroid-stimulating hormone (TSH)
   - D Corticotropin-releasing hormone (CRH)
   - E Antidiuretic hormone (ADH)

108. **The oxygen–haemoglobin dissociation curve is shifted to the left by what?**
   - A An increase in Pco_2
   - B A fall in pH
   - C A rise in temperature
   - D An increase in 2,3-DPG
   - E Fetal haemoglobin

109. **Which of the following cells are cytotoxic?**
   - A CD4 T-cells
   - B CD8 T-cells
   - C B-cells
   - D TH1 cells
   - E TH2 cells

110. **A 3-week-old baby exhibits projectile vomiting shortly after feeding, and failure to thrive. On examination, an olive-shaped mass is palpable in the right upper quadrant of the abdomen. A clinical diagnosis of pyloric stenosis is made. What biochemical laboratory features would support the diagnosis?**
   - A Hypokalaemia, metabolic alkalosis, low urinary pH
   - B Hyperkalaemia, metabolic acidosis, high urinary pH
   - C Hypokalaemia, metabolic acidosis, high urinary pH
   - D Hyperkalaemia, metabolic alkalosis, low urinary pH
   - E Hypokalaemia, metabolic alkalosis, high urinary pH

111. **A sample of cerebrospinal fluid (CSF) is obtained following a lumbar puncture. What is a feature of normal CSF?**
   - A Is produced within arachnoid granulations
   - B Has a composition identical to that of plasma
   - C Has a protein content that is 0.5 per cent that of plasma
   - D Has a higher potassium content than that of plasma
   - E Its pH is heavily buffered

112. **A patient on the surgical ward has chronic renal impairment. The plasma creatinine is 225 μmol/L and the glomerular filtration rate (GFR) is 25 mL/min. Which statement is correct regarding the patient's renal function?**
   - A The GFR is the main factor determining the rate of urine production
   - B GFR can be measured by para-aminohippuric acid (PAH)
   - C The normal GFR is 50 mL/min
   - D Inulin clearance can be used to estimate GFR
   - E A normal plasma creatinine implies normal renal function

113. **Gastric acid secretion is stimulated by which of the following?**
   - A Somatostatin
   - B Gastrin
   - C Secretin
   - D The glossopharyngeal nerve
   - E Cholecystokinin

114. **Carbon dioxide is principally transported in the blood in which form?**
   - A CO_2 physically dissolved in solution
   - B Carboxyhaemoglobin

C Bicarbonate
D Carbaminohaemoglobin
E Carbonic anhydrase

115. The plateau phase of the cardiac action potential is due to what?
A Magnesium influx
B Potassium influx
C Calcium influx
D Chloride efflux
E Sodium influx

116. A patient with a 6 cm abdominal aortic aneurysm is scheduled for elective repair. As part of the preoperative work-up, an echocardiogram is requested. The ejection fraction is defined as what?
A The ratio of end-diastolic volume to stroke volume
B The ratio of stroke volume to end-diastolic volume
C End-diastolic volume minus end-systolic volume
D End-systolic volume divided by stroke volume
E The ratio of stroke volume to end-systolic volume

117. Bile salt reuptake principally occurs where?
A In the duodenum
B In the jejenum
C In the ileum
D In the colon
E In the caecum

118. A 40-year-old patient is brought into the A&E unit with head injury. The cardiovascular effects of raised intracranial pressure include (BP = blood pressure; HR = heart rate; CPP = cerebral perfusion pressure):
A ↓ BP, ↓ HR, ↓ CPP
B ↓ BP, ↑ HR, ↓ CPP
C ↑ BP, ↑ HR, ↓ CPP
D ↑ BP, ↓ HR, ↓ CPP
E ↓ BP, ↑ HR, ↑ CPP

119. A patient is diagnosed with Conn's syndrome. Aldosterone is secreted from where?
A Liver
B Zona glomerulosa of the adrenal cortex
C Juxtaglomerular apparatus
D Adrenal medulla
E Zona fasciculata of the adrenal cortex

120. Which of the following gastrointestinal fluids is richest in potassium?
A Salivary
B Pancreatic
C Gastric
D Bile
E Small bowel

121. Which one of the following is the most potent inhibitor of gastric acid secretion?
A Chlorphenamine
B Misoprostol
C Ranitidine
D Omeprazole
E Gaviscon®

122. The following changes occur at birth:
A The left umbilical vein becomes the ligamentum venosum
B The urachus becomes the medial umbilical ligament
C The ligamentum arteriosum is a remnant of the umbilical arteries
D The foramen ovale closes in all cases at birth
E The vitellointestinal duct may persist as a Meckel's diverticulum

123. With regard to phototransduction:
A Photoreceptors depolarize in response to light exposure
B It is a vitamin D-dependent process
C Upon exposure to light, cGMP levels within the photoreceptor fall
D Opening of cGMP-gated cation channels occurs in response to light
E Light photons are absorbed by transducin

124. Which of the following is a feature of the adaptive (acquired) immune response?
A Acute inflammation
B Secretion of tears
C Natural killer cells
D Surface epithelia
E Self/non-self discrimination

125. **With regard to the thyroid gland, which of the following is true?**
   - A Tri-iodothyronine is the principal hormone of the gland
   - B Calcitonin is produced by follicular cells
   - C Organification involves the binding of tetra-iodothyronine to amino acids
   - D It is stimulated to produce thyroxine (T4) by TRH
   - E Thyroglobulin is stored in the colloid of follicles

126. **Which one of the following is a depolarizing neuromuscular blocker?**
   - A Atracurium
   - B Atropine
   - C Guanethidine
   - D Suxamethonium
   - E Neostigmine

127. **With regard to genital development:**
   - A The mesonephric (Wolffian) ducts differentiate into the female genitalia
   - B Female development is hormonally regulated through the actions of anti-Mullerian hormone and testosterone
   - C Gender is principally determined by the presence or absence of two X chromosomes
   - D Anti-Mullerian hormone is secreted by Leydig cells
   - E The testes and ovaries descend from their original position at the 10th thoracic level

128. **With regard to visual field pathways:**
   - A The axons contained within the optic nerve are derived from photoreceptors
   - B The optic tracts synapse in the medial geniculate nucleus of the thalamus
   - C Decussation is complete at the optic chiasm
   - D The macula region is grossly over-represented in the visual cortex
   - E Compression at the optic chiasm results in a homonymous hemianopia

129. **With regard to neutrophils (polymorphonuclear leucocytes):**
   - A They are the predominant cell type in chronic inflammation
   - B They have bilobed nuclei
   - C They have a life-span of only a few hours in inflamed tissue
   - D They may fuse to form multinucleate giant cells
   - E They carry out oxygen-dependent microbial killing by lysosomal enzymes

130. **Which one of the following regarding myoglobin in skeletal muscle is correct?**
   - A It binds and stores oxygen for rapid release during falling Po_2
   - B It contains a magnesium cofactor
   - C It releases oxygen at high Po_2
   - D It exhibits cooperative binding with O_2 (sigmoid dissociation curve)
   - E It is devoid of iron

131. **The following are classes of antihypertensive agents, *except*:**
   - A ACE inhibitors
   - B Beta-blockers
   - C Alpha-blockers
   - D Angiotensin II receptor antagonists
   - E Calcium-channel agonists

132. **With regard to development of the limbs:**
   - A Occurs in the second trimester of pregnancy
   - B Shaping of the hands and feet is brought about through apoptosis
   - C Is independent of the apical ectodermal ridge
   - D Thalidomide most commonly causes clinodactyly
   - E Under some circumstances limb regeneration occurs to a small degree in adult humans following amputation

133. **With regard to the organization of the cerebral cortex:**
   - A The right cerebral hemisphere is normally dominant
   - B The primary visual cortex is located within Brodmann area 17
   - C The primary auditory cortex is located within Broca's area
   - D The primary motor cortex is located within the post-central gyrus
   - E The primary somatosensory cortex is located within the pre-central gyrus

134. **The germinal centre of a lymph node:**
   - A Contains mainly T-lymphocytes

B Contains Langerhans dendritic cells
C Generates immunoglobulin-producing plasma cells
D Is characteristically enlarged in established infectious mononucleosis
E Contains the cords and sinuses

135. All eukaryotic cells have membrane-bound organelles. Which one of the following organelles is self-replicating?
A Golgi body
B Ribosome
C Rough endoplasmic reticulum
D Mitochondria
E Lysosome

136. With regard to antidiabetic agents, which drug stimulates release of insulin from the pancreas?
A Actrapid
B Gliclazide
C Metformin
D Rosiglitazone
E Acarbose

137. With regard to development of the kidney:
A It is derived from endoderm
B The transcription factor WT-1 is necessary for the competence of the mesenchyme to be induced
C There are two phases of kidney development
D The kidneys descend during development to their final site
E The metanephric blastema gives rise to the collecting ducts

138. With regard to cerebrospinal fluid (CSF):
A It is produced by arachnoid granulations
B It is produced at a rate of 30 mL/min
C It is situated within the subdural space
D It flows between the lateral ventricles and third ventricle via the Foramen of Magendie
E It turns over approximately 4–5 times daily

139. With regard to antibodies (immunoglobulins):
A They are produced by mast cells
B The antigen binding region is located in the constant region
C Antibody class is defined by the structure of the light chain
D Diversity is partly achieved through somatic hypermutation
E They are composed of one heavy chain and two light chains

140. A patient is diagnosed as having iron deficiency anaemia. Which of the following is the peripheral blood film likely to show?
A Macrocytic anaemia
B Microcytic anaemia
C Ring sideroblasts
D Sickle-shaped cells
E Howell–Jolly bodies

141. Which one of the following diuretics acts mainly on the distal convoluted tubule to decrease water reabsorption?
A Furosemide
B Acetazolamide
C Bendroflumethiazide
D Metolazone
E Vasopressin

142. With regard to diaphragmatic development:
A Is formed by the fusion of two separate elements
B Develops in the thoracic region
C The left pleuroperitoneal canal is larger and closes later than the right
D The central tendon arises from the pleuroperitoneal membranes
E The septum transversum migrates cranially (rostrally) in development

143. With regard to cerebrospinal fluid (CSF) composition:
A CSF is produced through a passive process
B The composition of CSF is identical to that of plasma
C The protein content of CSF is 0.5 per cent that of plasma
D The potassium content of CSF is higher than that of plasma
E The pH of CSF is heavily buffered

144. With regard to IgM antibodies:
A They cross the placenta

B They are characteristically produced in a secondary immune response
C They can activate complement
D They are usually found lining mucosal surfaces
E They are usually monomeric

145. Epinephrine is an endogenous catecholamine. Its effects include which one of the following?
A Decreased glucagon secretion by pancreatic alpha cells
B An effect mainly on alpha-adrenoceptors
C Increased glycogen synthesis in liver
D Increased glycogen synthesis in muscles
E Increased lipolysis

146. Which antibiotic acts by inhibiting protein synthesis?
A Penicillin
B Erythromycin
C Cefuroxime
D Trimethoprim
E Co-trimoxazole

147. With regard to craniofacial development:
A The human face forms from the fusion of four swellings
B Alcohol is the most common cause of holoprosencephaly
C The palate forms from the medial extensions of the mandibular swellings
D Craniofacial abnormalities account for 5 per cent of all human congenital defects
E The nasolacrimal groove forms between the medial and lateral nasal processes

148. The speed of nerve conduction decreases with:
A Increasing axonal diameter
B Increasing membrane capacitance
C Decreasing axonal resistance
D Myelination by Schwann cells
E Increasing temperature

149. The human major histocompatibility complex (MHC):
A Resides on chromosome 11
B Is composed of six human leukocyte antigen (HLA) genes
C Codes for three classes of antigens
D Will be identical in dizygotic twins
E Codes for blood group antigens

150. Which one of the following statements regarding von Willebrand's disease is true?
A It commonly exhibits an autosomal dominant pattern of inheritance
B It presents with reduced bleeding times
C It always has associated reduced factor VIII levels
D It is associated with reduced or abnormal platelets
E It is X-linked recessive

151. Which one of the following lipid-lowering agents acts by inhibiting HMG CoA reductase?
A Nicotinic acid
B Bezafibrate
C Colestyramine
D Simvastatin
E Omega-3 fatty acids

152. With regard to intestinal development:
A The gut is a mesodermal derivative
B The whole of the foregut apart from the stomach undergoes rotation
C The stomach is a midgut derivative
D Rupture of the cloacal membrane creates the mouth
E Midgut development involves herniation of bowel into the umbilicus

153. With regard to skeletal muscle fibres:
A They are each normally innervated by more than one motor neurone
B They become less excitable as the extracellular ionized calcium levels fall
C Calcium is taken up by the sarcotubular system when they contract
D Actin and myosin filaments shorten when they contract
E They contain intracellular stores of calcium ions

154. With regard to the major histocompatibility complex (MHC):
A CD4 (helper) T-cells recognize antigen only in the context of MHC Class I
B Class II MHC is expressed on all nucleated cells of the body
C Class II MHC contains β_2-microglobulin
D Class II MHC presents exogenous antigens
E Class II MHC is expressed in low levels on the surface of dendritic cells

155. In acute inflammation, which is the predominant cell type involved?
   A Basophil
   B Eosinophil
   C Lymphocyte
   D Monocyte
   E Neutrophil

156. Which antiarrhythmic drug acts by inhibiting potassium channels?
   A Lignocaine
   B Atenolol
   C Amiodarone
   D Verapamil
   E Diltiazem

157. With regard to the branchial arches:
   A Apart from the first cleft, the other branchial clefts are normally obliterated by overgrowth of the second branchial arch
   B Six pairs of branchial arches develop in humans
   C The muscles of facial expression are first-arch derivatives
   D All parathyroid glands originate from the same branchial arch
   E The tongue principally develops from the second branchial arch

158. With regard to nerve fibres:
   A Impulses can travel in one direction only
   B They continue to conduct impulses when extracellular sodium is replaced by potassium
   C An action potential has an amplitude varying directly with the strength of the stimulus
   D The equilibrium potential for an ion species depends on the ratio of the concentrations of the ion outside to inside of the cell
   E Resting nerve cell membranes are more permeable to Na^+ ions than to K^+ ions

159. The classic pathway of complement activation:
   A Starts with the activation of the C3 component
   B Is activated by lipopolysaccharide cell-wall constituents
   C Is activated by IgA immune complexes
   D Is activated by IgM immune complexes
   E Is evoluntionarily older than the alternative pathway

160. The plateau stage of the cardiac action potential is caused by which one of the following mechanisms?
   A Ingress of calcium ions
   B Ingress of potassium ions
   C Efflux of potassium ions
   D Ingress of sodium ions
   E Efflux of sodium ions

161. Which of the following anti-Parkinsonian drugs is a COMT (catechol-O-methyltransferase) inhibitor?
   A Selegiline
   B L-Dopa
   C Entacapone
   D Benzatropine
   E Bromocriptine

162. With regard to development of the nervous system:
   A Neural tube development requires signals from the underlying mesoderm
   B The nervous system is derived from endoderm
   C Neural tube defects originate during the final trimester of pregnancy
   D The notochord forms the spinal cord in adults
   E Neural tube defects result from the incomplete migration of neural crest cells

163. With regard to smooth (visceral) muscle:
   A Excitation depends more on the influx of extracellular calcium than release from internal stores
   B It contains no actin or myosin filaments
   C It classically relaxes when it is stretched
   D It contains an extensive T-tubular system
   E It is innervated through somatic motor nerve endings

164. A young man has a skull fracture involving the posterior cranial fossa. The fracture is most likely to have injured:
   A The temporomandibular joint (TMJ)
   B The temporal lobe
   C Mandibular division of trigeminal nerve (Vc)
   D Abducens nerve in the cavernous sinus

E Cranial nerve VIII as it enters the internal acoustic meatus

165. The incubation period for hepatitis A is:
A 2–10 days
B 15–40 days
C 40–60 days
D 60–160 days
E More than 160 days

166. In the treatment of asthma, the drug salbutamol principally acts by which of the following mechanisms?
A α_1-adrenoceptor antagonism
B β_1-adrenoceptor agonism
C β_2-adrenoceptor agonism
D β_2-adrenoceptor antagonism
E Muscarinic antagonism

167. A Meckel's diverticulum:
A Is a remnant of the urachus
B Is found in 10 per cent of the population
C Is most commonly situated immediately adjacent to the vermiform appendix
D Is completely asymptomatic and an incidental finding
E May contain ectopic tissue

168. With regard to the structure of cardiac muscle:
A The T-tubules are located at the junction of the A and I bands
B It has no visible striations in the cytoplasm
C It has an underdeveloped sarcoplasmic reticulum
D Specialized intercellular junctions exist between myocytes
E Muscle fibres are typically multinucleate with peripherally located nuclei

169. With regard to the acute-phase response:
A Bacterial endotoxin induces the acute-phase response
B Exogenous pyrogens act on the liver to release tumour necrosis factor (TNF)α
C The acute-phase response is mediated through interleukin-10
D Serum albumin levels increase during the acute-phase response
E TNFα decreases catabolic activity

170. Which one of the following areas of the central nervous system contains structures that are considered to be the phylogenically the oldest parts of the brain:
A Frontal lobe
B Limbic system
C Cerebellum
D Visual cortex
E Parietal lobe

171. With regard to organelles:
A Smooth endoplasmic reticulum makes polypeptides
B Mitochondria perform anaerobic respiration
C Mitochondria can multiply independently
D Prokaryotic cells have membrane-bound organelles
E The Golgi apparatus is involved in the degradation of proteins

172. Which one of the following cranial nerves carries parasympathetic fibres?
A V
B IV
C VI
D III
E II

173. With regard to properties of cardiac muscle:
A A fused tetanic response can be produced by repetitive stimulation
B The cardiac muscle action potential lasts approximately 2–3 ms
C Excitation–contraction coupling requires calcium-induced calcium release
D The force of contraction is independent of the length of the muscle fibre
E The plateau phase of the cardiac action potential is principally due to sodium influx

174. With regard to fever:
A It results from the direct action of microorganisms on the brain
B It depends on the action of prostaglandins within the hypothalamus
C It is always maladaptive and serves no purpose
D It only results from infectious causes

E The antipyretic action of aspirin results from boosting of the immune response

175. A patient presents with a torn medial collateral ligament of his left knee. Which of the following signs may be elicited on physical examination?
- A Posterior displacement of the tibia
- B Anterior displacement of the tibia
- C Abnormal lateral rotation during extension
- D Abnormal passive abduction of the extended knee
- E Inability to lock knee on full extension

176. Which of the following is a technique used to identify specific sequences of DNA?
- A Northern blotting
- B Southern blotting
- C Polymerase chain reaction (PCR)
- D Western blotting
- E Reverse-transcription PCR

177. Which one of the following is true concerning the larynx?
- A The posterior crico-arytenoids are the only muscles that separate the vocal cords
- B All the intrinsic muscles are supplied by the recurrent laryngeal nerve
- C The vocal cords are lined by pseudostratified columnar ciliated epithelium ('respiratory' epithelium)
- D The epiglottis is composed largely of hyaline cartilage
- E The cricoid cartilage and tracheal rings are all complete rings of cartilage

178. With regard to chemical neurotransmitters:
- A Noradrenaline is the predominant neurotransmitter found between first- and second-order sympathetic neurones
- B The nerve endings of second-order parasympathetic neurones release acetylcholine that acts on nicotinic cholinergic receptors
- C The neuromuscular junction releases acetylcholine that acts on muscarinic cholinergic receptors
- D The nucleus accumbens and substantia nigra are rich in dopamine
- E The locus coeruleus and periaqueductal grey are rich in acetylcholine

179. Which of the following is *not* an immunologically privileged site?
- A Central nervous system
- B Skin
- C Eye
- D Uterus
- E Testis

180. Pathogenic bacteria enter the body by various routes, and entry mechanisms are critical for understanding the pathogenesis and transmission of the each agent. Which pathogen is correctly linked with its mode of entry?
- A *Neisseria meningitidis* – sexually transmitted entry
- B *Corynebacterium diphtheriae* – food-borne entry
- C *Clostridium tetani* – inhalation entry
- D *Borrelia burgdorferi* – arthropod vector-borne entry
- E *Rickettsia rickettsii* – contaminated wound with soil entry

181. With regard to gene expression:
- A Translation occurs in the nucleus of eukaryotes
- B Introns code for proteins
- C DNA polymerases manufacture DNA in a 3′–5′ direction
- D RNA polymerase II gives rise to protein encoding mRNA
- E Codons are formed from groups of three amino acids

182. Concerning the thyroid gland, which one of the following is correct?
- A Blood supply is through the internal carotid and subclavian arteries
- B Embryologically starts out at the foramen caecum of the tongue
- C Venous drainage is by way of the external jugular vein
- D Produces thyroid stimulating hormone (TSH)
- E Is attached to the thyroid cartilage by Berry's ligament

183. Opioids:
   A Commonly cause diarrhoea
   B Act only centrally
   C Mediate most of their beneficial effects and side-effects through ς-receptors
   D Lead to tolerance
   E Can be reversed by flumazenil

184. Type I hypersensitivity:
   A Is caused by antigen reacting with IgM antibodies
   B Results in mast-cell degranulation
   C Is characterized by the Arthus reaction
   D Takes 48–72 hours to develop
   E Is caused by the formation of antibody–antigen complexes

185. Which one of the following statements concerning referred pain is true?
   A Pain from the transverse colon is usually referred to the midline area below the umbilicus
   B Somatic pain is usually referred in a diffuse, poorly localized pattern
   C The mechanism of referred pain is well understood
   D Diaphragmatic pain is usually referred to the inguinal area
   E Pain from an inflamed appendix is referred to the medial thigh

186. With regard to cell division:
   A Transfer of genetic information between homologous chromosomes occurs in metaphase I of meiosis
   B Mitosis always produces genetically identical daughter cells
   C It is controlled externally by cyclins
   D Cyclins are activated by dephosphorylation
   E p53 is an oncogene

187. With regard to the tongue:
   A All muscles of the tongue are innervated via the hypoglossal nerve
   B Special taste sensation on the anterior two-thirds of the tongue is through the mandibular division of the trigeminal nerve
   C It is composed of smooth musculature
   D Genioglossus muscle protrudes the tongue
   E Its epithelium is of the glandular columnar variety

188. With regard to the relationship of the electrocardiogram to the cardiac cycle:
   A The P-wave results from atrial repolarization
   B The QRS complex is due to ventricular repolarization
   C The Q-T interval gives a rough indication of the duration of ventricular systole
   D The first heart sound occurs at the same time as the P-wave
   E The second heart sound occurs at the same time as the QRS complex

189. Type III hypersensitivity:
   A Is mediated by specifically sensitized T-lymphocytes
   B May cause allergic rhinitis
   C Is a feature of nickel sensitivity
   D May occur in systemic lupus erythematosus
   E Is cell-mediated

190. Which one of the following proteins binds to penicillin?
   A Alanine racemase
   B 30S ribosomes
   C Porin
   D Transpeptidase
   E Peptidoglycan

191. With regard to DNA:
   A Adenine pairs only with thymine
   B Cytosine always pairs with guanine
   C The DNA double helix has 12 base-pairs per turn
   D Uracil is an example of a purine base
   E All bases are paired by two non-covalent hydrogen bonds

192. With regard to the parathyroid glands:
   A They secrete calcitonin
   B They are always four in number
   C They are third branchial pouch derivatives
   D They are all supplied by the inferior thyroid artery
   E They have an invariable position in the neck

193. A woman has warts caused by human papilloma virus (HPV). The infectious HPV is most likely to be found:
   A In terminally differentiated squamous cells

B In the basal layer of the warts
C In the surface cell layer of the warts
D In transformed cancer cells
E Throughout the warts

194. Hyperacute rejection:
A Is a cell-mediated response
B Occurs 48 hours after transplantation
C Can occur in autografts
D May be reversed by high-dose steroids
E May be minimized by blood-group matching

195. A total of 100 hypertensive patients are followed over a 4-week period for the effects of a diuretic drug on potassium concentrations. The statistical test used to compare the potassium serum levels before and after medication is most likely to be:
A Discriminant analysis
B Paired *t*-test
C Regression analysis
D Pearson correlation
E Chi-squared test

196. Gene transcription is initiated by:
A Exons
B Promoters
C Silencers
D Introns
E Enhancers

197. With regard to extra-ocular muscles:
A Superior rectus is supplied by the trochlear nerve
B Levator palpebrae superioris is supplied solely by the occulomotor nerve
C The superior oblique muscle is innervated by the occulomotor nerve
D Lateral rectus is supplied by the abducens nerve
E The inferior oblique muscle moves the eye inferiorly

198. Which of following substances is a vasodilator?
A Angiotensin II
B Nitric oxide
C Noradrenaline
D Vasopressin
E Thromboxane A2

199. Autoimmune diseases:
A Are usually congenital
B Are overall more common in men than in women
C Arise when an immune response is mounted against a foreign antigen
D Result from a breakdown in immunological tolerance
E Are always humoral-mediated

200. Hodgkin's lymphoma can be distinguished from other forms of lymphoma by the presence of:
A Reed–Sternberg cells
B Philadelphia chromosome
C Auer rods
D Decreased quantities of leukocyte alkaline phosphatase
E Pappenheimer bodies

201. A disease inherited as an autosomal dominant disorder:
A Requires that both parents carry the abnormality
B Usually prevents reproduction
C Affects males and females equally
D Affects all the children of the affected adult
E May be transmitted by a carrier who does not manifest the disease

202. With regard to the Palatine tonsil:
A It lies on the middle pharyngeal constrictor muscle
B It is supplied by the superior pharyngeal artery
C It is lined by columnar epithelium
D Inflammation may cause referred pain to the ear
E Bleeding after tonsillectomy is usually due to arterial bleeding

203. With regard to coronary blood flow:
A Blood flow to the left ventricle increases in early systole
B Local metabolic activity is the chief factor determining rate of blood flow to the heart
C Coronary blood flow to the left ventricle increases in hypothermia
D Coronary blood flow is increased in aortic stenosis

E The myocardium extracts 25 per cent of the oxygen from the coronary blood

204. With regard to bacterial structure and classification:
- A Gram-positive bacteria contain lipopolysaccharide
- B Gram-positive bacteria retain an iodine purple dye complex
- C Gram-negative bacteria possess thicker layers of peptigoglycan than Gram-negative bacteria
- D The endotoxin part of lipopolysaccaride is the O-antigen portion
- E All cocci are Gram-positive

205. Derivatives of the hindgut are typically supplied by the:
- A Coeliac artery
- B Ductus arteriosus
- C Inferior mesenteric artery
- D Superior mesenteric artery
- E Umbilical artery

206. Which one of the following is an autosomal dominant disorder?
- A Christmas disease
- B Phenylketonuria
- C Haemophilia A
- D Cystic fibrosis
- E Marfan's syndrome

207. The spinal accessory nerve supplies which of the following muscles?
- A Buccinator
- B Latissimus dorsi
- C Trapezius
- D Stylopharyngeus
- E Palatoglossus

208. With regard to cardiac conducting tissue:
- A Purkinje fibres lead to contraction of the apex before the base of the heart
- B Sinoatrial node cells are found in both atria
- C Sinoatrial node cells are unable to generate impulses when completely denervated
- D Sinoatrial node cells are connected to the AV node by fine bundles of Purkinje tissue
- E The pacemaker of the heart is the region of the heart that has the slowest intrinsic firing rate

209. Splenectomy increases susceptibility to which of the following organisms?
- A *Streptococcus pyogenes*
- B *Schistosomiasis haematobium*
- C *Bacteroides fragilis*
- D *Neisseria meningitidis*
- E *Staphylococcus aureus*

210. During a cholecstectomy, the cystic artery must be located and ligated. This arterial supply most commonly arises from the:
- A Gastroduodenal artery
- B Hepatic artery proper
- C Right hepatic artery
- D Left hepatic artery
- E Superior pancreatico-duodenal artery

211. A teenager would like genetic counselling. His mother has phenylketonuria, or PKU (which is inherited as autosomal recessive). He has a brother with PKU. What is the chance that he is a carrier of the disease?
- A 0 per cent
- B 25 per cent
- C 50 per cent
- D 75 per cent
- E 100 per cent

212. With regard to the parotid gland:
- A It contains within it branches of the facial nerve deep to the retromandibular vein
- B It consists of superficial, middle and deep lobes
- C Secreto-motor innervation is via the glossopharyngeal and auriculotemporal nerves
- D Its duct pierces the masseter muscle to enter the mouth opposite the upper second molar tooth
- E It produces mainly a mucous secretion

213. With regard to circulating red blood cells (erythrocytes):
- A They have a normal lifespan of 6–8 weeks
- B They are broken down in the bone marrow
- C They contain the enzyme glutaldehyde anhydrase

D They lack nuclei and mitochondria
E They swell to bursting point when suspended in 0.9% saline

214. With regard to *Helicobacter pylori* (*H. pylori*):
A It is a Gram-positive organism
B It is a known carcinogen
C Approximately 5 per cent of the population are infected with *H. pylori*
D It is destroyed by the acidic environment present within the stomach
E Infection can be prevented through vaccination

215. Cells in the pancreas that secrete glucagon and insulin are:
A A- and B-cells
B Acinar cells
C D cells
D Pancreatic D1 cells
E Pancreatic polypeptide cells

216. Which one of the following karyotypes is associated with short stature?
A 45XO
B 46YO
C 46XO
D 47XYY
E 47XXY

217. With regard to the cavernous sinus:
A It contains the external carotid artery
B It lies within the anterior cranial fossa
C The pituitary and sphenoidal air sinus lie in its medial wall
D Blood flows from anterior to posterior by way of valves
E It contains the optic nerve

218. Which of the following is true of erythrocytes?
A They travel at slower velocity in venules than in capillaries
B They are normally spherical
C They make little contribution to the buffering capacity of the blood
D Following haemolysis, erythrocytes release erythropoietin which stimulates the production of more erythrocytes
E They deform as they pass through the capillaries

219. Cholera:
A Is transmitted by the blood-borne route
B Is caused by infection with *Shigella sonnei*
C Is usually accompanied by marked mucosal inflammation and ulceration
D Is caused by a toxin which increases adenylate cyclase activity
E Is caused by endotoxin

220. The glossopharyngeal nerve provides the parasympathetic innervation of the:
A Submandibular salivary gland
B Sublingual salivary gland
C Parotid salivary gland
D Lacrimal gland
E Nasal mucous glands

221. With regard to Down's syndrome:
A Alzheimer's in seen in all individuals by the age of 45 years
B It is caused by trisomy 23
C It most commonly results from a chromosomal translocation
D The risk of having a child with Down's syndrome is approximately 1 in 1000 if the mother is 30 years old
E Individuals most commonly die prematurely from lung cancer

222. Which of the following muscles is *not* a muscle of mastication?
A Medial pterygoid
B Buccinator
C Masseter
D Lateral pterygoid
E Temporalis

223. With regard to blood clotting:
A The haemostatic response comprises two key events
B Blood platelets have a small single-lobed nucleus
C The conversion of fibrinogen to fibrin is catalysed by prothrombin
D It is reversed by plasmin (fibrinolysin)
E Liver failure results in a prothrombotic state

224. With regard to hepatitis B:
A It is an RNA virus
B Infection is more commonly cleared if acquired in childhood than later in life

C It is the second commonest human carcinogen worldwide
D It is commonly acquired by the faeco-oral route
E It is effectively treated by hepatitis B vaccination

225. A skydiver lands forcefully on his right lower limb and suffers a fracture of the acetabulum, with a dislocation of the femoral head into the pelvis. The acetabulum is formed by the ilium, ischium and pubis. These three bones are completely fused by:
A Birth
B 6 years of age
C Puberty
D 16 years of age
E 23 years of age

226. Huntington's disease (Huntington's chorea):
A Is an autosomal recessive condition
B Is a CTG trinucleotide repeat disorder
C Causes polyglutamine repeats within the fibrillin protein
D Is characterized clinically by a triad of bradykinesia, rigidity and tremor
E Exhibits a genetic phenomenon known as 'anticipation'

227. With regard to the Circle of Willis (circulus arteriosus):
A It is formed from the anastomosis of the internal and external carotid arteries
B The anterior communicating artery joins the two anterior cerebral arteries
C The posterior cerebral artery is the terminal branch of the internal carotid artery
D The posterior communicating artery joins the two posterior cerebral arteries
E It is fascinating, but clinically unimportant

228. With regard to the microcirculation and formation of lymph:
A At the arterial end of the capillary, the plasma colloid osmotic pressure exceeds the capillary hydrostatic pressure
B At the venous end of the capillary, the capillary hydrostatic pressure exceeds the plasma colloid osmotic pressure
C Oedema results from a rise in colloid osmotic pressure
D Interstitial fluid hydrostatic pressure is normally negative
E All the fluid that is filtered from the capillary flows into lymph vessels

229. Human immunodeficiency virus (HIV):
A Is a DNA virus
B Contains RNA polymerase
C Is transmitted by the faeco-oral route
D Establishes persistence through antigenic variation
E Principally targets CD8 T-cells

230. Typical physical and laboratory findings in hyperthyroidism include which of the following:
A Bradycardia
B Delayed reflexes
C High serum cholesterol
D Thick, rough skin
E Tremor

231. With regard to cystic fibrosis:
A Inheritance is sex-linked
B It is caused by a genetic defect on chromosome 6
C It is the most common inherited disease in Caucasians
D Patients can expect a normal life expectancy
E Gene therapy is a well established treatment option

232. With regard to the cranial meninges:
A The dura mater is a single layer thick
B The pia mater is the outermost layer (closest to the skull)
C A subdural haematoma lies in the plane between the dura and arachnoid mater
D A subarachnoid haematoma forms on the outside of the dura mater
E The dura mater is poorly innervated

233. With regard to the cerebral circulation:
A Cerebral blood flow is mainly governed by cardiovascular reflexes
B Cerebral blood flow is very sensitive to changes in the pCO_2 of the perfusing blood
C Cerebral blood flow increases steeply with increasing blood pressure

D It comprises functional end-arteries
E Raised intracranial pressure results in hypotension and tachycardia

234. With regard to influenza:
A It is a DNA virus
B It belongs to the Picornaviridae family of viruses
C Antigenic drift is responsible for pandemics
D Mutations in the haemagglutinin molecule are responsible for antigenic drift
E It can be prevented by administration of a live vaccine

235. Risk factors for developing osteoporosis include:
A Obesity
B Low calcium intake
C Late menopause
D Excessive rigorous physical exercise
E Abstinence from alcohol

236. Haemophilia A:
A Is more common in females than males
B Is due to an abnormal gene on the Y chromosome
C Is synonymous with Christmas disease
D Is due to a deficiency in factor IX
E Affects the intrinsic, rather than the extrinsic, pathway for blood coagulation

237. With regard to the facial nerve:
A It carries taste sensation from the posterior third of the tongue
B It innervates the levator palpebrae superioris muscle
C It is secreto-motor to the lacrimal gland
D It is associated with the third branchial arch
E It supplies the principal muscles of mastication

238. Which one of the following statements concerning lung volumes is true?
A The functional residual capacity is the sum of the tidal volume and residual volume
B The vital capacity is the sum of the inspiratory reserve volume, the expiratory reserve volume and the tidal volume
C The functional residual capacity can be measured directly by spirometry
D The residual volume is the volume of air left in the lungs after normal quiet expiration
E The normal tidal volume is approximately 2 litres

239. The pathogenicity of the tubercle bacillus is primarily due to which one of the following?
A Ability to multiply within macrophages
B Delayed hypersensitivity reaction against the bacteria
C Direct toxic effect on host cells
D Effective antibody response
E Necrosis caused by expanding granulomas

240. A 36-year-old man has a neck tumour. It has damaged his left cervical sympathetic chain ganglion. Which of the following physical signs would you expect:
A Increased sweat secretion on the left side of the face
B Lateral deviation of the left eye
C Pale skin on the left side of his face
D Ptosis on the left
E Pupil dilatation of the left eye

241. With regard to sickle cell anaemia:
A The inheritance pattern is autosomal dominant
B It is caused by a mutation within the haemoglobin alpha chain
C Mutation is a valine–alanine substitution
D It is more common in regions of the world in which malaria is endemic
E It causes splenomegaly in adulthood

242. With regard to the spinal cord and vertebral column:
A The spinal cord terminates at the level of L4
B The intervertebral joints are secondary cartilaginous joints
C It is supplied by two anterior spinal arteries and one posterior spinal artery
D Batson's vertebral venous plexus contains valves
E Intervertebral disc prolapse at L4/5 causes L4 root compression

243. With regard to surfactant:
- A It increases the surface tension of the film of liquid lining the alveoli
- B It reduces lung compliance
- C It is secreted by type I pneumocytes
- D The surface tension of fluid containing surfactant increases as the surface area of the fluid decreases
- E It helps to prevent the formation of pulmonary oedema

244. *Mycobacterium* tuberculosis:
- A Is a Gram-negative organism
- B Is an anaerobic microorganism
- C Typically affects the apical lung in post-primary TB
- D Is treated with penicillin
- E Is impossible to acquire following BCG vaccination

245. What are the insensible losses of water (i.e. skin and lung) over 24 hours in a typical adult male at room temperature?
- A 0 mL
- B 100–300 mL
- C 500–1000 mL
- D 2500–3500 mL
- E 4000–5000 mL

246. With regard to disorders of haemoglobin:
- A Sickle cell disease is due to the decreased production of normal globin
- B Haemoglobin binds more avidly to oxygen than carbon monoxide
- C Defective haem synthesis results in porphyria
- D Thalassaemia is due to the production of abnormal globin
- E Cyanide kills by blocking the interaction between oxygen and haemoglobin

247. With regard to the breast:
- A It drains to the tracheobronchial group of lymph nodes
- B It is supplied mainly by the anterior intercostal arteries
- C It sits on the pectoralis minor muscle
- D Lymphatics of the breast have connections with those of the opposite breast
- E It involutes during pregnancy

248. With regard to pulmonary blood flow:
- A Dilatation of pulmonary blood vessels occurs in response to hypoxia
- B The pulse pressure in the pulmonary artery is about the same as that in the aorta
- C During exercise, blood flow to the upper portion of the lung increases
- D The ventilation/perfusion ratio is the same in all parts of the lung in a standing man
- E Pulmonary vascular resistance is six times greater than that of the systemic circulation

249. With regard to tetanus:
- A It is caused by a Gram-negative bacillus
- B It is caused by an aerobic organism
- C It results from the secretion of exotoxin
- D It is caused by *Clostridium perfringens*
- E It is caused by bacterial invasion of the nervous system

250. Nitric oxide (NO) results in induction of vascular smooth muscle relaxation in response to acetylcholine. The production of NO requires which amino acid?
- A Lysine
- B Glutamine
- C Cysteine
- D Aspargine
- E Arginine

251. With regard to ABO blood grouping:
- A Blood group O is the universal recipient
- B The mode of inheritance is autosomal recessive
- C Blood group AB is the universal donor
- D Blood group O is recessive to A and B
- E Individuals of blood group O are resistant to *Plasmodium vivax*

252. With regard to the intercostal spaces:
- A The neurovascular bundle lies between the external intercostal and inner intercostal muscle layers
- B The direction of fibres of the external intercostal muscle is downwards and medial
- C The intercostal vein lies below the intercostal nerve
- D The neurovascular bundle lies in a groove just above each rib

E The intercostals are the main muscles of respiration

253. With regard to chemoreceptors:
- A The carotid bodies have a blood flow per unit volume similar to that of the brain
- B The carotid bodies are stretch receptors in the walls of the carotid arteries
- C Central chemoreceptors are located in the aortic arch
- D Carotid bodies primarily respond to hypoxia
- E The response of the peripheral chemoreceptors to arterial pCO_2 is more important than that of the central chemoreceptors

254. With regard to malaria:
- A It is caused by a virus
- B It is transmitted by the Aedes mosquito vector
- C The most virulent strain is *Plasmodium malariae*
- D It may cause blackwater fever
- E It is effectively prevented by vaccination

255. The neurotransmitters adrenaline, noradrenaline and dopamine are derived from which amino acid?
- A Tyrosine
- B Arginine
- C Aspargine
- D Phenylalanine
- E Tryptophan

256. Adult polycystic kidney disease:
- A Is inherited as an autosomal recessive condition
- B Affects only one kidney
- C Is associated with berry aneurysms of the Circle of Willis
- D Commonly presents at birth
- E Is due to a mutation in polycystin-1 in all cases

257. With regard to the oesophagus:
- A It is a segmental muscular tube composed entirely of smooth muscle
- B Epithelium is always stratified squamous throughout its whole length
- C Blood supply is from the descending thoracic aorta along its entire length
- D It lacks a true serosal surface
- E It measures approximately 40 cm in length

258. With regard to carbon dioxide transport:
- A Carbon dioxide is mainly carried in the blood in its dissolved form
- B It is carried as carboxyhaemoglobin on the haemoglobin molecule
- C The Haldane effect describes changes in the affinity of the blood for CO_2 with variations in the PaO_2
- D Venous blood has a higher pH than arterial blood
- E Carbon dioxide is less soluble in plasma than is oxygen

259. With regard to the malaria life cycle:
- A Sporozoites invade erythrocytes
- B Parasites may remain dormant in the liver as hypnozoites
- C Trophozoites invade hepatocytes
- D Schizonts are contained within the mosquito's salivary glands
- E Fertilization and formation of a zygote occurs in humans

260. A 42-year old woman has a genetic defect and cannot produce J-chains that are important in the structure of immunoglobulins. Most likely she will have:
- A Increased serum IgM and decreased IgE
- B Increased IgA in the intestine
- C Decreased serum IgM
- D Decreased mature T-lymphocytes
- E Decreased mature B-cells

261. The decline in incidence of serious infections during the nineteenth and twentieth centuries is mainly due to:
- A Better sanitation
- B Antibiotics
- C Immunization programmes
- D A decline in the virulence of organisms
- E Advances in medical science

262. With regard to oesophageal constrictions:
- A The lower oesophageal sphincter is a true anatomical sphincter
- B They may be caused by the right principal bronchus
- C The narrowest part of the oesophagus is at the level of cricopharyngeus

D They may be caused normally by the left atrium
E They may be caused by the descending thoracic aorta

263. Which one of the following is true of the haemoglobin oxygen/dissociation curve?
A It is a rectangular hyperbola
B It is shifted to the left by an increase in PCO_2
C Fetal haemoglobin shifts the curve to the right
D The Haldane effect describes the changes in affinity of the haemoglobin chain for oxygen following variations in PCO_2
E The shape of the curve is explained by the physico-chemical properties of haemoglobin

264. With regard to schistosomiasis:
A It is caused by a protozoan
B The intermediate host is the sandfly
C *Schistosoma mansoni* causes urinary schistosomiasis
D Disease results from the immune response to schistosome eggs
E It is treated with quinine

265. An 83-year-old man has chest pain, breathlessness and ankle oedema. On clinical examination, cardiomegaly is identified and a subsequent diagnosis of viral myocarditis is made. Which of the following microorganisms is most likely responsible for this illness:
A Rhinovirus
B Mumps
C Coronavirus
D Adenovirus
E Coxsackie B

266. Which one of the following changes in disease patterns have occurred in Europe and North America over the past 50 years?
A The death rate from lung cancer in females has fallen
B The death rate from lung cancer in males has risen in recent years
C The numbers infected with the HIV virus has fallen
D The death rate from suicide has fallen
E The death rate from gastric carcinoma has fallen

267. With regard to the diaphragm:
A It is composed of smooth muscle
B It contracts with expiration
C It forms the main muscle of respiration at rest
D Motor innervation is through right and left phrenic nerves and lower intercostal nerves
E Sensation is via lower intercostals nerves only

268. At high altitude when the atmospheric pressure is halved, which one of the following changes occurs?
A Decreased pulmonary arterial pressure
B Decreased arterial pH
C Increased arterial PO_2
D Decreased pulmonary ventilation
E Increased blood viscosity

269. Prions:
A Are infectious microorganisms
B Are destroyed by sterilization
C Contain nucleic acid
D Cause disease by inducing mutations in the DNA of the host
E Are responsible for causing Kuru in humans

270. Which of the following is the best neutrophil and macrophage chemotactant?
A C5a
B HLA-A
C HLA-B
D J-chain
E Variable region of heavy-chain IgG

271. The most common cause of death from cancer in women is currently:
A Ovarian cancer
B Breast cancer
C Lung cancer
D Endometrial cancer
E Colon cancer

272. With regard to diaphragmatic openings:
A The inferior vena cava passes through the muscular part of the diaphragm at T8

B The aortic opening lies at the T10 level
C The oesophageal opening transmits the right phrenic nerve
D The left phrenic nerve passes with the oesophagus through the oesophageal opening
E The sympathetic trunks pass posterior to the medial arcuate ligament

273. With regard to gas exchange:
A The rate of diffusion across the alveolar wall is directly proportional to its thickness
B Under resting conditions, equilibration between alveoli PO_2 and red blood cell PO_2 occurs one-third of the way along the pulmonary capillary
C At rest, the red blood cell spends approximately 5 seconds within the pulmonary capillary
D The rate of diffusion across the alveolar wall is inversely proportional to the surface area available for diffusion
E Chlorine is the gas of choice for measuring the diffusion properties of the lung

274. Which of the following definitions is correct?
A Hyperplasia is an increase in tissue growth through an increase in cell size
B Dysplasia is a change from one type of differentiated tissue to another
C Carcinoma-in-situ is a carcinoma with stromal invasion
D Anaplasia is almost a complete lack of differentiation
E Metaplasia is the disordered development of cells with loss of organization

275. A 92-year-old man has died secondary to lobar pneumonia. At post-mortem he is diagnosed with red hepatization. What pathological process within the lung was responsible?
A Desquamation of tracheal and bronchial epithelial cells
B Fibroblast proliferation
C Alcoholic toxic necrosis
D Leucocytes, erythrocytes and fibrin filling of the alveolar spaces
E Pleural deposits of fibrin and low molecular proteins

276. Which one of the following diseases is water-borne?
A Tuberculosis
B Cholera
C Hepatitis C
D Bubonic plague
E Malaria

277. With regard to the thoracic duct:
A It drains into the confluence of the right internal jugular and subclavian veins
B It lies anterior to the oesophagus as it passes through the diaphragm
C It crosses the midline at the level of T5
D It has no valves
E If it is injured, a haemothorax may result

278. With regard to the mechanics of respiration:
A Compliance is defined as the change in pressure per unit volume
B Compliance is synonymous with elastance
C Sighing serves no physiological purpose
D The lung follows the same behaviour in inflation and deflation
E Emphysema results in increased lung compliance

279. Which one of the following statements is true?
A Adenoma is a malignant tumour of glandular epithelium
B Sarcoma is a benign tumour of connective tissue
C Leiomyosarcoma is a malignant tumour of skeletal muscle
D Lymphoma is a benign tumour of lymphoid cells
E Liposarcoma is a malignant tumour of adipose tissue

280. Budd–Chiari syndrome is:
A A congenital inability to metabolize bilirubin
B A dietary deficiency of an essential amino acid
C Agenesis of the hepatic lobe
D Occlusion of the hepatic venous drainage

E Malignant transformation of the biliary epithelium

281. Which one of the following is true concerning retrospective and prospective studies?
A Prospective studies are also known as case–control studies
B Prospective studies allow direct determination of incidence rates
C The retrospective approach has the advantage that there is little or no bias
D In a prospective study, the cohort consists of people who are found to have the disease in question
E The prospective approach is usually used to determine the aetiology of a rare disease

282. With regard to the lungs:
A The left lung has three lobes
B The horizontal fissure is present in the left lung
C Each lung has eight bronchopulmonary segments
D A foreign body is more likely to enter the left bronchus than the right
E The lungs receive a dual blood supply

283. Which one of the following is true of haemoglobin?
A Most haemoglobin circulates as free protein in plasma
B Oxygen attaches to the globin chains
C Each haemoglobin molecule combines with eight oxygen atoms
D In normal adult haemoglobin, iron exists in the ferric state
E Normal adult haemoglobin contains two alpha and two gamma chains

284. With regard to metaplasia:
A It is irreversible
B It is most important in the upper oesophagus
C Metaplasia in the bronchus involves a change from columnar to stratified squamous epithelium
D It is harmless
E Barrett's oesophagus involves a change from glandular to stratified squamous epithelium

285. A 52-year-old man presents with episodic hypertension, an adrenal mass and elevated catacholamines. The most likely diagnosis is:
A Adrenal cortical carcinoma
B Adrenal cortical hyperplasia
C Phaeochromocytoma
D Ganglioneuroma
E Neuroblastoma

286. Which one of the following studies is regarded as the gold standard in epidemiological research?
A Cross-sectional study
B Case–control study
C Case report
D Randomized controlled trial
E Non-randomized controlled trial

287. With regard to the pleura:
A The pleura ends level with the 12th rib posteriorly
B It extends above the clavicle superiorly
C The visceral layer is richly innervated
D It extends above the neck of the 1st rib superiorly
E The pleural reflection on the right side matches that on the left side identically

288. Which one of the following is true of erythropoietin?
A It is a polypeptide
B Secretion is decreased at high altitude
C In adults, it is mainly made in the liver
D It acts via a secondary messenger
E Production is decreased by local hypoxia

289. Which of the following is a defining characteristic of a malignant tumour?
A Increase in size with time
B Chromosomal abnormalities
C Presence of a pseudo-capsule
D Invasion beyond the basement membrane
E Well-ordered maturation

290. Following a lethal overdose of paracetamol, the post-mortem will demonstrate:
A Pulmonary necrosis
B Hepatic necrosis
C Acute renal tubular necrosis

D Splenic infarction
E Meningeal inflammation

291. You are involved in running a diabetes screening service. Two thousand people, aged between 60 and 75, are screened. Both the mean and median random glucose measurement is 9.5 and the standard deviation is 1.4. Which statement is correct?
A Five per cent of subjects will have a glucose greater than 10.9
B The distribution is not a normal distribution
C Ninety-five per cent of subjects will have a blood glucose between 6.7 and 12.3
D Sixty-eight per cent of subjects have a blood glucose between 6.7 and 12.3
E Ninety-five per cent of the observations lie between two standard errors of the mean

292. With regard to the pericardium:
A It is two layers thick
B It is poorly innervated
C It is responsible for the formation of the transverse and oblique sinuses
D Pericardiocentesis may be detrimental in the management of cardiac tamponade
E It is essential in order to maintain a normal cardiac output

293. Which one of the following is true of aldosterone?
A It is a steroid hormone secreted by the adrenal medulla
B Production is decreased by angiotensin-converting enzyme inhibitors
C Secretion results in increased potassium reabsorption from the nephron
D Secretion results in a rise in urinary pH
E Production ceases following the removal of the kidneys and their juxtaglomerular cells

294. Which of the following are cytological features of malignancy?
A Hyperchromatism
B Pyknosis
C Karyorrhexis
D Decreased nuclear to cytoplasmic ratio
E Low mitotic index

295. A 63-year-old male has a progressive history of congestive cardiac failure. At post-mortem, the heart demonstrates extensive replacement of the myocardium by an acellular, eosinophilic material. This material is most likely to be:
A Cholesterol
B Calcium salt deposits
C Myocyte fibrinoid necrosis
D Post-infarctive cicatrix (scar)
E Amyloid

296. Which one of the following statements is true?
A The standard error provides a measure of the spread of observations around the mean
B The standard deviation is equal to the standard error divided by the square-root of the sample size
C The standard error is generally larger than the standard deviation
D In a positively skewed distribution, the median is greater than the mode, but greater than the mean
E The mean and standard deviation of a random sample will generally be different from the mean and standard deviation of the true population

297. Which of the following regarding the coronary arteries is correct:
A The sinoatrial node is supplied by the left coronary artery in most cases
B The atrioventricular node is supplied by the left coronary artery in most cases
C The circumflex artery is a branch of the right coronary artery
D Occlusion of the anterior interventricular artery (left anterior descending artery) results in an anterior myocardial infarction
E Angina is always due to atherosclerosis of the coronary vessels

298. With regard to the renin–angiotensin system:
A Angiotensinogen is secreted by the juxtaglomerular apparatus
B The lung catalyses the conversion of angiotensinogen to angiotensin I
C Activation results in the stimulation of aldosterone release

D Angiotensin II is a potent vasodilator
E Angiotensin-converting enzyme is found principally in the liver

299. Carcinomas most often metastasize by which of the following routes?
A Bloodstream
B Lymphatics
C Trans-coelomic
D Peri-neural
E Implantation

300. A 73-year-old man works in a plastics factory and is exposed to vinyl chloride. This industrial exposure has increased his likelihood of developing:
A Focal nodular hyperplasia
B Hepatic adenoma
C Hepatic angiosarcoma
D Hepatic fibroma
E Hepatocellular carcinoma

301. In a certain trial, the mean ± standard error is 0.5 ± 0.2, with a *p*-value under 0.005. This implies that:
A Ninety-five per cent of the values lie between 0.1 and 0.9
B This difference would have arisen by chance alone less than one time in 200
C This difference would have arisen by chance alone less than one time in 20 000
D One can be 95 per cent confident that the true population mean lies somewhere within the interval 0.3–0.7
E There is a 2.5 per cent chance that the true population mean lies outside the range 0.1–0.9

302. With regard to the inguinal canal:
A The superficial inguinal ring is a hole in transversalis fascia
B The canal runs from the anterior superior iliac spine to the pubic tubercle
C The conjoint tendon is formed by fusion of external and internal oblique muscles
D The posterior wall of the canal is bounded by transversalis fascia and the conjoint tendon medially
E A direct inguinal hernia passes through both the deep and superficial inguinal rings

303. With regard to the juxtaglomerular apparatus:
A The macula densa is a specialized region of the afferent arteriole
B Renin is secreted at the macula densa
C Renin is secreted in response to a raised sodium at the macula densa
D A fall in pressure in the afferent arteriole promotes renin secretion
E The juxtaglomerular (granular) cells are located in the wall of the distal convoluted tubule

304. Which of the following malignant neoplasms rarely metastasizes to distant sites:
A Bronchial carcinoma
B Breast carcinoma
C Astrocytomas
D Renal-cell carcinoma
E Melanoma

305. A 56-year-old man presents with a productive cough and weight loss. Chest X-ray demonstrates a large hilar mass. Sputum cytology shows oval cells with hyperchromatism, paucity of cytoplasm and inconspicuous nuclei. These malignant cells are most likely associated with:
A Clara cells
B Metaplastic bronchial epithelial cells
C Neuroendocrine cells
D Type I alveolar pneumocytes
E Type 2 alveolar pneumocytes

306. The following table shows the results for a screening test for pancreatic cancer in 100 people:

	Disease positive	*Disease negative*
Test positive	4	5
Test negative	1	90

Which of the following is true?
A The positive predictive value is 0.95
B The sensitivity is 0.95
C The specificity is 0.8
D The negative predictive value is 0.99
E The sensitivity and specificity depends on the disease prevalence

307. With regard to the epiploic foramen (of Winslow), which of the following is true?
   A The posterior wall is formed from the lesser omentum
   B The portal vein lies in its posterior wall
   C Superiorly lies the quadrate lobe of the liver
   D The common bile duct sits in the free edge of the greater omentum anteriorly
   E It forms the entrance to the lesser sac

308. With regard to antidiuretic hormone (arginine vasopressin):
   A It increases in response to a loss of circulating volume of at least 10 per cent
   B It is secreted by the pars distalis (adenohypophysis)
   C Increased secretion occurs in response to hypo-osmolar blood
   D It causes water reabsorption from the Loop of Henle
   E Insufficiency results in diabetes mellitus

309. Sarcomas:
   A Are derived from epithelium
   B Are more common than carcinomas
   C Have a peak incidence in those less than 50 years of age
   D Metastasize more commonly by lymphatic than haematogenous routes
   E Have a long in-situ phase

310. One sensitive indicator of heavy alcohol dependence is:
   A Decreased mean cell volume (MCV)
   B Decreased serum alkaline phosphatase
   C Elevated serum creatinine
   D Elevated serum gamma-glutamyl transpeptidase
   E Elevated serum indirect bilirubin

311. Which of the following are features of small bowel?
   A Valvulae conniventes
   B Haustra
   C Sacculations
   D Appendices epiploicae
   E Taeniae coli

312. With regard to acid–base balance:
   A The normal pH of arterial blood is 7.85–7.95
   B The pH of the blood fluctuates widely
   C The kidneys respond most rapidly to a change in pH
   D The kidney is able to generate new bicarbonate from glutamine
   E The renal tubule reabsorbs hydrogen ions and actively excretes bicarbonate

313. Which is true of tumour kinetics?
   A The smallest clinically detectable tumour is 1000 cells
   B Tumour growth obeys Gompertzian kinetics
   C In most tumours, the growth fraction is greater than 90 per cent
   D Tumour growth is characterized by contact inhibition
   E The clinical phase of tumour growth is long in comparison to the preclinical phase

314. The activity of what structure in the pons is suppressed by opiates, clonidine and GABA, and produces the most noradrenergic input to the brain?
   A Substantia nigra
   B Nucleus solitarius
   C Nucleus pulposus
   D Mammillary bodies
   E Locus coeruleus

315. With regard to the gall bladder:
   A Epithelium is stratified squamous
   B It has a normal capacity of around 10 mL
   C It is supplied by the cystic artery, a branch of the left hepatic artery
   D It is stimulated to contract by cholecystokinin
   E It is essential for life

316. With regard to renal blood flow:
   A The kidneys receive 5 per cent of the cardiac output
   B Angiotensin II vasoconstricts the afferent more than the efferent arteriole
   C It can be accurately measured by the use of inulin
   D The low blood flow in the vasa recta assists in the formation of concentrated urine
   E A fall in arterial blood pressure decreases glomerular filtration rate (GFR)

317. **With regard to angiogenesis:**
   - A It is the process of programmed cell death
   - B It is highly dependent on vascular endothelial growth factor (VEGF)
   - C It is impaired when tumours grow larger than 1 mm^3
   - D It is always pathological
   - E Granulation tissue is rich in cytokines that inhibit angiogenesis

318. **Serum electrolytes reveal sodium 150 mEq/L and potassium 5.2 mEq/L. The most likely diagnosis is:**
   - A Alzheimer's disease
   - B Delirium
   - C Pick's disease
   - D Secondary dementia
   - E Seizure disorder

319. **With regard to gall bladder disease:**
   - A Courvoisier's law states that in the presence of obstructive jaundice an impalpable gall bladder is always due to gallstones
   - B It may refer pain to the right shoulder tip
   - C The surface marking of the gall bladder is the right sixth intercostal space, mid-clavicular line
   - D Gallstones are usually composed of calcium carbonate
   - E Gallstones always cause symptoms

320. **With regard to glomerular filtration:**
   - A The GFR is the main factor determining the rate of urine production
   - B GFR can be measured by para-aminohippuric acid (PAH)
   - C The normal GFR is 50 mL/min
   - D The glomerular filtration barrier comprises three layers
   - E A normal plasma creatinine implies normal renal function

321. **An increased frequency of tumours caused by occupational carcinogen exposure has been proven in the following groups, *except*:**
   - A Transitional cell carcinoma bladder in dye workers
   - B Scrotal carcinoma in chimney sweeps
   - C Mesothelioma with asbestos exposure
   - D Hepatocellular carcinoma with polyvinyl chloride exposure
   - E Malignant melanoma with sunlight exposure

322. **Which of the following decreases insulin resistance:**
   - A Cortisol
   - B Exercise
   - C Obesity
   - D Pregnancy
   - E Growth hormone

323. **With regard to the liver:**
   - A It is completely surrounded by peritoneum
   - B The ligamentum venosum is a remnant of the umbilical vein
   - C It receives oxygen from the hepatic artery only
   - D It is surrounded by Gerota's fascia
   - E The right subhepatic space or hepatorenal pouch (of Rutherford–Morison) is the most dependent part of the peritoneal cavity

324. **With regard to tubular function:**
   - A Fifty per cent of the filtered sodium is reabsorbed in the distal convoluted tubule
   - B Most glucose is reabsorbed in the Loop of Henle
   - C The ascending limb of the Loop of Henle is permeable to water
   - D Drinking seawater is better than drinking nothing at all if lost at sea
   - E The maximum concentrating ability of the human kidney is 1200 mOsm/L

325. **For which one of the following tumours is there an association with Epstein–Barr virus (EBV) infection?**
   - A Bronchial carcinoma
   - B Cervical carcinoma
   - C Burkitt's lymphoma
   - D Hepatocellular carcinoma
   - E Kaposi's sarcoma

326. **Which of the following is the most common thyroid neoplasm in the UK?**
   - A Medullary thyroid cancer
   - B Lymphoma
   - C Papillary thyroid cancer

D Follicular cancer
E Metastases

327. With regard to portosystemic anastomoses:
A They occur at sites at which arterial blood meets venous blood
B They feature at the lower end of the oesophagus
C They become highly significant in renal failure
D They are most clinically significant at the lower end of the anal canal
E They feature at the splenic hilum

328. With regard to saliva:
A Secretion is equivalent to 200 mL/day
B Secretion from the parotid gland is mainly mucinous
C It contains the trypsin enzyme
D It is richer in potassium than any other gastrointestinal secretion
E Secretion is a passive process

329. With regard to oncogenes:
A They behave in a dominant fashion
B They encode proteins that negatively regulate growth
C BRCA1 is an oncogene implicated in breast carcinoma
D Transcription of oncogenes is dysregulated in normal cells
E Oncogenes are present only in tumour cells

330. The neurotransmitter released from the cerebellar Pukinke cells is:
A Glutamate
B GABA
C Acetylcholine
D Glycine
E Serotonin

331. With regard to the spleen:
A It lies under cover of ribs 9–11 on the right
B It is the major site of erythropoietin secretion
C It is normally the site of haematopoiesis in adults
D Accessory spleens are rare
E Splenectomized patients are at high risk of post-splenectomy sepsis

332. Which of the following cells secretes intrinsic factor?
A Goblet cells
B Kupffer cells
C Peptic cells
D Chief cells
E Parietal cells

333. With regard to tumour suppressor genes:
A They encode proteins that positively regulate growth
B They behave in a dominant fashion
C Gain-of-function of tumour suppressor genes results in neoplastic growth
D p53 and Rb-1 are tumour suppressor genes
E p53 normally functions as an anti-apoptotic factor

334. Which one of the following muscles is innervated by the facial nerve?
A Temporalis
B Anterior belly of digastric
C Buccinator
D Masseter
E Lateral pterygoid

335. With regard to the transpyloric plane (of Addison):
A It is half way between the suprasternal notch and umbilicus
B It lies at the level of T12
C It lies at the origin of the inferior mesenteric artery
D It lies level with the hilum of the kidneys
E It is the point at which the aorta bifurcates

336. With regard to gastric acid secretion:
A It is inhibited by gastrin
B It is potentiated by histamine
C It commences only when food enters the stomach
D It is stimulated by the glossopharyngeal nerve
E It is stimulated by somatostatin

337. Retinoblastoma:
A Is inherited as an autosomal recessive condition
B Is due to a defective gene located on chromosome 5

C Is familial in 90 per cent of cases
D In its inherited form, carries minimal risk of extraretinal malignancies
E Results from loss of heterozygosity of the normal Rb gene

338. From which branchial (pharyngeal) pouch does the inferior parathyroid gland arise?
A First
B Second
C Third
D Fourth
E Fifth

339. With regard to the adrenal gland (suprarenal gland):
A The suprarenal vein on each side drains into the corresponding renal vein
B The adrenal gland is situated within the same fascial compartment as the kidney
C The zona glomerulosa forms the innermost layer of the adrenal cortex
D The anterior surface of the right adrenal gland is overlapped by the inferior vena cava
E The adrenal medulla is derived from embryonic mesoderm

340. Which one of the following is true of gastrin?
A It is secreted in the body of the stomach
B It is stimulated by low pH
C It stimulates gastric acid production
D It inhibits gastric motility
E Decreased secretion results in the Zollinger–Ellison syndrome

341. Lung carcinoma:
A Is the third most common cause of death from neoplasia in the UK
B Has rarely metastasized at the time of presentation
C May produce paraneoplastic syndromes
D Is most commonly due to small-cell (oat-cell) carcinoma
E Is most commonly caused by asbestos exposure

342. Prokaryotes differ from eukaryotes in that prokaryotes have:
A Peptidoglycan
B Sterols in their membranes
C 2 to 6 chromosomes
D An endoplasmic reticulum
E Larger 80S ribosomes

343. With regard to the vermiform appendix:
A It is most often situated in a pelvic position
B It receives blood via the right colic branch of the superior mesenteric artery
C It lies at McBurney's point (half way between the anterior superior iliac spine and umbilicus)
D It is unimportant in humans
E It is a retroperitoneal structure

344. With regard to the exocrine pancreas:
A It secretes digestive juices with a pH of 4–5
B It develops from a single ventral pancreatic bud
C Secretion is inhibited by cholecystokinin
D The main stimulation for secretion occurs during the intestinal phase
E It produces secretin

345. Which one of the following is the commonest intracerebral neoplasm:
A Astrocytoma
B Oligodendroglioma
C Meningioma
D Neuronal tumour
E Secondary carcinoma

346. A 67-year-old male undergoes an elective right colectomy for adenocarcinoma of the caecum. If distant non-nodal metastases are discovered, which organ would be affected first?
A Brain
B Lung
C Adrenal
D Liver
E Bone

347. With regard to acute appendicitis:
A It is most common at the extremes of age
B It may result in thrombosis of the appendicular artery (endarteritis obliterans)
C It often resolves with conservative management such as antibiotics
D If untreated it is rarely life-threatening
E Classically it refers pain to the epigastric region

348. Which one of the following is true of pancreatic enzymes:
   A Trypsin is a powerful activator of other pancreatic proteolytic enzymes
   B The pancreas secretes enterokinase (enteropeptidase)
   C Chymotrypsinogen activates trypsinogen to form trypsin
   D The pancreas secretes proteases in their activated form
   E The pancreas normally contains a trypsin activator

349. Which one of the following is the commonest malignant tumour of bone?
   A Chondroblastoma
   B Giant-cell tumour
   C Osteosarcoma
   D Chondrosarcoma
   E Secondary carcinoma

350. A research assistant is studying the production of an anthrax vaccine. He must destroy all vegetative cells and spores of *Bacillus anthracis* that have contaminated the pipette. What agent should he use?
   A Boiling
   B Ethanol alcohol
   C Oxidizing agents
   D Autoclaving
   E Anionic detergents

351. With regard to the greater omentum:
   A It has no surgical importance
   B It is supplied by the right and left gastric arteries
   C It is two layers thick
   D It provides a route of access to the lesser sac
   E The anterior layers descend from the lesser curvature of the stomach

352. With regard to the endocrine pancreas:
   A It secretes hormones into a highly branched ductal system
   B Glucagon is secreted from β-islet cells
   C Islets of Langerhans make up only 2 per cent of the volume of the gland
   D Somatostatin is secreted from α-islet cells
   E Glucagon stimulates glycogenesis

353. Apoptosis:
   A Is always a pathological event
   B Involves the death of large contiguous areas of cells
   C Is usually accompanied by inflammation
   D May be seen in histological section
   E Leaves a permanent clump of cellular debris

354. The virus responsible for causing acquired immunodeficiency sydrome (AIDS) has which one of the following features?
   A A double-stranded genome
   B Lacks a viral evelope
   C Lacks reverse transcriptase
   D Is a member of the adenovirus group
   E Destroys CD4 T-lymphocytes

355. With regard to the ureters:
   A They are lined by stratified squamous epithelium
   B They enter the bladder obliquely forming a flap valve
   C The point of narrowest calibre is at the pelviureteric junction
   D The arterial supply of the lower third of the ureter is by way of the descending abdominal aorta
   E In the female, the ureters are crossed below by the uterine arteries in the broad ligament

356. Which one of the following is true of bile?
   A Bile salts are derived from the waste products of haemoglobin
   B It is actively concentrated in the gall bladder
   C Thirty per cent is reabsorbed by the enterohepatic circulation
   D Bile contains enzymes required for the digestion of fat
   E Accumulation of bile salts is responsible for causing jaundice

357. With regard to acute inflammation:
   A The predominant cell type involved is the macrophage
   B Inflammation is usually initiated by cell-mediated immunity
   C Inflammation may last for many months
   D Inflammation is intimately connected with the clotting system
   E Inflammation is always due to infection

358. A man is bleeding from the carotid artery. In order to temporary control the bleeding, the surgeon should compress the artery against the anterior tubercle of which of the following?

A Second cervical vertebra
B Third cervical vertebra
C Fouth cervical vertebra
D Fifth cervical vertebra
E Sixth cervical vertebra

359. With regard to the spermatic cord:

A It contains within it the ilioinguinal nerve
B It contains the femoral branch of the genitofemoral nerve
C It is surrounded by two fascial coverings
D It contains the pampiniform plexus
E It has dartos muscle contained in its wall

360. With regard to intestinal absorption:

A A greater volume of water is absorbed from the colon than from the small intestine
B Gastric acid assists in the absorption of iron
C Glucose is absorbed by a potassium-cotransport mechanism
D Vitamin B_{12} is absorbed from the duodenum
E Sodium is absorbed at a rate proportional to body needs

361. The following are possible outcomes of acute inflammation, *except*:

A Resolution
B Chronic inflammation
C Abscess formation
D Amyloidosis
E Death

362. A man falls on an outstretched hand. X-rays indicate an anterior dislocation of one of the carpal bones. Which carpal bone is most commonly dislocated?

A Capitate
B Lunate
C Scaphoid
D Trapezoid
E Triquetrum

363. With regard to the testis:

A It is supplied by the testicular artery which arises from the internal iliac artery
B It drains via the pampiniform plexus to the inferior vena cava
C Lymph drainage is to the inguinal group of lymph nodes
D It is supplied by T10 sympathetic nerves
E A fluid collection around the testis is known as a varicocele

364. In the setting of starvation:

A Glycogen stores last for two weeks
B Glucose is the only metabolic fuel that can be used by neurones
C The brain uses free amino acids when glucose levels begin to fall
D Protein is spared until relatively late
E Death occurs at around 21 days

365. With regard to chronic inflammation:

A It is always preceded by an acute inflammatory phase
B It usually heals by organization and repair
C It is characterized by less tissue destruction than acute inflammation
D It usually results in resolution
E Neutrophils are the predominant cell type

366. Under normal conditions, virtually 100 per cent of the filtered load of glucose is reabsorbed by the kidney tubules. Which part of the nephron shown in Figure 1 is expected to have the highest reabsorption of glucose?

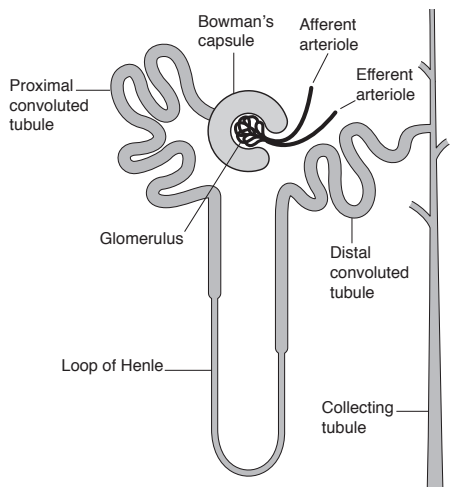

Figure 1 The nephron.

A Proximal convoluted tubule
B Thin descending Loop of Henle

C Thick ascending limb of Loop of Henle
D Distal convoluted tubule
E Collecting duct

367. With regard to the ovary:
A It is retroperitoneal
B It lies medial to the obturator nerve and anterior to the ureter
C It drains lymph to the internal iliac nodes
D It receives a parasympathetic supply from the pudendal nerve
E It gives rise to referred pain in the suprapubic region

368. Which one of the following hormones is secreted by the anterior pituitary?
A Testosterone
B Oxytocin
C Thyroid-stimulating hormone (TSH)
D Corticotropin-releasing hormone (CRH)
E Antidiuretic hormone (ADH)

369. Which of the following inflammatory processes often involves granulomas?
A Lobar pneumonia
B Bronchopneumonia
C Tuberculosis
D Granulation tissue
E Ulcerative colitis

370. An intravenous drug user presents with pyrexia and haematuria. Clinical examination demonstrates splenomegaly and splinter haemorrhages. Of which of the following heart valves would vegetations be expected?
A Aortic
B Pulmonary
C Mitral
D Tricuspid
E Bicuspid

371. With regard to the rectum:
A It is drained by tributaries of both the inferior mesenteric and internal iliac veins
B It is suspended by a mesentery
C It receives its blood supply from the external iliac artery
D It is lined by transitional epithelium
E It is supplied by parasympathetic nerve fibres from the vagus

372. Which one of these statements regarding type 2 diabetes mellitus is true?
A It usually presents with weight loss
B Ketones are found
C It is associated with HLA DR3/4
D Identical twins show 90 per cent concordance
E It usually presents in the teen years

373. With regard to wound healing:
A Granulation tissue actively contracts
B Granulation tissue is defined by the presence or absence of granulomas
C Repair implies the complete restitution of normal tissue architecture and function
D In first-intention healing, the wound is unapposed
E Scar formation is absent in second-intention healing

374. A 62-year-old industrial chemist presents with painless haematuria, urinary frequency and urgency. He is diagnosed with bladder cancer. Which is the most likely type?
A Adenocarcinoma
B Sarcoma
C Papilloma
D Squamous cell carcinoma
E Transitional cell carcinoma

375. With regard to the uterus:
A It usually lies in a retroverted, anteflexed position
B The broad ligament is a remnant of the gubernaculum
C The Pouch of Douglas lies between the bladder anteriorly and uterus posteriorly
D The ovarian artery is intimately related to the ureter
E The ureter is closely related to the lateral fornix of the cervix

376. In diabetes mellitus:
A A fasting glucose of 6.5 mM is compatible with a diagnosis
B A random glucose of 9 mM on two occasions is compatible with a diagnosis
C A fasting glucose of 7.5 mM on two occasions is consistent with a diagnosis
D A glucose of 10 mM after a 2-hour glucose tolerance test is compatible with a diagnosis

E A 50 g glucose challenge is used in the glucose tolerance test

377. Which one of the following tissues is likely to regenerate following damage?
A Cerebral cortex
B Peripheral neurones
C Skeletal muscle
D Cardiac muscle
E Spinal cord

378. Deficiencies of which of the following factors usually predispose to thrombosis rather than bleeding?
A Factor V
B Factor VIII
C Factor IX
D Factor X
E Factor XII

379. With regard to the blood supply of the stomach:
A The right half of the lesser curvature is supplied by the right gastoepiploic artery
B The left half of the greater curvature is supplied by the left gastric artery
C The fundus of the stomach is supplied by the left gastric artery
D The gastroduodenal artery is a branch of the common hepatic artery
E The right gastric artery is most commonly implicated in a bleeding duodenal ulcer

380. Which one of these statements regarding insulin is true?
A Insulin receptors use cAMP as their signal transducer
B It is secreted by alpha-cells of the pancreas
C Secretion is stimulated by somatostatin
D It is an anabolic hormone
E Release is inhibited by the ingestion of amino acids

381. With regard to necrosis:
A It is a physiological or pathological process
B Single cells are involved
C Liquefactive necrosis classically occurs in the brain
D Necrotic cells are phagocytosed by adjacent cells
E Caseous necrosis is the commonest type

382. A Swan–Ganz catheter is inserted into a patient with acute respiratory distress syndrome (ARDS). His pulmonary artery pressure is 6 mmHg. The same pressure would be expected in which of the following structures?
A Aorta
B Left atrium
C Left ventricle
D Right atrium
E Systemic veins

383. With regard to the femoral triangle, which of the following is correct?
A The femoral vein lies lateral to the femoral artery
B The femoral nerve lies within the femoral sheath
C The femoral artery lies at the mid-point of the inguinal ligament
D The femoral nerve is the most medially placed structure
E Cloquet's node lies most medially within the femoral canal

384. With regard to the hypothalamo-pituitary axis:
A Oxytocin is synthesized in the posterior pituitary gland
B Prolactin is under dominant inhibitory regulation
C Thyroxine is a steroid hormone
D Thyroid-stimulating hormone (TSH) acts via tyrosine kinase receptors
E GH binds to intracellular receptors

385. Which one of the following is the best definition of gangrene?
A Digestion of living tissue by saprophytic bacteria
B Digestion of dead tissue by saprophytic bacteria
C Gas production in dead tissue
D Necrosis of tissue caused by bacterial toxins
E Necrosis of tissue caused by ischaemia

386. A woman has episodic abdominal pain which is worse after fatty meals. Which hormone is responsible for her post-prandial worsening of symptoms?
A Somatostatin
B Secretin

C Pepsin
D Cholecystokinin
E Gastrin

387. With regard to the shoulder (glenohumeral) joint:
A It is a ball-and-socket fibrocartilagenous joint
B It has high mobility at the expense of stability
C It is supported mainly by way of ligaments
D It lies in close relation to the musculocutaneous nerve
E It most commonly dislocates posteriorly

388. Which one of the following is true of cortisol?
A It is a protein
B It lowers blood glucose
C It is an anabolic hormone
D It is stimulated by renin
E It has a peak hormonal concentration in the morning

389. Which one of the following increases the risk of thrombosis?
A Immobility
B Thrombocytopenia
C Reduced blood viscosity
D An intact endothelium
E Heparin

390. When inserting a subclavian central line, the first bony landmark that can be palpated below the inferior margin of the medial portion of the clavicle is:
A Acromion
B Atlas
C First rib
D Second rib
E Third rib

391. With regard to the hip joint, which of the following is true?
A The blood supply to the femoral head arises from a single source
B It may refer pain to the knee
C It is the most commonly dislocated joint in the body
D It lies deep to the sciatic nerve
E The fibrous capsule is strengthened by two ligaments

392. With regard to calcium homeostasis:
A The active form of vitamin D is 25-hydroxycholecalciferol
B PTH secretion is stimulated by the pituitary gland
C Activated vitamin D decreases calcium absorption from the intestine
D PTH acts directly on osteoblasts in bone
E In the kidney, PTH increases calcium excretion and increases phosphate reabsorption from the urine

393. With regard to an embolus:
A It most often arises from a thrombus formed within arteries
B It is the same as a thrombus
C Embolus due to thrombus is impossible to distinguish from post-mortem clot
D Embolus is always due to thrombus
E It generally has a worse outcome than thrombus

394. Which of the following veins empties into the left renal vein?
A Hepatic
B Left suprarenal
C Right gonadal
D Left phrenic
E Right renal

395. With regard to the anatomical snuffbox:
A Tenderness at its base is indicative of a fractured hamate
B It is bounded medially by the abductor pollicis longus
C The basilic vein begins in its roof
D The skin overlying it is supplied by cutaneous branches of the median nerve
E The pulsation of the radial artery may be felt at its base

396. With regard to thyroxine:
A The thyroid gland produces more T3 than T4
B TRH directly results in thyroxine release from the thyroid gland
C Thyroxine promotes the growth and development of the brain
D Thyroxine decreases basal metabolic rate
E Thyroxine acts on cell surface receptors

397. Ischaemia:
- A Refers to generalized tissue death due to toxins, trauma or vascular occlusion
- B Is synonymous with the term 'infarction'
- C Is an abnormal reduction of the blood supply to, or drainage from, an organ or tissue
- D Is always due to vascular occlusion
- E Leads to a worse outcome in tissues with a collateral circulation

398. The Brunner glands secrete an alkaline product that helps maintain an optimal pH for pancreatic enzyme activity. Where are these glands located?
- A At the base of the villi throughout the small intestine
- B Epithelium of the Ampulla of Vater
- C Submucosa of the ileum
- D Submucosa of the jejunum
- E Submucosa of the duodeneum

399. With regard to the knee joint:
- A It is a synovial, pivot joint
- B The cruciate ligaments are intracapsular and intrasynovial
- C The suprapatellar bursa (pouch) communicates with the knee joint
- D Inflammation of the prepatellar bursa is known as 'clergyman's knee'
- E The menisci play an important role in the locking and unlocking mechanism of the knee joint

400. During diabetic ketoacidosis:
- A The pH of the blood is high
- B Cheyne–Stokes breathing is characteristic
- C Hyperkalaemia occurs
- D Blood glucose levels are typically low
- E Volume status is euvolaemic

401. With regard to acute myocardial infarction:
- A It usually results from an embolus
- B It always causes chest pain
- C It induces acute inflammatory changes, maximal at 1–3 days post-infarct
- D Infarcts less then 12 hours old are clearly visible on macroscopic examination
- E The infarcted tissue is replaced by new cardiac muscle

402. A woman sprains her ankle while running down a flight of stairs. Which ligament did she most likely injure?
- A Deltoid
- B Anterior talo-tibial
- C Medial collateral
- D Calcaneo-fibular
- E Calcaneo-tibial

403. With regard to the brachial plexus:
- A It has principal root values C6–T2
- B The serratus anterior muscle is innervated by the subscapular nerve
- C A lesion involving the lower roots of the brachial plexus results in a classic Erb–Duchenne palsy
- D Cords lie in relation to the third part of the axillary artery
- E Roots lie in the neck between the scalenus anterior and medius muscles

404. With regard to adrenal gland disorders:
- A Adrenal insufficiency results in hypokalaemia and hypernatraemia
- B Conn's syndrome results in hyperkalaemia
- C Cushing's disease is due to a cortisol-producing tumour of the adrenal cortex
- D Phaeochromocytoma is due to oversecretion of cortisol by a tumour of the adrenal medulla
- E Congenital adrenal hyperplasia (adrenogenital syndrome) results in virilization and salt wasting

405. Atherosclerosis:
- A Is irreversible
- B Most commonly occurs at branching points within the circulation
- C Is a disease that primarily affects the tunica media of arteries
- D Is accompanied by acute inflammation
- E Is accelerated by hypocholesterolaemia

406. What structure is involved in tarsal tunnel syndrome with heel pain?
- A Anterior tibial artery
- B Deep peroneal nerve
- C Peroneal artery
- D Superficial peroneal nerve
- E Tibial nerve

407. With regard to the brachial plexus:
   A The ulnar nerve arises from the posterior cord
   B The radial nerve arises from the lateral cord
   C The musculocutaneous nerve arises from the lateral cord
   D The median nerve arises from the anterior cord
   E The axillary nerve arises form the lateral cord

408. Which one of the following is true of testosterone?
   A Secretion occurs only in males
   B It is secreted from the Sertoli cells of the testis
   C It is a peptide hormone
   D It is essential for spermatogenesis
   E It depends on FSH for secretion

409. Which of the following regarding local anaesthetics is true?
   A Cocaine is an amide
   B Addition of adrenaline increases systemic absorption of the local anaesthetic
   C One of the first signs of toxicity is perioral paraesthesia
   D They work by blocking potassium channels in the nerve endings
   E They inhibit the propagation of impulses in Aβ fibres first

410. A surgeon's finger is placed in the epiploic Foramen of Winslow. The superior margin is:
   A Common bile duct
   B First part of the duodenum
   C Head of pancreas
   D Hepatic veins
   E Caudate lobe of the liver

411. With regard to the carpal tunnel:
   A It is a fibro-osseous tunnel containing the extensor tendons
   B It contains within it the ulnar nerve and artery
   C Entrapment of the median nerve within it is known as cubital tunnel syndrome
   D It contains ten tendons within it
   E It contains within it the palmar cutaneous branch of the median nerve

412. With regard to the female reproductive system:
   A The menopause is associated with an increase in follicle stimulating hormone
   B Oestrogen concentration peaks just prior to menstruation
   C Both oestrogen and progesterone are necessary for ovulation to take place
   D Oestrogen production is confined to ovarian tissue
   E Fertilization of the human ovum normally takes place in the uterus

413. Aspirin (acetylsalicylic acid):
   A Is a lipo-oxygenase inhibitor
   B Inhibits the coagulation cascade
   C Inhibits platelet aggregation
   D Is a reversible cyclo-oxygenase inhibitor
   E Works by acetylating an aspartate residue at the active site

414. Cancer of the testis most likely metastases to which set of lymph nodes?
   A Aortic
   B Deep inguinal
   C Superficial inguinal
   D Common iliac
   E Internal iliac

415. With regard to the arterial supply of the lower limb:
   A The femoral artery is a direct continuation of the common iliac artery
   B The posterior tibial pulse is posterior to the lateral malleolus at the ankle
   C The popliteal pulse is the most superficial structure within the popliteal fossa
   D The femoral pulse lies at the mid-point of the inguinal ligament
   E The dorsalis pedis pulse is lateral to the extensor hallucis longus tendon

416. With regard to thermoregulation:
   A Brown fat (non-shivering thermogenesis) plays a significant role in adults
   B Acclimatization of the sweating mechanism occurs in response to heat
   C Apocrine sweat glands play an important role in heat loss by evaporation
   D Thermoregulation is one of the principal functions of the thalamus

E Heat adaptation takes approximately 3–5 days to develop

417. Aspirin damages the gastric mucosa through which of the following mechanisms?
- A Reduced surface mucus secretion
- B Increased mucosal blood flow
- C Increased surface bicarbonate secretion
- D Reduced acid secretion by gastric parietal cells
- E Delayed gastric emptying

418. Internal haemorrhoids are painless and only sensitive to stretch. They are formed from folds of the mucous membrane and the submucosa of the anal canal which contain varicose branches of the:
- A Superior rectal vein
- B Inferior rectal vein
- C Superior rectal artery
- D Middle rectal artery
- E Inferior rectal artery

419. With regard to the superficial veins of the extremities:
- A The cephalic vein lies within the deltopectoral groove
- B The long (great) saphenous vein lies behind the medial malleolus at the a nkle
- C The short (small) saphenous vein enters the femoral vein
- D The basilic vein pierces clavipectoral fascia
- E The long saphenous vein has no tributaries draining into it

420. With regard to antiemetics:
- A Cyclizine acts on the histaminergic system
- B Ondansetron primarily acts on the dopaminergic system
- C Prochlorperazine acts on the cholinergic system
- D Metoclopramide is the drug of choice for motion sickness
- E Metoclopramide is the antiemetic of choice in Parkinson's disease

421. A 'claw hand' is usually associated with injury to which of the following nerves?
- A Axillary nerve
- B Musculocutaneous nerve
- C Radial nerve
- D Median nerve
- E Ulnar nerve

422. With regard to the hand:
- A All the lumbricals are supplied by the median nerve
- B All the interossei are supplied by the ulnar nerve
- C The palmar interossei abduct the fingers
- D It is supplied by a single palmar arterial arch
- E Dupuytren's contracture is caused by ischaemic contracture of the intrinsic muscles of the hand

423. Which one of the following agents is a thrombolytic?
- A Warfarin
- B Aspirin
- C Fibrinogen
- D Streptokinase
- E Heparin

SBA answers and explanations

1E: Tear of quadriceps tendon

A 21-year-old male has sustained an injury of sudden onset, associated with swelling and an inability to extend at the knee joint and an absent knee reflex. This is consistent with an injury to the quadriceps group of muscles that lie in the anterior compartment of the thigh and act as the principal extensors of the knee joint. The mechanism of injury is inconsistent with a fractured patella.

2B: Increased stroke volume

During strenuous exercise there is an increase in heart rate, stroke volume and cardiac output. Remember cardiac output is a function of heart rate and stroke volume. During exercise, there is an increase in respiratory rate (hyperventilation) which will lead to a reduction in P_aCO_2. During exercise the oxygen demand of skeletal muscle rises, therefore leading to a reduction in mixed venous blood oxygen concentration. Renal blood flow is autoregulated, so renal blood flow is preserved and will tend to remain the same. Mean arterial blood pressure is a function of cardiac output and total peripheral resistance and will increase with exercise, mainly as a result of the increase in cardiac output that occurs.

3C: Bronchial carcinoma

Thrombophlebitis migrans (or migratory thrombophlebitis) is a condition that results in recurrent episodes of venous inflammation (phlebitis) associated with thrombosis, that occurs in different locations (migratory). It is generally caused by inflammatory, or malignant, conditions where the patient is tipped into a hypercoagulable state. When associated with malignant conditions it is known as Trousseau's syndrome and is generally associated with visceral malignancies (adenocarcinomas), such as gastric, pancreatic, bronchial carcinomas. It is a non-metastatic (or paraneoplastic) effect of malignancy and is related to factors secreted by tumours.

4D: Long thoracic nerve of Bell

The serratus anterior muscle acts to protract the upper limb at the shoulder joint (the 'boxing' muscle). It is innervated by the long thoracic nerve of Bell which is a branch of the brachial plexus and has root values C5, 6 and 7. This may be remembered by the old aphorism 'C5, 6, 7 – Bells of Heaven'. A problem with either the nerve or muscle (e.g. nerve injury following axillary lymph node clearance for breast cancer, some forms of muscular dystrophy) leads to loss of the normal function of the muscle and winging of the scapula when the patient is asked to push against a wall. This is an important clinical sign.

5C: Renal tubular cells

Peripheral nerve cells, unlike nerve cells of the central nervous system, do regenerate following injury. It is a slow process that occurs at about 1 mm/day and may be followed with nerve conduction studies. Schwann cells are responsible for myelination of nerve fibres which increases the axonal speed of conduction. Following injury (Wallerian degeneration), they are able to regenerate. Mucosal cells are epithelial cells which behave like stem cells and can therefore continuously renew themselves. Liver cells (hepatocytes) under certain circumstances can be stimulated to divide. Renal tubular cells lack the ability to regenerate following injury. This is why renal blood flow is so carefully autoregulated. It is also why acute tubular necrosis is taken so seriously, because damage to renal tubular cells is irreversible and will lead to end-stage renal failure, requiring renal replacement therapy in the form of dialysis or transplantation.

6D: Prostatic carcinoma commonly spreads via the blood

Metastasis may be defined as the survival and growth of cells that have migrated or have otherwise been transferred from a malignant tumour to a site or sites distant from the primary.

Tumours commonly spread via the lymphatic and haematogenous routes, so spread generally follows the pattern of these two routes. Other routes are less common (transcoelomic, perineural spread, through cerebrospinal fluid, iatrogenic). Although there are some exceptions, as a general rule, adenocarcinomas spread via the lymphatic route and sarcomas typically spread haematogenously (through the bloodstream). Therefore osteosarcomas typically spread via the bloodstream. Basal cell carcinomas rarely metastasize (thereby excluding answer B) and tend to cause destruction through local invasion. Adenocarcinoma of the prostate tends to metastasize haematogenously through the basivertebral vertebral venous plexus to bone.

7C: Skull fracture

A biconvex-shaped haematoma on a head CT scan is consistent with an extradural haematoma (unlike a crescenteric-shaped haematoma which is caused by a subdural haematoma) and this would explain the patient's fluctuating GCS score. Extradural haematomas are caused by arterial bleeds (typically the important middle meningeal artery which is a branch of the maxillary artery and passes through the foramen spinosum). Usually the artery is torn during a traumatic episode around the region of the pterion which is the weakest part of the skull. The middle meningeal artery forms a close relation to the pterion of the skull. A fracture in this region leads to a torn middle meningeal artery and an extradural haematoma. Management is resuscitation with immediate evacuation through burr holes to prevent a deterioration in neurological function.

8A: Fibroblasts

The stages of wound healing include:

- haemostasis/coagulation
- acute inflammation
- formation of granulation tissue (endothelial cells, fibroblasts, macrophages)
- angiogenesis
- epithelialization, fibroplasia, wound contraction (myofibroblasts)
- remodelling.

During the wound contraction phase (which is responsible for forming a mature scar), fibroblasts change phenotypes and take on contractile properties (forming myofibroblasts). They are primarily responsible for drawing the two wound edges together. Macrophages are responsible for engulfing foreign and particulate matter through phagocytosis and also release cytokines that assist in the inflammatory and healing phases of the injury response. Reticulocytes are immature red blood cells (erythrocytes) and play no significant role in wound contraction. Giant cells are formed from a coalescence of macrophages and are seen in granulomatous conditions but again play no significant role in wound contraction.

9A: Typically encapsulated

An adenoma is defined as a benign tumour of epithelial cells. Table 1 distinguishes the main features of benign and malignant tumours.

Table 1 Features of benign and malignant tumours

Benign	Malignant
Non-invasive	Invasive
No metastasis	Capable of metastasis
Resembles tissue of origin (well-differentiated)	Variable resemblance to tissue of origin
Slowly growing	Rapidly growing
Normal nuclear morphology	Abnormal nuclear morphology
Well circumscribed	Irregular border
Rare necrosis/ulceration	Common necrosis/ulceration

Benign tumours do *not* spread beyond the basement membrane, nor metastasize to distant sites. They are typically encapsulated and have a pseudocapsule caused by compression of the normal surrounding tissues as a result of their slow growth.

Some cells may be dysplastic within a benign tumour (dysplasia means 'precancerous', or disordered, cells but importantly without the ability to invade through the basement membrane and metastasize to distant sites, so technically by definition are still benign). Dysplasia represents an important step in the progression to a malignant tumour and severe dysplasia is synonymous with carcinoma-in-situ. Examples of adenomas that may contain dysplastic cells include some types of bowel polyps (e.g. tubular, villous and tubulovillous polyps/adenomas).

Most adenomas are solid nodules, rather than being annular or circumferential lesions. Rectal carcinomas (that are malignant) can form annular or circumferential lesions.

10B: Damage to the external laryngeal nerve

Two important nerves are at risk in a thyroidectomy.

- The recurrent laryngeal nerve supplies all the intrinsic muscles of the larynx with the exception of the cricothyroid muscle. Damage on either side leads to vocal fold paralysis and resulting hoarseness. Bilateral injury leads to stridor which may necessitate a tracheostomy to maintain a reasonable airway (Semon's law).
- The external branch of the superior laryngeal nerve supplies the cricothyroid which is responsible for lengthening and shortening of the vocal cords, thereby controlling voice pitch.

11D: Woven bone

During fracture healing, provisional callus is composed of woven bone. This is gradually replaced with lamellar bone. Woven bone is characterized by a haphazard organization of collagen fibres and is mechanically weak. Lamellar bone has a regular parallel alignment of collagen into sheets (lamellae) and is mechanically strong.

12C: Anal cancer

The key word in this question is 'sole'. Anal carcinoma is the only cancer featured in the list that may be treated solely with radiotherapy. Current best available treatments for the other cancers require combination treatments (surgery, chemotherapy, radiotherapy).

13D: Retromandibular vein

There are several important structures to be aware of during parotid surgery. From superficial to deep are the following structures:

- facial nerve (VII cranial nerve)
- retromandibular vein – often large and responsible for causing troublesome bleeding
- external carotid artery – deep and rarely encountered.

Also at risk is the great auricular nerve (sensory to the ear-lobe and angle of mandible) and the risk of Frey's syndrome (gustatory sweating caused by misdirected reinnervation to the sweat glands through injury to the parasympathetic secretomotor fibres of the auriculotemporal nerve).

14E: Cardiac output divided by body surface area

The cardiac index is defined as the cardiac output relative to body surface area, thus relating heart performance to the size of the individual. The unit of measurement is litres per minute per square metre ($L/min/m^2$). Cardiac output (CO) is a function of heart rate (HR) and stroke volume (SV): $CO = HR \times SV$. Mean arterial blood pressure (MABP) is a function of cardiac output (CO) and total peripheral resistance (TPR): $MABP = CO \times TPR$.

15B: Bladder cancer

Beta-naphthylamine is a carcinogen that increases the risk of transitional cell carcinoma of the bladder. It was commonly used by workers in the aniline dye industry.

16D: Right occipital lobe

The man has a left homonymous hemianopia which means he is unable to view objects in the left visual field. This information is processed by the right primary visual cortex which lies in the right occipital lobe.

17C: Pressure on the eyeball

Heart rate increases when physiological demand increases (e.g. increased blood flow to skeletal muscles during exercise, to the gut after a heavy meal). Pressure on the sinoatrial node results in activation of the Bainbridge reflex (or atrial reflex) whereby an increase in heart rate occurs as a result of an increase in atrial pressure. During inspiration, intrathoracic pressure decreases. This triggers increased venous return which causes an increased heart rate through the Bainbridge reflex and Frank–Starling's law. Various vagotonic manoeuvres (e.g. Valsalva manoeuvre, carotid sinus massage, pressure on eyeballs, ice-water facial immersion, swallowing of ice-cold water) result in increased parasympathetic tone through the vagus nerve which results in a decrease in heart rate. Such manoeuvres may be clinically useful in terminating supraventricular arrhythmias.

18A: Plasma bicarbonate of 39 mmol/L

Respiratory failure is associated with hypoxia and either a normal/low CO_2 (type 1 respiratory failure) or a raised CO_2 (type 2 respiratory failure). Type 2 respiratory failure in the setting of a raised carbon dioxide leads to a respiratory acidosis. When respiratory failure is chronic, rather than acute, pH compensation occurs through the kidneys.

Renal compensation occurs whereby the renal tubules act to increase the resorption of bicarbonate thereby normalizing the plasma pH (a normal bicarbonate range is 22–30 mmol/L, so 39 mmol/L is raised). This is why patients with long-term, stable chronic obstructive pulmonary disease often have a normal pH but a raised plasma CO_2 and bicarbonate on their arterial blood gases. Renal compensation takes several days before it is fully functional (hence it is a sign of chronic respiratory failure, rather than acute).

19B: Glossopharyngeal nerve

The palatine tonsils are closely related to the glossopharyngeal nerve (cranial nerve IX) which is also the same nerve that supplies the middle ear (Jacobson's nerve). Pain from the tonsils is therefore commonly misinterpreted by the body as coming from the ear when it is in fact not. Referred otalgia is common after tonsillectomy and is also commonly seen in patients presenting with tonsillar and/or base of tongue tumours.

20E: Pampiniform plexus

The contents of the spermatic cord may be remembered by the "Rule of 3's" as follows:

- 3 *constituents*: vas deferens (round ligament uterus in females), lymphatics, obliterated processus vaginalis
- 3 *arteries*: testicular artery, artery to vas (a branch of the superior/inferior vesical), cremasteric artery (a branch of the inferior epigastric)
- 3 *nerves*: genital branch of the genitofemoral (motor to cremaster muscle, sensory to cord), ilioinguinal nerve (inside the inguinal canal but outside the cord), autonomics
- 3 *veins*: pampiniform venous plexus, vein from vas, cremasteric vein
- 3 *fascial coverings*: internal spermatic fascia, external spermatic fascia, cremasteric muscle and fascia.

The ilioinguinal nerve is inside the inguinal canal, but importantly lies outside the spermatic cord. The dartos muscle lies within the scrotal layers and is not to be confused with the cremaster muscle.

21C: Subcostal nerve

When the kidney is approached surgically through a posterior approach, the subcostal nerve is usually superficial and encountered before reaching the kidney. The kidney lies extraperitoneally

(retroperitoneal) and therefore A is incorrect. B and D are incorrect because the question is asking which structure is encountered before reaching the kidney. E is incorrect because the left kidney is being operated on and therefore the right hemidiaphragm should not be encountered. Always remember to read the question carefully!

22D: Right ureter

There are three important structures at risk in a right hemicolectomy that also form important relations to the right hemicolon:

- right ureter
- right gonadal vessels
- second part of the duodenum.

Vigilance and careful identification of these structures are needed to prevent inadvertent injury to them at the time of surgery.

23B: Left kidney

The head of the pancreas is related to the hilum of the right kidney but does not overlie it. It is, however, anterior to the left kidney.

24B: Pulmonary fibrosis

Pulmonary functional residual capacity (FRC) is the volume of air present in the lungs at the end of passive expiration. Obstructive diseases (e.g. emphysema, chronic bronchitis, asthma) lead to an increase in FRC due to an increase in lung compliance and air trapping. Restrictive diseases (e.g. pulmonary fibrosis) result in stiffer, less compliant lungs and a reduction in FRC.

25E: Released in hypovolaemia

Angiotensin II is one of the most potent vasoconstrictors in the human body. It is released as part of the renin–angiotensin system and is derived from angiotensin I (Figure 2). Angiotensinogen is converted to angiotensin I by renin. Angiotension I is converted to angiotensin II by angiotensin-converting enzyme (ACE) in the lungs. Angiotensin II stimulates secretion of aldosterone from the adrenal cortex (zona glomerulosa layer).

Hypovolaemia results in a decrease in intrarenal blood pressure which is sensed by the juxtaglomerular apparatus of the kidney, resulting in renin secretion and a rise in the levels of angiotension II.

26D: A fall in P_{CO_2}

The oxygen–haemoglobin dissociation curve is shifted to the right by a fall in pH (increased hydrogen ion concentration, or acidosis), a rise in temperature, an increase in 2,3-DPG (2,3-diphosphoglycerate), a rise in P_{CO_2}, exercise and HbS (sickle-cell haemoglobin). The dissociation curve is shifted to the left by a rise in pH, a fall in temperature, a decrease in 2,3-DPG, a fall in P_{CO_2}, fetal haemoglobin, high carbon monoxide levels (carboxyhaemoglobin) and methaemoglobinaemia (Figure 3).

Anaemia has no effect on the dissociation curve as the graph represents the degree of oxygen saturation of the existing haemoglobin, rather than the amount, or concentration, of haemoglobin in the blood.

27A: Hypoxia

The dominant control process of coronary perfusion is metabolic hyperaemia. GTN spray is used in angina and increases coronary blood flow through the vasodilatatory action of nitric oxide. Alpha-adrenoceptor stimulation increases systemic blood pressure and thereby increases coronary artery perfusion. All beta-adrenoceptor agonists dilate the coronary vessels thereby increasing coronary perfusion. ADH, or vasopressin, causes a strong vasoconstriction in most tissues, but the cerebral and coronary vessels, by contrast, respond to vasopressin with an EDRF-mediated

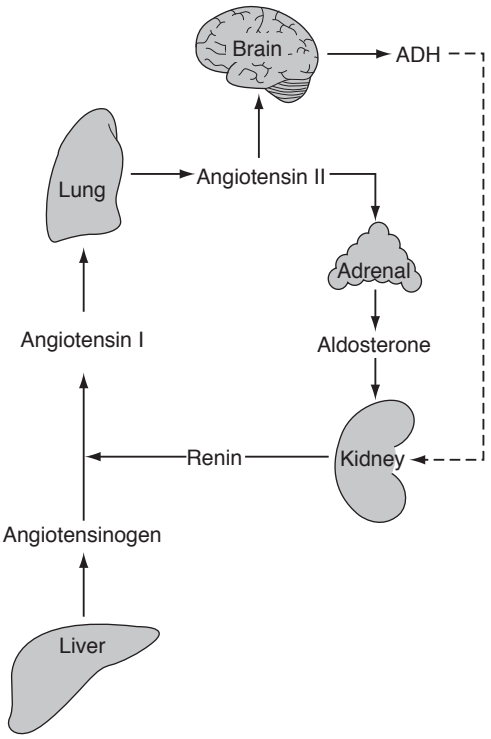

Figure 2 The renin–angiotensin–aldosterone system. Angiotensin I is a decapeptide and angiotensin II is an octapeptide. Renin is a proteolytic enzyme; angiotensin II is a converting enzyme. ADH, antidiuretic hormone.

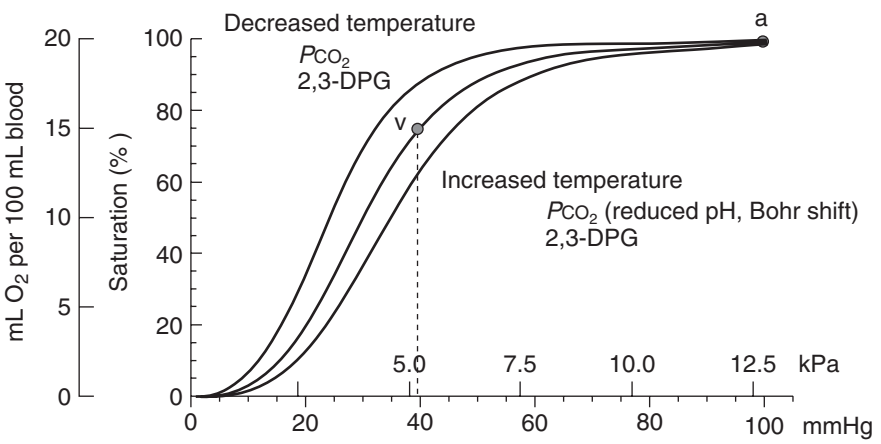

Figure 3 The carriage of oxygen by blood. v, venous; a, arterial.

dilatation (thereby increasing coronary flow). Vasopressin thus produces a redistribution of cardiac output in favour of brain and heart, which seems appropriate in hypovolaemia. Hypoxia reduces myocardial contractility and thereby decreases coronary perfusion.

28D: Bile salts

Resection of the terminal ileum interferes with the enterohepatic circulation, which is the route by which bile salts are recirculated in the body. Resection of the terminal ileum (e.g. in Crohn's disease) may therefore lead to a deficiency in bile salts. The clinical consequences of this are an increased risk of cholesterol gallstones. Vitamin B_{12} is also reabsorbed in the terminal ileum, so resection may also lead to deficiencies in vitamin B_{12} levels through malabsorption.

29A: Promotes protein synthesis

Insulin is produced by the beta-cells of the islets of Langerhans in the pancreas and has various actions, including: promoting uptake of glucose into cells; glycogen synthesis (glycogenesis); protein synthesis; stimulation of lipogenesis (formation of fat). Insulin functions to drive potassium into cells and is used to treat hyperkaelamia. Parathyroid hormone and activated vitamin D are the principal hormones involved in calcium/phosphate metabolism, rather than insulin.

30E: A rise in arterial Pco_2

Prolonged vomiting will lead to a hypochloraemic metabolic alkalosis (a rise in pH; raised bicarbonate), in addition to causing a hypokalaemia as gastric juices are rich in potassium. A hypovolaemic state will ensue with a raised urea concentration. pH compensation occurs through the respiratory system, resulting in hypoventilation which will tend to increase arterial Pco_2 levels.

31D: Lower protein concentration

Intracellular fluid contains a higher concentration of potassium, phosphate, protein and magnesium, but extracellular fluid contains a higher concentration of sodium, calcium and chloride and bicarbonate (Figure 4). Roughly two-thirds of the total body water content is intracellular and one-third is extracellular. The intracellular compartment is more acidic (lower pH; higher hydrogen ion concentration) due to nucleic acids (DNA and RNA) present within cells. The protein content inside cells is higher than the extracellular compartment; osmotic shock (cell lysis) is prevented by the $3Na^+/2K^+$-ATPase pump.

EXTRACELLULAR			INTRACELLULAR	
Na^+	143 mM	>	10 mM	Na^+
K^+	4 mM	<	140 mM	K^+
Ca^{2+}	1.5 mM	>	0.1 μM	Ca^{2+}
Mg^{2+}	1.0 mM	<	58 mM	Mg^{2+}
Cl^-	118 mM	>	10 mM	Cl^-
HCO_3^-	24 mM	>	10 mM	HCO_3^-
pH	7.4	>	7.0	pH

Figure 4 The ionic composition of intracellular and extracellular spaces.

32E: Can lead to a rise in blood pressure and bradycardia

The pressure–volume relationship between intracranial pressure (ICP), volume of cerebrospinal fluid (CSF), blood, and brain tissue, is known as the Monro–Kellie doctrine, or the Monro–Kellie hypothesis. This states that the cranial compartment is incompressible, and the volume inside the cranium is a fixed volume. The cranium, along with the relatively inelastic dura, forms a rigid container, such that the increase in any of its contents – brain, blood, or CSF – will tend to increase the ICP. This in turn will result in a fall in CPP, because CPP = MABP – ICP, where MABP is the mean arterial blood pressure. To compensate for a fall in CPP, the Cushing's reflex/response occurs, resulting in a rise in mean arterial blood pressure and, through the baroreceptor reflex, this causes a reflex bradycardia.

Raised intracranial pressure would not be caused by a shearing injury to the scalp as the injury sustained is outside the cranial vault. Following an acute subdural haematoma there is often a delay before a rise in ICP, because these are often caused by slow venous bleeds, and compensatory mechanisms occur to maintain the ICP within the normal range (displacement of CSF into the spinal canal; ability of the falx or tentorium to stretch). Chronic subdural haematomas, on the other hand, can result in a rise in ICP when compensation can no longer occur.

When the rise in ICP is significant, 'coning' may occur with compression of the 3rd cranial nerve on one side, causing a fixed, dilated pupil on the ipsilateral side.

33A: There is negative base excess

In metabolic acidosis there is a negative base excess. Bicarbonate is the main extracellular buffer, not intracellular. The main intracellular buffers are phosphate and proteins. Compensation in metabolic acidosis occurs through hyperventilation (an increase in alveolar ventilation) and blowing off of CO_2. The mainstay of treatment is to treat the underlying cause (e.g. treatment of hypoxia, shock, hypovolaemia, sepsis). Bicarbonate infusions are used as a last resort since they shift the oxygen–haemoglobin dissociation curve to the left.

34C: Sensory innervations from the internal laryngeal nerve

The posterior one-third of the tongue is innervated (light touch and special taste sensation) by branches of the glossopharyngeal (IX) and vagus (X) nerves. The chorda tympani supplies special taste sensation to the anterior two-thirds of the tongue, and light touch to the anterior two-thirds of the tongue is supplied by the lingual nerve.

Filiform (for gripping food) and fungiform (for sweet/salty taste) papillae are found on the anterior aspect of the tongue. Valate papillae are found further back but still on the anterior two-thirds of the tongue and are concerned with bitter taste. Foliate papillae are found on the sides of the tongue and are concerned with sour taste. The mucous membrane covering the posterior one-third of the tongue is devoid of papillae but has a nodular irregular surface caused by the presence of underlying lymphoid tissue, the lingual tonsil.

35C: The ACL is supplied by the middle geniculate artery

The popliteus tendon penetrates the capsule and is covered by synovial membrane. The suprapatellar bursa communicates with the joint space. The middle geniculate artery pierces the joint capsule to supply it and the cruciate ligaments. The iliotibial tract is attached to a smooth round facet on the anterolateral aspect of the lateral condyle of the tibia. Flexion occurs in the upper compartment and rotation in the lower compartment of the knee.

36B: Provides the same amount of oxygen to the liver as the portal vein

The liver has a rich blood supply derived from two sources: two-thirds from the portal vein, the remaining one-third from the hepatic artery. Portal vein blood is rich in nutrients absorbed from the intestine, but has a relatively low oxygen tension. Hepatic arterial blood contains few nutrients but is rich in oxygen. The hepatic artery supplies roughly 50 per cent of the oxygen

delivered to the liver and the portal vein the other 50 per cent of hepatic oxygen supply. The liver is divided into segments by planes defined by the main hepatic veins (Couinaud classification). Purposeful embolization of hepatic arterial branches may be used to treat hepatic metastases.

37C: Protracted vomiting

Metabolic alkalosis is commonly seen in protracted vomiting where there is a loss of hydrochloric acid. Aspirin (salicylic acid) poisoning will lead to a metabolic acidosis with a raised anion gap. A pancreatic fistula will lead to loss of bicarbonate-rich (alkaline-rich) digestive juices, resulting in a metabolic acidosis (normal anion gap). Hyperventilation will cause a respiratory, rather than a metabolic, alkalosis. Hypoglycaemia will lead to a metabolic acidosis secondary to lactic acidosis and the production of ketone bodies.

38A: Staphylococcus aureus

Osteomyelitis is most commonly caused by *S. aureus* in all age groups.

39A: May respond to pressure dressing

Keloid scars extend beyond the margins of the wound (unlike hypertrophic scars which are confined to the wound margins). Keloid scars are most common on the sternum and deltoid area. Re-excision will usually lead to recurrence. Steroid injections (e.g. triamcinolone) may reduce keloid scar formation around the time of surgery. Pressure dressings also help. The use of subcuticular sutures will not reduce keloid formation.

40C: Haemophilus influenzae

Splenectomized patients are at high risk of postsplenectomy sepsis, especially from encapsulated organisms such as:

- *Haemophilus influenzae*
- *Neisseria meningitidis* (meningococcus)
- *Streptococcus pneumoniae* (pneumococcus).

They are prevented by administering the relevant vaccinations and giving prophylactic penicillin. Patients are also at risk of malaria (especially *Plasmodium falciparum*).

41C: Deficiency of factor IX

Haemophilia B (also known as Christmas disease) is less common than haemophilia A and is due to a deficiency in factor IX. Haemophilia A is due to a deficiency in factor VIII.

42A: Dysphagia

Iron deficiency may be associated with a postcricoid web resulting in dysphagia, koilonychia (spoon-shaped nails), glossitis and angular cheilitis. The association is known as Plummer–Vinson syndrome (also known as George–Paterson–Brown-Kelly syndrome, or sideropenic dysphagia). Such patients are usually female and are at an increased risk of postcricoid tumours.

43D: Increase in tidal ventilation

During haemorrhagic shock, catecholamine levels increase as a result of secretion by the adrenal medulla during the 'fright, fight or flight' (stress) response. A hypovolaemic state stimulates antidiuretic hormone (ADH) secretion. Hypoxia as a result of haemorrhage stimulates chemoreceptors, resulting in increased ventilation (tidal ventilation). The carotid body peripheral chemoreceptors are most sensitive. There is also stimulation of baroreceptors located in the carotid sinus and aortic arch, that act to maintain blood pressure. Haemorrhagic shock leads to hypothermia and a reduction in $P\mathrm{CO}_2$ (secondary to hyperventilation) and consequently a shift in the oxygen–haemoglobin dissociation curve to the left, thereby increasing the affinity of haemoglobin for oxygen.

44B: Acute gastric dilatation

Major burns are associated with splanchnic vasoconstriction on both the arteriolar and venous sides of the circulation. Curling's ulcers are stress ulcers related to major burns, not to be confused with Cushing's ulcers which occur in the setting of head injury. They were once a common complication of major burns and commonly resulted in perforation and haemorrhage, more often than other forms of intestinal ulceration, with correspondingly high mortality rates. Major burns are associated with paralytic ileus, rather than mechanical bowel obstruction.

45C: During growth

Following trauma, sepsis, surgery or any other catabolic state, nitrogen balance is negative. Metabolic rate increases and protein from muscle stores is mobilized for repair and energy, which results in increased urea production and a net nitrogen loss. This may be prolonged for many weeks if sepsis or multiorgan failure occurs. Adrenocorticotropic hormone (ACTH) stimulates cortisol secretion, leading to a catabolic state and a negative nitrogen balance. During growth there is a positive nitrogen balance as protein synthesis occurs.

46A: Prolactin

The anterior pituitary gland (adenohypophysis or pars distalis) synthesizes and secretes the following six hormones: FSH (follicle-stimulating hormone), LH (luteinizing hormone), growth hormone, prolactin, ACTH (adrenocorticotropic hormone) and TSH (thyroid-stimulating hormone). The posterior pituitary gland (neurohypophysis) produces only two hormones: ADH (antidiuretic hormone, also known as vasopressin) and oxytocin. These hormones are synthesized by the hypothalamus and then stored and secreted by the posterior pituitary gland into the bloodstream.

47E: Lies deep to the prevertebral layer of the deep cervical fascia

Scalenus anterior arises from the anterior tubercles of the transverse processes of the 3rd, 4th, 5th and 6th cervical vertebrae and descends almost vertically to insert into the scalene tubercle on the inner border of the 1st rib and into the ridge on the upper surface of the rib in front of the subclavian grove. It lies deep to the prevertebral layer of the deep cervical fascia in the posterior triangle of the neck. The important anterior relations include the phrenic nerve and subclavian vein. Important posterior relations include the second part of the subclavian artery and the roots of the brachial plexus (anterior rami of lower cervical and first thoracic nerves).

48D: 125 mL/min

The normal glomerular filtration rate (GFR) in humans is 125 mL/min. After the age of 40, GFR decreases progressively by about 0.4–1.2 mL/min per year.

49B: Lung cancer

The three most common cancers in the female population in the UK in descending order of frequency are lung, breast and colorectal. In the male population the three most common in descending order of frequency are lung, prostate and colorectal.

50C: 30 per cent

Patients diagnosed with pancreatic cancer typically have a poor prognosis, partly because the cancer usually causes no symptoms early on, leading to locally advanced or metastatic disease at the time of diagnosis. Median survival from diagnosis is around 3–6 months. Even in those suitable for resectional surgery, 5-year survival rates are still only 30 per cent.

51C: Elemental fluids require minimal digestion by the patient

Enteral tube feeding may be administered in the presence of a functional gastrointestinal tract and may be achieved by a nasogastric tube, gastrostomy or enterostomy. Most patients will tolerate a non-lactose, iso-osmolar non-elemental feed, but those suffering from intestinal fistulae, short bowel syndrome or inflammatory bowel disease benefit from an elemental diet which requires minimal digestion. Diarrhoea is a possible complication, but less likely if feeds are given

continuously rather than in bolus and if iso-osmolar rather than hyperosmolar fluid administration. Osmolality is increased when the feed contains glucose, and is lowered when the feed contains sucrose or glucose polymers as the carbohydrate source. Enteral feeding is more cost-effective, safer and requires less monitoring than parental feeding. Moreover, the enteral route allows maintenance of the structural and functional integrity of the intestine.

52D: Does not take into account the presence of metastases

Duke's classification is a histological staging system (defines how far the tumour has spread). The individual stage gives valuable information for the prognosis and management of the patient. A grading system describes the degree of cellular differentiation. Stage A represents a tumour confined to the wall of the bowel, stage B when the tumour has penetrated the serosal surface and stage C when there is local lymph node involvement. Stage D was added later and represents widespread distant metastases, as this is a histological not a clinical staging system. A more detailed method is the TNM system which addresses many more details about tumour spread.

53B: Acute inflammation causes a rise in intraosseous pressure

Osteomyelitis is an infection of bone caused by pyogenic bacteria. *Staphylococcus aureus* is the commonest causative organism. Acute inflammation causes a rise in intramedullary pressure resulting in pain and vessel thrombosis. The classical pathological sequelae are as follows. Bone death results in the formation of a sequestrum, but healing is by new bone formation (the involucrum). A cloacae forms (holes in the involucrum through which pus formed in the medulla discharges). Finally, a tract from drainage from cloaca to the skin is apparent (sinus). Early plain radiographs are often normal, but after 7–10 days bone rarefaction, periosteal new bone and sequestra may be seen. Patients with sickle cell disease are prone to osteomyelitis caused by *Salmonella*.

54B: Abdominal pain, pyrexia and tachycardia are suggestive of a leak

Anastomoses involving the large bowel are more likely to leak than the small bowel. The small bowel has a better blood supply (perfusion), more fluid contents and lower intraluminal pressure compared to the large bowel. Surgical technique plays an important role in preventing leakage. Anastomatic leaks may be apparent in the immediate postoperative period, but it is more usual for signs and symptoms to develop at day 5/6 when bowel peristalsis commences. Abdominal pain, pyrexia and tachycardia are all suggestive of a leak. The appearance of bowel contents through the abdominal wound is not proof of a leak. Extensive dissection may be caused by injury to an unrelated portion of bowel, which had necrosed and leaked. In general, early leaks are best treated by exterioration of the anastomatic ends, or by creating a proximal defunctioning stoma. Late leaks often result in adhesions, abscesses or fistulae. Urgent laparotomy is rarely indicated and conservative management should be adopted.

55A: Cyclophosphamide

The main alkylating agents in regular use are cyclophosphamide, chlorambucil, melphelan and nitrogen mustard. Their mechanism of action is that they bind to proteins and DNA, thereby inhibiting their normal function. Both 5-FU and 6-mercaptopurine are classified as antimetabolites because they inhibit specific synthetic pathways and prevent cell division. Vincristine is a vinca alkaloid, which disrupts the integrity the spindle apparatus and arrest cells during mitosis.

56A: Occurs in normal tissue

Metastatic calcification is a process that involves calcium deposition in normal tissue due to elevated serum calcium levels in the blood. Altered calcium metabolism results in increased absorption, or decreased excretion of calcium and related minerals. Metastatic calcification is a different process to dystrophic calcification (normal serum calcium levels in the blood) and associated with tissue abnormalities or degeneration resulting in mineral deposition. Dystrophic calcification is the calcification occurring in degenerated or necrotic tissue, as in hyalinized scars,

degenerated foci in leiomyomas, and caseous nodules. This occurs as a reaction to tissue damage. The former process is general in nature and the latter is a localized phenomenon. Psammoma bodies are associated with the following tumours: papillary carcinomas (thyroid, renal cell, ovarian), meningiomas, mesotheliomas and prolactinomas.

57D: Neuroma formation

Joint contractures affecting the hip joint are a contraindication to offering a patient an above-knee amputation. Sudek's atrophy is the type I form of complex regional pain syndrome and does not demonstrate nerve lesions. This is not commonly associated with amputation. Myoglobinuria is the presence of myoglobin in the urine and is associated with rhabdomyolyis or muscle destruction. Amputation neuroma is a tumour that may occur near the stump following an amputation. Amyloid is a family of unusual proteins, all characterized by beta-pleated sheets, and associated with chronic infections, chronic inflammatory diseases and certain neoplasms.

58A: Begins in the region of the anatomical snuffbox

The cephalic vein is a superficial vein of the upper limb that arises within the anatomical snuffbox. It communicates with the basilic vein by the median cubital vein at the elbow and is located in the superficial fascia along the anterolateral surface of the biceps muscle. At the elbow, it is superficial to the lateral cutaneous nerve of the forearm. Superiorly, the cephalic vein passes between the deltoid and pectoralis major muscles (deltopectoral groove) and through the deltopectoral triangle, where it empties into the axillary vein. As it is a vein, it contains valves.

59B: Proximal myopathy

The patient is generally a young female and the condition may be familial. The thyroid is usually moderately diffusely enlarged and soft and a bruit may be heard. The patient may be hot, with moist and warm skin due to peripheral vasodilatation. Weight loss may be a feature despite increased food intake. Fine hand tremor with hyperkinesias and increased bowel mobility is also common. Cardiac enlargement and abnormal heart sounds are suggestive of Cushing's syndrome. Eye signs are usual. Menstrual irregularity and infertility are common.

60B: Left homonymous hemianopia

Occlusion of the posterior cerebral artery results in the following signs and symptoms:

- contralateral loss of pain and temperature sensations
- prosopagnosia with bilateral lesions of the lingual and fusiform gyri
- medial midbrain syndrome (Weber's syndrome)
- contralateral deficits of cranial nerves: facial (UMN), vagus and hypoglossal nerves
- ipsilateral deficit of occulomotor nerve (ophthalmoplegia)
- visual field defects (contralateral homoymous hemianopia with macular sparing)
- Horner's syndrome
- visual agnosia
- palinopsia, micropsia and macropsia (illusory phenomena)
- achromatopsia and dyschromatopsia (disorders of colour vision)
- memory impairment (amnesia).

61C: Femoral arterial branch, which takes part in the anastomosis around the knee

The adductor canal contains the femoral artery, femoral vein, and branches of the femoral nerve (the saphenous nerve and nerve to vastus medalis). The boundaries of the adductor canal are as follows:

- lateral: vastus medialis muscle
- posteromedially: adductor longus and adductor magnus muscles
- anteriorly: sartorius muscle
- roof: the sartorius and the subsartorial fascia.

62D: A cause of thoracic outlet syndrome

A cervical rib is an extra rib, which arises from the 7th cervical vertebra. It is a congenital abnormality that is located above the 1st rib. Thoracic outlet syndrome is caused by compression of the lower trunk of the brachial plexus or subclavian artery. It is associated with the formation of subclavian aneurysms. Chest radiographs with apical lordotic views and cervical spine radiographs are recommended. Onset is from the second to eighth decade with a peak in the fourth decade. It is more common in females.

63E: Is a cause of toe gangrene

An aneurysm is an abnormal dilation of a blood vessel. Abdominal aortic aneurysms between 5 and 5.9 cm have a growth rate 0.43 cm/year and an annual risk of rupture of 3–15 per cent. Ninety per cent of abdominal aortic aneurysm are infrarenal (below the level of the kidneys). If the aortic aneurysm grows at a rate of more than 1 cm/year, surgical treatment should be performed electively. It is associated with positive family history, smoking, atherosclerosis and other causes (infection, inflammation, trauma, etc.). There is no causative link with builders. Complications of aneurysms include: thrombosis, embolism, pressure effects, haemorrhage or ischaemia.

64A: Is formed by the union of the splenic and superior mesenteric veins

The hepatic portal vein is the venous drainage from the gastrointestinal tact and spleen into the liver. It is formed by the confluence of the superior mesenteric and splenic veins. The anterior boundaries of the epiploic foramen of Winslow is the hepatic portal vein. The portal vein is posterior to the common hepatic artery. The hepatic portal vein orginates behind the neck of the pancreas. Approximately 75 per cent of hepatic blood flow is derived from the hepatic portal vein, while the remainder is from the hepatic arteries.

65D: Predisposes to malignant change

Ulceration of the lower limb affects 1 per cent of the adult population and approximately 3.6 per cent of people over the age of 65. The majority of chronic lower limb ulceration is attributed to venous disease. Venous ulcers occur when there is venous insufficiency or following deep venous thrombosis in which the valves have been destroyed following recanalization. In both, the common denominator is venous stasis. Chronic limb ulceration is linked to Marjolin's ulcers (an aggressive ulcerating squamous cell carcinoma in areas of previously damaged skin). The use of compression bandages or graduated compression stockings exerts a pressure of 40 mmHg at the ankle. An ABPI of less than 0.5 is contraindicated for compression bandaging.

66A: Affects the lower limbs in 80 per cent of cases

Lymphoedema is the accumulation of tissue fluid as a result of a fault in the lymphatic system. It commonly affects the legs, arms, genitalia and face. Lymphoedema affects the legs in 80 per cent of cases. Lymphoedema presents with unilateral limb swelling. It may be classified as primary (unknown aetiology) or secondary due to infection/inflammation. Lymphoedema should be distinguished from systematic diseases (cardiac or renal failure), venous disease (post-thrombotic syndrome) or rarer causes (arteriovenous malformations). Delayed ilio-inguinal uptake of radionucleotide rhenium–antimony labelled technetium is diagnostic. Treatment of lymphoedema is conservative (compression stocks), medical (diuretics), or surgical (debulking operations: Homan's procedure, lymphovenous shunts and lymphatic bypass).

67C: Is characterized by Reed–Sternberg cells

Hodgkin's disease often presents with painless enlargement of one or more lymph nodes (usually in the cervical region) and is characterized histologically by the presence of Reed–Sternberg cells. Non-Hodgkin's disease is commonly seen in the gastrointestinal tract. The Ann Arbour system divided Hodgkin's disease into four stages, according to its extent, with A or B subtypes according to absence or presence of constitutional systems. The lymphocyte-depleted type of Hodgkin's disease is associated with the worse prognosis.

68E: Parasympathetic fibres to the submandibular gland

The facial nerve is the seventh (VII) of twelve paired cranial nerves. It emerges from the brainstem between the pons and the medulla, controls the muscles of facial expression, and provides taste sensations for the anterior two-thirds of the tongue and oral cavity. It also supplies preganglionic parasympathetic fibres to many head and neck ganglia (including the submandibular and sublingual glands via the chorda tympani). The vagus nerve (CN X) supplies the palatoglossus muscle and the trigeminal nerve (CN V) supplies the medial pterygoid, masseter and temporalis muscles.

69A: Lies between mylohyoid and hypoglossus muscle

The submandibular (Wharton's) duct is 5 cm long. First it lies between mylohyoid and hyoglossus muscles and then between the sublinguinal gland and geniohyoid muscle. The duct develops in the ectoderm from a groove in the floor of the mouth. It opens into the floor of the mouth adjacent to the frenulum. The facial nerve (CN VII) runs through the parotid gland.

70B: Is at more of a horizontal angle than in an adult

The Eustachian tube links the nasopharynx to the middle ear. It is noted to be more horizontal in shape in children compared to adults. A portion of the tube (1/3) proximal to the middle ear is comprised of bone and the remainder is composed of cartilage. It is derived from the first pharyngeal pouch. Otitis media commonly affects the Eustachian tube. Children under 7 years of age are more susceptible to this condition because the Eustachian tube is shorter and at more of a horizontal angle than in the adult ear.

71D: There is an association with Henoch–Schönlein purpura

Intussusception is an invagination of a portion of bowel into its own lumen. It occurs most commonly in boys aged 3–12 months. The majority of intussusceptions are ileo-colic, but ileo-ileal, ileo-ileocolic and colo-colic have also been described. Henoch–Schönlein purpura is a systemic vasculitis characterized by deposition of immune complexes containing the antibody IgA into the skin and kidney. There is an association with intussusception.

72D: Is associated with autoimmune diseases

Sjögren's syndrome is an autoimmune disease characterized by dryness of the mouth and eyes. There is a female predominance with an average age of onset in the late forties. Amyloid comprises a family of unusual proteins, all of which have characteristic beta-pleated sheet structure, and is not directly related to Sjögren's disease. Five per cent of patients with Sjögren's disease will develop lymphoma.

73C: Allows the biopsy of rectal tumours without anaesthetic

Rigid sigmoidoscopy examines the rectum. It rarely causes serious complications (<1 per cent). At about 15 cm the rectosigmoid junction will be encountered and usually this can be negotiated to show about 10 cm of the sigmoid. A proctoscope is used to examine haemorrhoids. Partial-thickness rectal biopsies are easy to carry out in clinic without anaesthesia. In the diagnosis of Hirschsprung's disease, a full-thickness biopsy at the anorectal junction is taken, usually under general anaesthetic or using a small anal retractor in neonates.

74B: Peptic ulcer

Parathyroid hormone increases serum calcium levels at the expense of phosphate. In 70 per cent of cases the condition is asymptomatic. Symptomatic forms are described as 'stones' (nephrolithiasis and nephrocalcinosis), 'bones' (bone pain and arthralgia), 'groans' (peptic ulcer disease and pancreatitis) and 'psychic overtones'. Calcium may increase gastrin secretion, which in turn may lead to peptic ulcer disease. The calcium may deposit in the eye leading to cataract formation. Hoarseness due to laryngeal spasm is associated with hypoparathyroidism.

75C: Has a roof pierced by the external jugular vein

The boundaries of the posterior triangle of the neck are: posterior border of sternocleidomastoid, anterior border of trapezium and the medial third of the clavicle. The roof is formed by investing fascia, platysma and the external jugular vein. The floor is comprised of prevertebral fascia covering muscles, subclavian artery, trunks of the brachial plexus and cervical plexus. The carotid sheath is contained in the anterior triangle of the neck.

76A: Develops from the first and third branchial arches

The tongue is a branchial arch derivative and is derived from the first and third branchial arches. Special taste to the anterior two-thirds of the tongue is from the chorda tympani nerve (a branch of the facial nerve, VII) and special taste sensation to the posterior one-third of the tongue derives from the glossopharyngeal nerve (IX). Somatic touch to the anterior two-thirds of the tongue is by way of the lingual nerve (Va) and to the posterior one-third is by way of the glossopharyngeal nerve (IX), as is the case with special taste.

The hypoglossal nerve (XII) supplies all the intrinsic muscles of the tongue, with the exception of palatoglossus which is supplied by the pharyngeal plexus of nerves (IX, X, sympathetics). A left hypoglossal nerve palsy will result in a deviated tongue to the left on tongue protrusion (but note the question says glossopharyngeal nerve!).

The tongue receives its blood supply primarily from the lingual artery, a branch of the external carotid artery. The fibrous septum dividing the two halves of the tongue prevents any significant anastomosis of blood vessels across the midline. In contrast, a significant feature of the tongue's lymphatic drainage is that lymph from one side, especially of the posterior part, may reach nodes on both sides of the neck (in contrast to the blood supply which remains unilateral). Because the lymphatic plexus freely communicates across the midline, cancer of the tongue frequently metastasizes bilaterally.

77A: Is more common in patients with Plummer–Vinson syndrome

Postcricoid tumours are more common in females. They are associated with iron deficiency anaemia and patients with Plummer–Vinson syndrome (also known as George–Paterson–Brown–Kelly syndrome) are at higher risk of developing such tumours. Such tumours require multimodal (combination) therapy (radiotherapy, chemotherapy and surgery). If surgically operable, they can be safely resected and reconstructed with a good chance of cure with minimal morbidity.

Postcricoid tumours are highly lethal with a poor prognosis and a 5-year survival generally ranging from 15 to 20 per cent.

78A: Thyroid dysfunction is unlikely

Retrosternal goitres are usually benign and multinodular. Although any thyroid malignancy can extend retrosternally (but especially anaplastic thyroid carcinomas and lymphomas), most cases are benign. In most cases the patient remains euthyroid with normal thyroid function tests and normal thyroid autoantibody tests. Tracheal deviation is not necessarily associated with stridor and many patients solely complain of shortness of breath on exertion. Recurrent laryngeal nerve palsy is a sign of thyroid malignancy and, as mentioned, most retrosternal goitres are benign.

79D: In the parotid gland can be reliably diagnosed by fine-needle aspiration

Although tumours seen within the minor salivary glands are more commonly malignant, malignant salivary gland carcinomas are still far more common in the major salivary glands (parotid, submandibular, sublingual). Frey's syndrome (gustatory sweating) is a postoperative complication of parotid surgery and is due to misdirected reinnervation of the secretomotor fibres of the auriculotemporal nerve into the sweat glands.

Salivary gland carcinomas are best diagnosed by ultrasound-guided fine-needle aspiration cytology (if the result is positive), although a negative test (benign result) does not exclude the presence of malignancy as the needle may have been directed into the wrong place. Risk factors

for salivary gland malignancies include prior radiation treatment. Tobacco and alcohol, which are highly associated with head and neck squamous cell carcinoma, have not been shown to play a role in the development of malignancies of the salivary glands. Salivary gland carcinomas are relatively resistant to radiotherapy. Carefully planned and executed surgical excision is the primary treatment for all primary salivary gland tumours.

80A: Is a cause of carpal tunnel syndrome

Colles' fracture is a distal fracture of the radius that is a known cause of carpal tunnel syndrome (compression of the median nerve in the carpal tunnel). It rarely results in ulnar nerve compression. A Colles' fracture is extra-articular by definition and does not extend into the wrist joint, otherwise this would make it an intra-articular fracture (Barton's fracture). The distal fragment in a Colles' fracture is displaced dorsally, unlike in a Smith's fracture where the distal fragment is displaced volarly (ventrally). Associated fracture of the ulnar styloid process may occur in more than 60 per cent of cases, although this does not form part of the true Colles' fracture (especially as it may not occur in all cases) and is a common associated injury.

81B: The left hip joint is not congenitally dislocated

The Trendelenburg test is a favourite of examiners, so it is worth spending a moment discussing it. Put simply, the test is an assessment of insufficiency of the hip abductor system.

Ask the patient to stand on his or her good leg and flex the other leg at the knee. The opposite side of the pelvis should rise to help to balance the trunk on the leg by bringing the centre of gravity over the weight-bearing foot. This involves the use of the hip abductors – the gluteus medius and minimus. This manoeuvre is then repeated by asking the patient to stand on the bad leg. The test is positive if the opposite side of the pelvis falls and the patient has difficulty standing. You may notice that the patient throws the upper part of the body over the affected hip in order to compensate for the loss of balance due to the pelvic dip on the contralateral side (Trendelenburg lurch).

In this scenario the left gluteal abductors (and left superior gluteal nerve), but not the psoas muscle, are working.

A Trendelenburg test can be positive for two main reasons – neurological or mechanical. Neurological causes can be due to generalized motor weakness as seen with myelomeningocele and spinal cord lesions, or more specific problems, such as superior gluteal nerve dysfunction/injury (e.g. following hip surgery). The mechanical causes include conditions that affect the abductor muscle lever arm, such as:

- congenital dislocation of the hip
- coxa vara
- fractures of the femoral neck
- dislocation or subluxation of the hip joint
- neuromuscular diseases (e.g. poliomyelitis)
- pain arising in the hip joint, inhibiting the gluteal muscles.

These conditions shorten the length of the muscle from its origin to its insertion, and significantly reduce its strength.

It should be noted that the test is not valid in children below the age of 4 years, and that it has a 10 per cent false-positive rate due to pain, generalized weakness, poor cooperation or bad balance.

82A: Has maximum velocity in the centre

In a vessel, laminar flow is governed by Poiseuille's law. Flow is maximal in the centre of a tube, with the highest concentration of cells in the centre. For flow in a pipe, laminar (smooth) flow occurs when the Reynold's number is less than 2300 and turbulent (rough) flow occurs when it is greater than 4000. Turbulent flow is a fluid regime characterized by chaotic, stochastic property

changes. This includes low-momentum diffusion, high-momentum convection, and rapid variation of pressure and velocity in space and time.

83D: Limitation of straight-leg raising

A right S1 radiculopathy secondary to a lumbar disc protrusion would result in right-sided pain in the posterior aspect of the leg and ankle, reduced power in plantar flexion and reduced sensation in the lateral foot, and reduced/absent ankle jerk. A femoral stretch test assesses for irritation of higher nerve roots (L4 and above). The straight-leg raise test (Lasègue's sign or Lasègue test) determines whether a patient with low back pain has an underlying herniated disk, mostly located at L5, S1 or S2 spinal nerves.

84E: Have small orifices and characteristically close spontaneously before the age of 5 years

Congenital umbilical hernia is a congenital malformation, common in infants of African descent. Among adults, it is three times more common in women than in men; among children, the gender ratio is roughly equal. Umbilical hernias in children are common with an incidence of 1 in 10. Obstruction and strangulation of the underlying hernia is rare because the underlying defect in the abdominal wall is larger compared to inguinal hernia of the newborn. The size of the base of the herniated tissue is inversely correlated with risk of strangulation (i.e. narrow base is more likely to strangulate). A persistence of a patent vitelline duct permits an intermittent discharge of enteric contents from the umbilicus. It is a very rare abnormality and may be associated with umbilical polyps. When the hernia's orifice is small (<2 cm), 90 per cent close by 5 years.

85E: Fluids and mannitol

Haemolytic transfusion reactions lead to hypotension and oliguria. The increased haemoglobin in the plasma will be cleared via the kidney, which leads to haemoglobinuria. Inserting a urinary catheter with subsequent demonstration of oliguria and haemoglobinuria not only confirms the diagnosis, but is also useful in monitoring therapy. Treatment commences with discontinuation of the transfusion, followed by aggressive fluid resuscitation to support the hypotensive episode and increased urine output. Inducing diuresis through fluid resuscitation and osmotic diuretics is an important step to eliminate the haemolysed red cell membranes and help prevent renal failure. Alkalinization of the urine (pH >7) helps prevent haemoglobin aggregation and renal failure. Steroids have a limited role in this context.

86E: Burst abdomen is preceded by serosanguinous discharge

Cutting through muscle produces more postoperative pain than muscle splitting incisions where the anatomical planes between muscle fibres are used. There is no evidence that closing the peritoneum reduces the development of adhesions. The release of collagenase near wound edges weakens the skin and therefore sutures should be placed 1 cm away. The tip of the first trocar cannot be visualized before the camera is inserted unless a small laparotomy incision is made. The 'pink sign' indicates impending wound disruption.

87E: Responds to treatment with vancomycin

Pseudomembranous colitis, also known as antibiotic-associated diarrhoea (AAD), is an infection of the colon. The main causative agent is *Clostridium difficile*. Patients present with diarrhoea, fever, abdominal pain and rectal bleeding. In severe cases, life-threatening complications can develop, including toxic megacolon. A major risk factor for this condition includes recent antibiotic usage. Clindamycin is the antibiotic classically implicated as the causative agent, but any antibiotic can cause the condition. Due to frequent administration, cephalosporin antibiotics (cefazolin and cephalexin) account for a large percentage of cases. Medical treatment of this condition includes metronidazole or vancomycin.

88A: Ultrasound

There are no blood tests that are specific and sensitive to establish the diagnosis of acute cholecystitis. (Raised alkaline phosphatase, bilirubin, WBC and CRP are only suggestive of

the underlying diagnosis.) However, ultrasound, CT scan and hepatobiliary scintigraphy with technetium-99m DISIDA (bilirubin) analogue are all sensitive and specific modalities for the diagnosis of acute cholecystitis. Plain radiographs are not beneficial.

89A: Albumin of 30 g/L

The modified Glasgow scoring system is an indicator of prognostic severity (Table 2). One point is scored for each criterion met on admission and again at 48 hours after admission (1–2 points is associated with a mortality of <1 per cent, 3–4 points with 15 per cent, and 6 points with a mortality approaching 100 per cent).

Table 2 Modified Glasgow scoring

Po_2	<8 kPA (60 mmHg)
Age	>55 years
Neutrophils/WCC	$>15 \times 10^9$/L
Ca (corrected)	<2 mmol/L
Raised urea	>16 mmol/L
Enzymes (LDH)	>600 IU/L
Albumin	<32 g/L
Sugar (glucose)	>10 mmol/L

90D: Is anteriorly bounded by to the seminal vesicles and prostate

The blood supply of the rectum is supplied by the superior rectal artery (first two-thirds of rectum) and the middle rectal artery (last third of rectum). The venous drainage is the superior and middle rectal veins. The nerve supply comprises the inferior anal nerves and inferior mesenteric ganglia. The lymphatic drainage comprises the inferior mesenteric, pararectal and internal iliac lymph nodes. In males, the anterior border of the rectum comprises the rectovesical pouch, small bowel, Denonvillier's fascia, bladder, vas, seminal vesicles and prostate.

91E: Is attached to the diaphragm by the falciform ligament

The liver weighs 1500 g and is the largest organ in the body. It receives 30 per cent of the body's total cardiac output (1500 mL blood flow/min). The liver is drained by the hepatic veins into the inferior vena cava. The nerve supply of the liver is by the right vagus nerve via the celiac ganglia and left vagus, which is supplied directly into the porta hepatis. Sympathetic innervation is carried on vessels. The liver is attached to the diaphragm by the falciform ligament.

92B: Iron deficiency may develop

Choledochal cysts are dilations of the bile duct that may present with cholangitis, biliary obstruction or as an abdominal mass. They are major risk factors for cholangiocarinoma and are rare except in the Far East. One-third of cases present in adulthood. Treatment consists of excising the cyst and fashioning a Roux-en-Y choledochojejunal anatomosis. Multiple intrahepatic dilations occur in Caroli's disease, which is associated with cirrhosis and with medullary sponge kidney. Of note, Casoni's complement fixation test is for hydatid disease.

93E: Is treated by operative correction and may result in articular damage and foot stiffness

Talipes equinovarus is a structural deformity of the hindfoot and forefoot. Conservative treatment should address the problem by stretching and splinting in the following order: first the forefoot adduction, then the supination, and finally the equines deformity. It is more common in males and is bilateral in 30–50 per cent of cases.

94A: There is an association between osteosarcoma and Paget's disease of the bone

Bone tumors are rare. The three predominant malignant tumours are the osteosarcomas, chondrosarcomas and Ewing's sarcoma. Chondrosarcomas commonly occur in the middle-aged and elderly. Chemotherapy is now given routinely for osteosarcomas and Ewing's sarcoma, but

has a limited role for chondrosarcomas. Metastasis usually occurs via the bloodstream. Pain and swelling are the two most common features.

95D: Costodiaphragmatic recess of the pleura

The posterior relations of the kidney include:

- diaphragm and costo-diaphragmatic recess of the pleura
- psoas muscle
- quadratus lumborum muscle
- 12th rib
- subcostal neurovascular bundle (vein, artery and nerve)
- iliohypogastric and ilio-inguinal nerves.

96C: May contain heterotropic pancreas

Meckel's diverticulum is the anatomical remnant of the vitello-intestinal duct. In the developing fetus the vitello-intestinal duct connects the primitive midgut to the yolk sac and plays a part in intestinal rotation. It is present in 2 per cent of the population. It is often observed as a 5 cm intestinal diverticulum projecting from the antimesenteric wall of the ileum and about 60 cm from the ileocaecal valve. Its blind end may contain ectopic tissue, namely gastric mucosa (10 per cent of cases), liver, pancreatic tissue, carcinoid or lymphoid tissue. It is about twice as common in males.

97A: Radiotherapy

Recognized curative treatment for localized carcinoma of the prostate includes primarily surgery, radiation therapy, and proton therapy. Alternative treatments (hormonal therapy, chemotherapy, cryosurgery, and high-intensity focused ultrasound (HIFU)) can halt the progression of disease, but not provide a cure. Tamsulosin is an α_{1a}-selective alpha-blocker used in the symptomatic treatment of benign prostatic hyperplasia (BPH).

98C: Is no more likely to have secondary hyperparathyroidism than someone on CAPD for the same period

Patients with end-stage renal failure, whether they are on haemodialysis or continuous ambulatory peritoneal dialysis (CAPD), are at an increased risk of secondary hyperparathyroidism – an increase in parathyroid hormone as a physiological response to hypocalcaemia as a result of low levels of activated vitamin D in chronic renal failure. Many years following renal transplantation, a condition known as tertiary hyperparathyroidism may develop where the parathyroid glands begin to function autonomously and complications may ensue. In such situations a parathyroidectomy may be indicated. Bisphosphonates following surgery would be counterproductive as they would lower calcium even further (bisphosphonates inhibit osteoclasts and thereby decrease calcium). Vascular calcification causes hardening and sclerosis of the blood vessels and is irreversible. Patients on haemodialysis who have taken aluminium hydroxide (to control high levels of phosphate) over long periods are at increased risk of osteomalacia (not osteoporosis).

99A: Will affect 1 in 15 women

Breast carcinoma is the most common female cancer in the UK. There is a genetic element (i.e. BRAC 1 and 2 genes) to the disease, but the risk is only about three times the normal in those with a first-degree relative with pre-menopausal disease. Oestrogen exposure has been linked. For example, early menarche, late menopause and nulliparous women are at a higher risk. Breast feeding is protective.

100D: Non-parametric tests could be used

A normal distribution is shown be a symmetrical bell-shaped curve on a graph. A population is defined in terms of its mean and its standard deviation. The mean, median and mode have the same value. A chi-squared test can be applied to a normally distributed population, whereas non-

parametric tests can be applied whether a population is distributed normally or otherwise. One standard deviation from the mean contains 68 per cent of the population, two standard deviations include 95 per cent, and three standard deviations include 99.7 per cent. Twenty-five out of 1000 individuals (2.5 per cent) would be expected to be more than two standard deviations from the mode.

101E: Parietal cells

Goblet cells are mucus-secreting cells, widely distributed throughout epithelial surfaces, but especially dense in the gastrointestinal and respiratory tracts. Kupffer cells have phagocytic properties and are found in the liver; they participate in the removal of ageing erythrocytes and other particulate debris. The gastric mucosa contains many cell subtypes, including acid-secreting cells (also known as parietal or oxyntic cells), pepsin-secreting cells (also known as peptic, chief or zymogenic cells) and G-cells (gastrin-secreting cells). Peptic cells synthesize and secrete the proteolytic enzyme, pepsin. Parietal cells actively secrete hydrochloric acid into the gastric lumen, accounting for the acidic environment encountered in the stomach. However, parietal cells are also involved in the secretion of the glycoprotein, intrinsic factor.

Intrinsic factor plays a pivotal role in the absorption of vitamin B_{12} from the terminal ileum. Autoimmune damage to parietal cells leads to a lack of intrinsic factor and hydrochloric acid, leading to vitamin B_{12} deficiency and achlorhydria. This is known as pernicious anaemia. Pernicious anaemia is associated with a 3-fold increase in gastric cancer risk.

102D: Neisseria meningitidis

The spleen plays an important role in the removal of dead and dying erythrocytes and in the defence against microbes. Removal of the spleen (splenectomy) leaves the host susceptible to a wide array of pathogens, but especially to encapsulated organisms.

Certain bacteria have evolved ways of evading the human immune system. One way is through the production of a 'slimy' capsule on the outside of the bacterial cell wall. Such a capsule resists phagocytosis and ingestion by macrophages and neutrophils. This allows them not only to escape direct destruction by phagocytes, but also to avoid stimulating T-cell responses through the presentation of bacterial peptides by macrophages. The only way that such organisms can be defeated is by making them more 'palatable' by coating their capsular polysaccharide surfaces in opsonizing antibody.

The production of antibody against capsular polysaccharide primarily occurs through mechanisms that are independent of T-cells. The spleen plays a central role in both the initiation of the antibody response and the phagocytosis of opsonized encapsulated bacteria from the bloodstream. This helps to explain why the asplenic individuals are most susceptible to infection from encapsulated organisms, notably *Streptococcus pneumoniae* (pneumococcus), *Neisseria meningitidis* (meningococcus) and *Haemophilus influenzae*.

The risk of acquiring these infections is reduced by immunizing individuals against such organisms and by placing patients on prophylactic penicillin, in most cases for the rest of their life. In addition, asplenic individuals should be advised to wear a MedicAlert bracelet to warn other healthcare professionals of their condition.

103E: Upon assuming the upright position

Stimulation of the sympathetic nervous system results in a rise in heart rate and stroke volume and therefore cardiac output increases. Cutting the vagus nerves to the heart results in an increase in heart rate because of the abolition of vagal tone and therefore cardiac output increases.

If the end-diastolic volume of the heart (preload) is increased, under normal physiological circumstances, cardiac output is increased by the Frank–Starling mechanism. The exception is in the failing heart where the law of LaPlace becomes more important and cardiac output actually falls.

Arterial blood pressure is homeostatically regulated through the action of baroreceptors, principally located in the carotid sinus and the wall of the aortic arch. If the carotid sinus pressure is reduced, the baroreceptors become inactive and lose their inhibitory effect on the vasomotor centre in the brainstem. The result is activation of the sympathetic nervous system. This produces a rise in heart rate, stroke volume, mean systemic filling pressure and venous return, leading to an increase in cardiac output and return of the mean arterial blood pressure to its original value.

Cardiac output falls when one stands up owing to the pooling of blood on the venous side of the circulation, which has a large capacitance. Stepping out of a hot bath exacerbates this pooling effect because superficial cutaneous veins dilate in response to heat, increasing their capacitance even further. Under normal circumstances, activation of the baroreceptor reflex compensates to some degree, preventing syncope. However, in the elderly, or in patients on antihypertensives, inadequate compensation from the baroreceptor reflex may result in a vasovogal syncope, or othostatic hypotension.

104E: It is directly proportional to the fourth power of the radius

The Hagen–Poiseuille law states that the flow through a vessel is:

- *directly* proportional to the *pressure* head of flow
- *directly* proportional to the *fourth power* of the radius
- *inversely* proportional to the *viscosity*
- *inversely* proportional to the *length* of the tube.

The radius of the tube is therefore the most important determinant of flow through a blood vessel. Thus, doubling the radius of the tube will lead to a 16-fold increase in flow at a constant pressure gradient. The implications of this are several fold.

First, owing to the fourth-power effect on resistance and flow, active changes in radius constitute an extremely powerful mechanism for regulating both the local blood flow to a tissue and central arterial pressure. The arterioles are the main resistance vessels of the circulation and their radius can be actively controlled by the tension of smooth muscle within its wall.

Second, in terms of intravenous fluid replacement in hospital, flow is greater through a peripheral cannula than through central lines. The reason is that peripheral lines are short and wide (and therefore of lower resistance and higher flow) compared to central lines, which are long and possess a narrow lumen. A peripheral line is therefore preferential to a central line when urgent fluid resuscitation, or blood, is required.

105D: The sum of the residual volume and the expiratory reserve volume

Spirometry traces are easy to understand if you remember the following two rules:

1. There are four lung volumes and five capacities that you need to remember.
2. A capacity is made up of two or more lung volumes.

The *four lung volumes* are:

- *Tidal volume* = volume of air inspired or expired with each normal breath in quiet breathing; approximately 500 mL
- *Residual volume* = volume of air that remains in the lung after forced expiration
- *Inspiratory reserve volume* = extra volume of air that can be inspired over and above the normal tidal volume
- *Expiratory reserve volume* = extra volume of air that can be expired by forceful expiration after the end of a normal tidal expiration.

The *five lung capacities* are:

- *Functional residual capacity* = volume of air that remains in the lung at the end of quiet expiration, equal to the sum of the residual volume and the expiratory reserve volume
- *Inspiratory capacity* = inspiratory reserve volume + tidal volume

- *Expiratory capacity* = expiratory reserve volume + tidal volume
- *Vital capacity* = inspiratory reserve volume + tidal volume + expiratory reserve volume (or total lung capacity – residual volume)
- *Total lung capacity* = vital capacity + residual volume.

The residual volume (and therefore functional residual capacity and total lung capacity) cannot be measured directly by spirometry. They are measured by either whole-body plethysmography, or by using the helium dilution or nitrogen washout techniques.

106C: Is increased in emphysema

Compliance is expressed as volume change per unit change in pressure. Elastance is the reciprocal of compliance. The pressure–volume curve of the lung is nonlinear with the lungs becoming stiffer at high volumes. The curves which the lung follows in inflation and deflation are different; this behaviour is known as 'hysteresis'. The lung volume at any given pressure during deflation is larger than during inflation. This behaviour depends on structural proteins (collagen, elastin), surface tension and the properties of surfactant.

Surfactant is formed in, and secreted by, type II pneumocytes. The active ingredient is dipalmitoyl phosphatidylcholine. It helps prevent alveolar collapse by lowering the surface tension between water molecules in the surface layer. In this way it helps to reduce the work of breathing (makes the lungs more compliant) and permits the lung to be more easily inflated.

Various disease states are associated with either a decrease or an increase in the lung compliance. Fibrosis, atelectasis and pulmonary oedema all result in a decrease in lung compliance (stiffer lungs). An increased lung compliance occurs in emphysema where an alteration is elastic tissue is probably responsible (secondary to the long-term effects of smoking). The lung effectively behaves like a 'soggy bag' so that a given pressure change results in a large change in volume (i.e. the lungs are more compliant). However, during expiration the airways are less readily supported and collapse at higher lung volumes, resulting in gas trapping and hyperinflation.

107C: Thyroid-stimulating hormone

The pituitary gland (hypophysis) is the conductor of the endocrine orchestra. It is divided into an anterior part and a posterior part. The *anterior pituitary* (adenohypophysis or pars distalis) secretes six hormones, namely:

- FSH/LH: reproduction
- ACTH: stress response
- TSH: basal metabolic rate
- GH: growth
- prolactin: lactation.

The *posterior pituitary* (neurohypophysis or pars nervosa) secretes only two hormones:

- ADH (vasopressin): osmotic regulation
- oxytocin: milk ejection and labour

Testosterone is produced from Leydig cells in the testis and from the adrenal glands. CRH is produced by the median eminence of the hypothalamus.

108E: Fetal haemoglobin

The haemoglobin oxygen dissociation curve is sigmoidal in shape, which reflects the underlying biochemical properties of haemoglobin. The significance of the sigmoidal curve is that haemoglobin becomes highly saturated at high oxygen partial pressures (and is therefore highly efficient at collecting oxygen), and releases a significant amount of oxygen at pressures that are fairly low, but not extremely so (with the result that haemoglobin is highly effective at supplying oxygen where it is needed).

The effect of things that shift the curve to the right (raised CO_2, lowered pH, increased temperature, increase in 2,3-DPG) is to increase oxygen availability in the tissues. The effect of CO_2/H^+ on O_2 carriage is known as the Bohr shift or effect. This is exactly what is needed in metabolizing tissues; release of acids or CO_2 thus liberates O_2 to fulfil the metabolic needs of the tissue. Do not confuse this with the effect of changes in O_2 on CO_2 carriage, which is called the Haldane effect.

A shift of the oxygen dissociation curve to the left is characteristic of fetal haemoglobin. When compared with adult haemoglobin, it is composed of two alpha and two gamma chains, instead of the usual two alpha and two beta chains of adult haemoglobin. This arrangement assists in the transfer of oxygen across the placenta from the maternal to the fetal circulation. The corollary of this is that fetal tissue oxygen levels have to be low to permit the release of oxygen from the haemoglobin.

109B: CD8 T-cells

Lymphocytes can be divided into two main subtypes – T-cells and B-cells. B-cells (or plasma cells) secrete antibodies. T-cells can be divided into two further subtypes – CD4 T-cells and CD8 T-cells. CD4 (helper) T-cells can recognize antigen only in the context of MHC Class II, whereas CD8 (cytotoxic) T-cells recognize cell-bound antigens only in association with Class I MHC. This is known as MHC restriction.

CD4 and CD8 T-cells perform distinct but somewhat overlapping functions. The CD4 helper T-cell can be viewed as a master regulator. By secreting cytokines (soluble factors that mediate communication between cells), CD4 helper T-cells influence the function of virtually all other cells of the immune system including other T-cells, B-cells, macrophages and natural killer cells. The central role of CD4 cells is tragically illustrated by the HIV virus which cripples the immune system by selective destruction of this T-cell subset. In recent years two functionally different populations of CD4 helper T-cells have been recognized – TH1 cells and TH2 cells, each characterized by the cytokines that they produce. In general, TH1 cells facilitate cell-mediated immunity, whereas TH2 cells promote humoral-mediated immunity.

CD8 cytotoxic T-cells mediate their functions primarily by acting as cytotoxic cells (i.e. they are T-cells that kill other cells). They are important in the host defence against cytosolic pathogens. Two principal mechanisms of cytotoxicity have been discovered – perforin–granzyme-dependent killing and Fas–Fas ligand dependent killing.

110A: Hypokalaemia, metabolic alkalosis, low urinary pH

Following a diagnosis of pyloric stenosis, the first concern is to correct the metabolic abnormalities that invariably coexist with the condition. The serum electrolytes and capillary gases should be measured and corrected prior to surgery.

With prolonged vomiting, the infant becomes dehydrated, with a hypochloraemic metabolic alkalosis. The alkalosis is a result of loss of unbuffered hydrogen ions in gastric juice with concomitant retention of bicarbonate.

Fluid loss stimulates renal sodium reabsorption, but sodium can be reabsorbed only either with chloride, or in exchange for hydrogen and potassium ions (to maintain electroneutrality). Gastric juice has a high concentration of chloride and patients losing gastric secretions become hypochloraemic. This means that less sodium than normal can be reabsorbed with chloride.

However, it appears that the defence of extracellular fluid volume takes precedence over acid–base homeostasis and further sodium reabsorption occurs in exchange for hydrogen ions (perpetuating the alkalosis) and potassium ions (leading to potassium depletion). This explains the apparently paradoxical finding of acidic urine in patients with pyloric stenosis. Potassium is also lost in the gastric juice and thus patients frequently become potassium-depleted and yet are losing potassium in their urine.

111C: Has a protein content that is 0.5 per cent that of plasma

Most of the CSF is produced by the choroid plexus, which is situated in the lateral, third and fourth ventricles. CSF is absorbed directly into the cerebral venous sinuses through the arachnoid villi, or granulations, by a process known as mass or bulk flow.

The composition of CSF is different from plasma. The concentrations of K^+, Ca^{2+}, bicarbonate and protein are lower in CSF than in plasma. This is to prevent high concentrations of these electrolytes inadvertently exciting neurones present within the brain substance. The potassium content of the CSF in this respect is particularly important. Further buffering of the K^+ content of CSF takes place through astrocytes.

Likewise, the low protein content of the CSF (the CSF protein content is 0.5 per cent that of plasma) is deliberate to prevent some proteins and amino acids acting as 'false neurotransmitters'. The CSF is more acidic than plasma because pH of the CSF plays a critical role in the regulation of pulmonary ventilation and cerebral blood flow. Another reason why the CSF protein is kept deliberately low is to prevent proteins buffering pH. The result is that the pH of the CSF accurately reflects carbon dioxide levels of the blood. In this way changes in pH act as a powerful regulator of the respiratory system (through the action of pH on central chemoreceptors) and on cerebral blood flow.

112D: Inulin clearance can be used to estimate GFR

In the normal adult human the GFR (or normal renal clearance) averages 125 mL/min, or 180 L/day. The entire plasma volume (about 3 L) can therefore be filtered and processed by the kidney approximately 60 times each day. The rate of urine production in humans is dominated by tubular function and not by GFR. The GFR remains relatively constant through autoregulation.

After 35 years of age, GFR falls at about 1 mL/min/year. By the age of 80, GFR has fallen to about 50 per cent of its youthful level. GFR can decrease by as much as 50 per cent before plasma creatinine rises beyond the normal range. Consequently, a normal creatinine does not necessarily imply normal renal function, although a raised creatinine does usually indicate impaired renal function.

A substance used to measure the GFR must be freely filtered at the glomerulus, not be secreted by the tubules, not be reabsorbed, not be metabolized or synthesized in the body, not alter the renal function/GFR, be non-toxic and soluble in plasma. Such a substance is the polyfructose molecule, inulin. However, it is too cumbersome to use in routine clinical practice. Instead, GFR is more commonly quantified by measuring the 24-hour urinary creatinine excretion. Para-aminohippuric acid is used to measure renal blood flow and not GFR.

113B: Gastrin

Gastric acid is *stimulated* by three factors:

- acetylcholine, from parasympathetic neurones of the vagus nerve that innervate parietal cells directly
- gastrin, produced by pyloric G-cells
- histamine, produced by mast cells. This stimulates the parietal cells directly and also potentiates parietal cell stimulation by gastrin and neuronal stimulation. H_2 blockers such as ranitidine are therefore an effective way of reducing acid secretion.

Gastric acid is *inhibited* by three factors:

- somatostatin
- secretin
- cholecystokinin.

There are *three classic phases of gastric acid secretion*:

- *Cephalic* (preparatory) phase [significant]: results in the production of gastric acid before food actually enters the stomach – triggered by the sight, smell, thought and taste of food acting via the vagus nerve
- *Gastric* phase [most significant]: initiated by the presence of food in the stomach, particularly protein-rich food
- *Intestinal* phase [least significant]: the presence of amino acids and food in the duodenum stimulate acid production.

114C: Bicarbonate

Carbon dioxide is transported in the blood in various forms:

- Bicarbonate accounts for about 80–90 per cent of the total CO_2 in the blood
- Carbamino compounds account for 5–10 per cent
- Only 5 per cent is physically dissolved in solution.

Carbon dioxide is carried on the haemoglobin molecule as carbamino-haemoglobin; carboxyhaemoglobin is the combination of haemoglobin with carbon monoxide.

Erythrocytes contain the enzyme carbonic anhydrase that catalyses the reaction $CO_2 + H_2O = H^+ + HCO_3^-$ and requires zinc as a cofactor. This plays an important role in carbon dioxide transport and in the buffering of pH.

115C: Calcium influx

The most important source of activator calcium in cardiac muscle remains its release from the sarcoplasmic reticulum. Calcium, however, also enters from the extracellular space during the plateau phase of the action potential. This calcium entry provides the stimulus that induces calcium release from the sarcoplasmic reticulum (calcium-induced calcium release).

The result is that tension generated in cardiac, but not in skeletal, muscle is profoundly influenced both by extracellular calcium levels and by factors that affect the magnitude of the inward calcium current. This is of practical value in two key clinical situations; in heart failure where digoxin is utilized to increase cardiac contractility (by increasing the intracellular calcium concentration) and in hyperkalaemia where calcium gluconate is used to stabilize the myocardium.

The plateau phase of the action potential in cardiac muscle (principally due to calcium influx) maintains the membrane at a depolarized potential for as long as 500 ms. The result is that the cell membrane is refractory throughout most of the mechanical response, largely due to the inactivation of fast sodium channels. This prevents tetany upon repetitive stimulation which would be detrimental to cardiac output. Furthermore, the prolonged refractory period in cardiac muscle allows the impulse that originates in the sinoatrial node to propagate throughout the entire myocardium just once, thereby preventing re-entry arrhythmias.

116B: The ratio of stroke volume to end-diastolic volume

During diastole, filling of the ventricles normally increases the volume of each ventricle to about 120 mL. This volume is known as the end-diastolic volume. Then, as the ventricles empty in systole, the volume decreases about 70 mL, which is known as the stroke volume. The remaining volume in each ventricle, about 50 mL, is known as the end-systolic volume and acts as a reserve which can be utilized to increase stroke volume in exercise.

The fraction of end-diastolic volume that is ejected is called the 'ejection fraction' – usually equal to about 60 per cent. The ejection fraction is often used clinically as an indirect index of contractility. It is a particularly useful in assessing the state of the myocardium prior to aortic aneurysm repair where cross-clamping of the aorta places particular stress on the myocardium.

117C: In the ileum

Between 90 and 95 per cent of the bile salts are absorbed from the small intestine and then excreted again from the liver; most are absorbed from the terminal ileum. This is known as the

enterohepatic circulation. The entire pool recycles twice per meal and approximately 6 to 8 times per day.

Disruption of the enterohepatic circulation, either by terminal ileal resection or through a diseased terminal ileum (e.g. Crohn's disease), results in decreased fat absorption and cholesterol gallstone formation. The latter is believed to result because bile salts normally make cholesterol more water-soluble through the formation of cholesterol micelles. Loss of reuptake also results in the presence of bile salts in colonic contents, which alters colonic bacterial growth and stool consistency.

118D: ↑BP, ↓HR, ↓CPP

The important relationship between cerebral perfusion pressure (CPP), mean arterial blood pressure (MABP) and intracranial pressure (ICP) is as follows: CPP = MABP – ICP. It stems from the fact that the adult brain is enclosed in a rigid, incompressible box, with the result that the volume inside it must remain constant (Monro–Kelly doctrine). A rise in intracranial pressure therefore decreases cerebral perfusion pressure (and hence cerebral blood flow).

In raised intracranial pressure, as the brainstem becomes compressed, local neuronal activity causes a rise in sympathetic vasomotor drive and thus a rise in blood pressure. This is known as the Cushing's reflex. This elevated blood pressure evokes a bradycardia via the baroreceptor reflex. The Cushing's reflex helps to maintain cerebral blood flow and protect the vital centres of the brain from loss of nutrition if the intracranial pressure rises high enough to compress the cerebral arteries.

119B: Zona glomerulosa of the adrenal cortex

The adrenal gland comprises an outer cortex and an inner medulla, which represent two developmentally and functionally independent endocrine glands within the same anatomical structure. The adrenal medulla secretes adrenaline (70 per cent) and noradrenaline (30 per cent). The adrenal cortex consists of three layers, or zones. The layers from the surface inwards may be remembered by the mnemonic GFR:

G = zona glomerulosa (secretes aldosterone)
F = zona fasciculata (secretes cortisol and sex steroids)
R = zona reticularis (secretes cortisol and sex steroids).

Aldosterone is a steroid hormone that facilitates the reabsorption of sodium and water and the excretion of potassium and hydrogen ions from the distal convoluted tubule and collecting ducts. Conn's syndrome is characterized by increased aldosterone secretion from the adrenal glands.

120A: Salivary

In humans, about 1–1.5 litres of saliva are secreted each day. Secretion is an active process. The two-stage hypothesis of salivation states that a primary secretion is first formed by secretory end-pieces (that resembles an ultrafiltrate of plasma), which is then modified as it flows along the duct system. Na^+ and Cl^- are absorbed and K^+ and HCO^{3-} are secreted as saliva flows along the ductal system. In addition, the ducts have a low water permeability.

The final saliva is hypotonic with respect to plasma and contains a higher potassium concentration than any other gastrointestinal secretion of the body. Any abnormal state in which saliva is lost to the exterior of the body for long periods can lead to a serious depletion of potassium, leading in occasional circumstances to serious hypokalaemia and paralysis.

121D: Omeprazole

Three main classes of drugs are used to combat gastric hyperacidity. From least to most potent they are:

- antacids
- H_2-receptor antagonists
- proton pump inhibitors (PPIs).

Only the H_2-receptor antagonists and PPIs reduce the secretion of acid from parietal cells. Of these, the PPIs (e.g. omeprazole, lansoprazole) are the most potent and have the longest duration of action. The reasons for this are two-fold. First, PPIs target the terminal stage in gastric acid secretion, namely the proton pump which is directly responsible for secreting H^+ ions into the gastric lumen. Second, the irreversible nature of the proton pump inhibition means that acid secretion only resumes after the synthesis of new enzyme. PPIs are extremely effective in promoting ulcer healing, even in patients who are resistant to H_2 antagonists.

H_2-receptor antagonists, however, should not be regarded as obsolete since they have a faster onset of action compared with PPIs. They are, however, less potent in inhibiting gastric acid secretion and have a relatively short duration of action compared with PPIs. H_2 antagonists (e.g. cimetidine, ranitidine) competitively inhibit histamine actions at all H_2 receptors. Acid secretion is not mediated via H_1 receptors, so chlorphenamine has no effect on acid secretion.

Antacids have no effect on the secretion of gastric acid from parietal cells but exert their effect by neutralizing the acid that is produced. Their efficacy is limited because the rise in pH stimulates gastrin secretion, which in turn stimulates more acid release (the 'acid rebound effect'). This effect does not occur with H_2-receptor antagonists and PPIs which act directly on parietal cells. Alginates (e.g. Gaviscon) are sometimes used and are believed to increase adherence of mucus to the mucosa, thereby increasing mucosal resistance to acid-pepsin attack.

Misoprostol is a synthetic prostaglandin analogue that promotes ulcer healing by stimulating protective mechanisms in the gastric mucosa (increased mucus, bicarbonate and blood flow) and by reducing acid secretion. It is sometimes co-administered with NSAIDs in the elderly to prevent peptic ulcer disease. However, misoprostol is not as efficacious as a PPI and use is limited by its tendency to cause troublesome diarrhoea.

122E: The vitellointestinal duct may persist as a Meckel's diverticulum

There are many important changes that take place at birth:

- The urachus (allantois) becomes the single, median umbilical ligament
- The umbilical arteries become the right and left, medial umbilical ligaments, respectively
- The ductus venosus becomes the ligamentum venosum
- The left umbilical vein becomes the ligamentum teres (round ligament) in the free edge of the falciform ligament
- The ductus arteriosus becomes the ligamentum arteriosum
- In 2 per cent of cases the vitellointestinal duct may persist as a Meckel's diverticulum
- The foramen ovale in most cases obliterates at birth to become the fossa ovalis, but remains patent into adulthood in some 20 per cent of cases.

Aberrations of this normal developmental process may lead to problems in adulthood. Failure of the urachus (which normally runs from the bladder to the umbilicus) to obliterate correctly may lead to a urachal fistula, sinus, diverticulum or cyst, often with leakage of urine from the umbilicus. Failure of the ductus arteriosus to obliterate at birth leads to a patent ductus arteriosus, resulting in non-cyanotic congenital heart disease. In 2 per cent of cases, the vitello-intestinal duct persists as a Meckel's diverticulum with its associated complications. In 20 per cent of cases the foramen ovale fails to obliterate completely at birth resulting in a patent foramen ovale. This may become the site for paradoxical embolism (where venous thrombus migrates and enters the systemic circulation through a patent foramen ovale), resulting in stroke.

123C: Upon exposure to light, cGMP levels within the photoreceptor fall

Phototransduction is the process by which light energy in the form of photons is converted to a change in membrane potential of the photoreceptor cell (rod or cone):

Incident light photons
→ Conformational change of rhodopsin

→ Activation of G-protein, transducin
→ Activation of cGMP phosphodiesterase
→ Decreased intracellular cGMP
→ Closure of Na^+ channels
→ Hyperpolarization
→ Decreased release of neurotransmitter
→ Response in bipolar cells and other retinal neurones.

The outer segment of the rod contains internal membranous discs which contain the light-sensitive protein, rhodopsin. Rhodopsin consists of opsin (seven transmembrane protein, or serpentine receptor) bound to retinal (the light-absorbing portion), a derivative of vitamin A. Deficiencies of vitamin A can therefore lead to night blindness and if untreated to deterioration of receptor outer segments and eventually total blindness. Slight differences among the opsins of each of the three types of cone results in differences in the wavelengths absorbed preferentially by each photopigment.

In the dark, non-selective cation channels in the outer segment are bound to cGMP and open, causing a predominant Na^+ influx. This is known as the 'dark current'. The level of cGMP in the outer segment depends on its rate of synthesis (by guanylate cyclase) and degradation (by phosphodiesterase). Absorption of a photon of light leads to isomerization of retinal (from the 11-*cis* to the all-*trans* configuration), structural activation of rhodopsin and activation of the G-protein, transducin. Activated transducin produces a fall in cGMP, closure of cGMP-gated cation channels and hyperpolarization. The hyperpolarization reduces the release of synaptic transmitter (glutamate) and this generates a signal that ultimately leads to action potentials in ganglion cells (the output cells of the retina). The action potentials are transmitted to the brain. In a sense, therefore, our photoreceptors are really 'dark receptors', depolarizing and releasing more transmitter as the level of illumination decreases. Presumably because we spend less than half our time in darkness, this arrangement is not as metabolically inefficient as it sounds at first.

This seemingly cumbersome process occurs very rapidly and results in great amplification. Photoactivation of a single rhodopsin molecule can lead to the hydrolysis of more than 10^5 molecules of cGMP per second. The amplification helps to explain the remarkable sensitivity of photoreceptors; rods are capable of producing a detectable response to as little as one photon of light. Several forms of retinitis pigmentosa, an inherited disorder of photoreceptors leading to blindness, are due to mutations within genes encoding members of the photoreceptor visual transduction cascade.

124E: Self/non-self discrimination

Innate (natural) immunity comprises:

- physical barriers (skin, mucosal membranes)
- physiological factors (pH, temperature, oxygen tension; e.g. low pH of stomach inhibits microbial growth, commensal flora)
- protein secretions (e.g. lysozyme in saliva and tears, complement, cytokines, acute phase proteins)
- phagocytic cells (neutrophils, macrophages, natural killer cells)
- acute inflammation (including mast cells, histamine etc.).

The two key features of adaptive (acquired) immunity are its specificity and memory.

The adaptive (acquired) arm of the immune response operates through both humoral and cell-mediated mechanisms and has a number of key features. Immunological tolerance is the exposure to self components in fetal life that leads to a state of specific immunological unresponsiveness (anergy). In adulthood the adaptive immune system is therefore able to discriminate self from non-self which is essential in preventing one's own immune system mounting a response against tissues. It may become defective resulting in autoimmune disease.

Immunological memory is a feature of the adaptive immune response and is essential for the rapid response to subsequent exposure of antigens. This concept is central to understanding how vaccines work.

125E: Thyroglobulin is stored in the colloid of follicles

The thyroid gland produces three hormones: tetra-iodothyronine (T4), which is the principal hormone; tri-iodothyronine (T3), which has shorter duration but is more potent than T4; and calcitonin, which is produced by parafollicular C-cells and is involved in calcium balance. The steps in the production of T4 and T3 can be summarized as follows:

- An active pump concentrates iodine into the thyroid follicular cells
- Iodine is oxidized into its active form (by peroxidase)
- Iodine binds with tyrosine, to form tyrosyl units (organification)
- Tyrosyl units bind to a protein core, to form thyroglobulin
- Tyrosyl units combine while bound to the protein core, to form either T3 or T4
- Thyroglobulin molecules are stored as colloid in follicles
- TRH (from the hypothalamus) stimulates the anterior pituitary gland to produce TSH
- TSH (thyroid stimulating hormone) stimulates the release of T3 and T4 into the blood.

126D: Suxamethonium

Neuromuscular blockers are commonly used drugs in anaesthetics. By specific blockade of the neuromuscular junction (NMJ) they relax skeletal muscles and induce paralysis. This enables light levels of anaesthesia to be employed with adequate relaxation of the muscles of the abdomen and diaphragm, thereby facilitating surgery. They also relax the vocal cords and allow the easy passage of a tracheal tube at anaesthetic induction, a procedure known as endotracheal intubation. They can be used *only* when mechanical ventilation is available because such drugs also paralyse the main muscles of respiration. Neuromuscular blockers can be divided into two main types: depolarizing and non-depolarizing.

Non-depolarising blockers (e.g. atracurium), also known as competitive muscle relaxants, compete with acetylcholine for receptor sites at the NMJ and their action can be reversed with anticholinesterases, such as neostigmine. Atropine is a muscarinic antagonist and is often given with neostigmine in order to prevent the muscarinic (parasympathomimetic) side effects of anticholinesterases (such as bradycardia, excessive salivation etc.).

Depolarizing blockers (e.g. suxamethonium, also known as succinylcholine) act by mimicking the action of acetylcholine at the NMJ but hydrolysis is much slower than for acetylcholine because it is resistant to degradation by cholinesterase. Depolarization is therefore prolonged, resulting in sodium-channel inactivation and neuromuscular blockade. Unlike non-depolarizing agents, its action cannot be reversed and recovery is spontaneous. Indeed, anticholinesterases such as neostigmine potentiate the neuromuscular block. Anticholinesterases are also used in myasthenia gravis to enhance neuromuscular transmission by prolonging the action of acetylcholine.

Suxamethonium has a half-life of only a few minutes and is rapidly hydrolysed by pseudocholinesterase. In patients with deficient or atypical pseudocholinesterase enzyme (an autosomal recessive condition), the metabolism is reduced and the half-life and duration of action of suxamethonium are prolonged, resulting in 'scoline apnoea', or prolonged paralysis. Assisted ventilation should be continued until muscle function is restored. In addition, suxamethonium may be responsible for triggering malignant hyperthermia in susceptible individuals – an autosomal dominant disorder that results in intense muscular spasm and hyperpyrexia and is associated with a high mortality.

Guanethidine inhibits the release of noradrenaline from postganglionic sympathetic nerve terminals. It has largely fallen out of use but is extremely effective in lowering blood pressure and may be useful in cases of resistant hypertension.

127E: The testes and ovaries descend from their original position at the 10th thoracic level

Genital development is principally determined by the presence or absence of a Y chromosome. Thus XO individuals (Turner's syndrome) are female and XXY individuals (Klinefelter's syndrome) are male. Presence of the sex-determining region of the Y chromosome (SRY) results in male development, absence of SRY leads to female development.

If the embryo is male, the SRY gene is transcribed and this initiates a cascade of events. The sex cord form the seminiferous tubules, some of the support cells become Sertoli cells and produce a hormone known as anti-Mullerian hormone (AMH), while other support cells become Leydig cells and secrete testosterone. This has the consequence that the paramesonephric (Mullerian) ducts regress due to AMH and the external genitalia become male (conversion of testosterone to dihydrotestosterone in the genital fold results in the formation of the penis and scrotum). The mesonephric (Wolffian) ducts grow to form the vas deferens and associated ducts. In females, where there is no SRY gene, the support cells do not form Sertoli cells. This has the consequence that no AMH is produced and no testosterone-secreting cells develop. The paramesonephric (Mullerian) ducts remain and form the uterus and fallopian tubes, the mesonephric (Wolffian) ducts regress and female external genitalia develop (labia majora and minora, clitoris). Aberrations of this process may lead to ambiguous genitalia and problems with gender assignment.

During embryonic and fetal life, the testes and the ovaries both descend from their original position at the 10th thoracic level. This explains the long course taken by the gonadal arteries and the site of referred pain from the gonads to the umbilicus (T10 dermatome). Descent is genetically, hormonally and anatomically regulated and depends on a ligamentous cord known as the gubernaculum. Furthermore, descent of the testis through the inguinal canal into the scrotum depends on an evagination of peritoneum known as the processus vaginalis. This normally obliterates at birth. Gonadal descent is a complicated process and therefore there are many ways in which it can go wrong. Most commonly, an undescended or maldescended testis may occur (cryptorchidism). A patent processus vaginalis may lead to the formation of a congenital hydrocele, or inguinal hernia.

128D: The macula region is grossly over-represented in the visual cortex

The visual pathway may be summarized as follows:

- Photoreceptors (rods, cones) within the retina convert light energy into electrical impulses (phototransduction)
- This is transmitted to ganglion cells, directly via bipolar cells, or indirectly via horizontal and amacrine cells
- Ganglion cells are the output cells of the retina. Axons from ganglion cells converge at the optic disc (blind spot) and travel in the optic nerve
- Incomplete decussation occurs at the optic chiasm; those from the nasal half of each retina (corresponding to the temporal halves of the visual field) cross over (decussate), while those from the temporal halves of each retina stay on the same side
- The optic tracts synapse in the various layers of the lateral geniculate nucleus of the thalamus before being relayed to the primary visual cortex in the occipital lobe via the optic radiation.

The macula is a region of the retina that subserves highest visual acuity. It is grossly over-represented in the visual cortex in a phenomenon known as 'cortical magnification'. This may partly explain why lesions located within the visual cortex may result in macula sparing.

The effects of lesions to the visual pathway may be easily predicted utilizing the above information:

- Lesions anterior to the optic chiasm (i.e. a transected optic nerve) result in a unilaterally blind eye

- Lesions of the optic chiasm (commonly from a pituitary tumour) result in a bitemporal hemianopia
- Lesions posterior to the optic chiasm (commonly due to ischaemic events) result in a homonymous hemianopia, with or without macula sparing.

129C: They have a life-span of only a few hours in inflamed tissue

Neutrophils are the most common type of leukocyte in the blood. They are present in large numbers in acute inflammation, but in chronic inflammation macrophages predominate. They have multilobed rather than bilobed nuclei, with 4–5 lobes but rising to 6–7 lobes in patients with vitamin B_{12} or folate deficiency. The ability to form multinucleate giant cells is a characteristic of macrophages rather than neutrophils and is classically seen in granulomatous conditions such as tuberculosis.

The phagocytic ability of neutrophils plays a vital role in the host defence against infection. Microbial killing results from both oxygen-dependent and oxygen-independent mechanisms. The former is more important and depends on the 'respiratory burst'. The respiratory burst follows activation of cell membrane NADPH oxidase by phagocytosis and results in the formation of powerful bacteriocidal agents (H_2O_2, superoxide anion and singlet oxygen). Oxygen-independent microbial killing is carried out by lysosomal enzymes, such as lysozyme. The importance of oxygen-dependent bacterial mechanisms is illustrated by the congenital disorder, chronic granulomatous disease. It results from inherited defects in the genes encoding several components of NADPH oxidase, rendering the patient susceptible to recurrent bacterial infections.

Neutrophils have a life-span of only a few hours in an inflammatory lesion, sometimes less. A severe local infection quickly becomes a graveyard of thousands of neutrophils. Their content, especially enzymes, spill out and may cause additional damage to host tissues. This is known as immune pathology and is the price to be paid for having a sophisticated immune system.

130A: It binds and stores oxygen for rapid release during falling Po_2

Myoglobin is a single-chain globular protein containing a haem group (iron-containing porphyrin) with eight alpha helices and a hydrophobic core. Being monomeric, it has instant binding with oxygen rather than the cooperative binding seen in haemoglobin. It has a hyperbolic dissociation curve. Its function is to store oxygen in muscle tissues for rapid release during times of need, as in exercise.

131E: Calcium-channel agonists

The following classes of antihypertensive drugs are currently in use (remembered by AAABCD):

- ACE inhibitors
- angiotensin II receptor antagonists
- alpha-blockers
- beta-blockers
- calcium-channel blockers (antagonists)
- diuretics.

Lowering raised blood pressure has successfully been shown (in both primary and secondary preventative settings) to reduce the risk of stroke, coronary events, heart failure and renal failure.

The choice of antihypertensive drug will depend on the relevant indications or contraindications for the individual patient. A single agent may not be enough, so additional blood-pressure–lowering drugs may have to be added until the blood pressure is well-controlled.

Alpha-blockers have largely been superseded by the other classes of antihypertensive agents. However, they still play an important role in the management of phaeochromocytoma (an adrenaline-secreting tumour of the adrenal medulla). In such instances α-receptors must be blocked prior to β-receptor blockade in order to prevent a dangerous hypertensive crisis developing.

Angiotensin II receptor antagonists are generally used as second-line agents when patients are unable to tolerate an ACE inhibitor. From 15 to 30 per cent of patients taking ACE inhibitors develop an intractable cough which is believed to result from the accumulation of bradykinin (angiotensin converting enzyme normally assists in the degradation of bradykinin and its derivatives). In such cases the patient may benefit from conversion to an angiotensin II receptor antagonist.

132B: Shaping of the hands and feet is brought about through apoptosis

The limb is the organ whose development is probably best understood and to understand abnormalities it is necessary to understand how the limb develops. Limb development takes places over a 4-week period, and by the end of the eighth week all the components of the upper and lower limbs are distinct. During this critical period, limb development is susceptible to the harmful effects of environmental teratogens, resulting in limb anomalies.

The limbs develop from small protrusions (the limb buds) that arise from the body wall of the embryo. Positioning and patterning the limb involves cellular interactions between the ectoderm surrounding the limb bud (apical ectodermal ridge) and the mesenchymal cells that form the core of the limb bud.

As the limb grows out the cells acquire a positional value that relates to their position in the bud with respect to all three axes, proximodistal, anteroposterior and dorsoventral. These positional values largely determine how the cells will develop. The positional value of the cells is acquired in the progress zone at the tip of the growing bud. Thalidomide, a drug commonly used in the late 1950s and early 1960s for morning sickness, was later found to interfere with the normal processes of limb development resulting in major limb defects such as phocomelia (short, ill-formed limbs resembling the flippers of a seal) and amelia (absent limbs).

Separation of the digits occurs by apoptosis (or programmed cell death). This is a good example of a situation in which apoptosis is physiological, rather than pathological.

Adult human limbs never regenerate following amputation, under any circumstances. Adult human limb loss is permanent and irreversible. Some amphibians, however, are unique among vertebrates in being able to regenerate entire limbs. This relates to their ability to revert to an embryonic state (dedifferentiate) in order to recapitulate embryogenesis. Elucidation of the mechanisms involved in amphibians and their possible relationship to limb development in higher organisms may one day enable us to regenerate a lost limb following an amputation.

133B: The primary visual cortex is located within Brodmann area 17

The human cerebral cortex is divided into about 50 distinct areas known as Brodmann areas, based on histological structural differences. The numbered areas have come to refer to the different functional areas of the human cortex.

In general, sensory signals from all modalities of sensation terminate in the cerebral cortex posterior to the central sulcus (with the primary somatosensory cortex area lying in the postcentral gyrus). On the other hand, the portion of the cortex anterior to the central sulcus is devoted almost entirely to motor control (with the primary motor cortical area lying in the precentral gyrus). A good way to remember this is 'Marks & Spencer' or 'M&S', with motor in front and sensory behind the central sulcus.

Visual signals terminate in the occipital lobe (Brodmann area 17 corresponds to the primary visual cortex) and auditory signals terminate in the temporal lobe (Heschl's gyrus).

There are two primary language centres within the brain: Broca's and Wernicke's areas. Broca's area is situated in the frontoparietal area and is concerned with the expression of speech. Wernicke's area lies in the temporoparietal area and deals primarily with the comprehension of speech. In the majority of people, the left cerebral hemisphere is dominant so that a stroke affecting the left cerebral cortex (resulting in a right-sided hemiparesis) interferes with the language centres, producing a corresponding dysphasia.

134C: Generates immunoglobulin-producing plasma cells

The germinal centres of lymph nodes contain mainly B-lymphocytes and follicular dendritic cells. Follicular dendritic cells are able to trap antigen on their cell surface for long periods. They help to initiate a B-cell response to antigens entering the lymph node and play an important role in affinity maturation (a process which results in an increase in the affinity of the antibodies produced during the course of a humoral immune response). Follicular dendritic cells should not be confused with Langerhans' dendritic cells which are professional antigen presenting cells found in the skin.

The cords and sinuses of a lymph node are situated in the medulla. The medullary cords are rich in plasma cells, whereas the sinuses are rich in macrophages. The paracortical zone (or interfollicular area) is rich in T-lymphocytes.

There is characteristically an expansion of the paracortex, rather then the germinal centres, in infectious mononucleosis (and many other viral infections), so-called reactive hyperplasia. This manifests clinically as lymphadenopathy.

135D: Mitochondria

Mitochondria are found in all eukaryotic cells. They contain their own DNA and are thought to be symbiotic prokaryotes that have been assimilated into eukaryotic cells in our biological past (endosymbiotic theory). They replicate by mitosis to form a clonal population. All the mitochondrial DNA in humans is derived from the clonal population of the ovum and therefore are maternally inherited.

136B: Gliclazide

Sulphonylureas (gliclazide and glibenclamide) are indicated when diet fails to control hyperglycaemia. Sulphonylureas stimulate insulin release from the pancreas, and are therefore of use only in patients who still have residual pancreatic islet cell function. Side effects include weight gain and hypoglycaemia.

Metformin increases the sensitivity to insulin at the receptor level, but should be avoided in patients with impaired renal function. Side effects include lactic acidosis, nausea, vomiting and diarrhoea.

Rosiglitazone is an example of a thiazolidinedione. This class of drugs act by increasing the sensitivity of insulin by binding to a nuclear receptor called PPAR-γ. It is not a first-line treatment and should be used in combination with metformin or a sulphonylurea. Rosiglitazone is currently contraindicated in heart failure as it is thought to worsen this condition.

Acarbose acts by delaying the digestion and absorption of starch and sucrose, through the inhibition of intestinal alpha-glucosidases. Its main side-effect is flatulence.

137B: The transcription factor WT-1 is necessary for the competence of the mesenchyme to be induced

The kidney develops from the intermediate column of mesoderm. There are three phases of kidney development, the definitive kidney developing in the last phase:

- stage 1: pronephros – primitive tubules
- stage 2: mesonephros – functional in the embryo, producing a dilute urine important in maintaining the composition of the amniotic fluid. They also contribute to the male genital system.
- stage 3: metanephros – true, hind kidneys.

The definitive metanephroi are induced early in the fifth week by the ureteric buds that sprout from the mesonephric ducts. The ureteric bud induces the mesenchymal cells to condense around it, forming the metanephric blastema. The development of the ureteric bud and the metanephric blastema depends on reciprocal induction, neither being able to develop in the absence of the other. The metanephric blastema causes the ureteric bud to grow and bifurcate and the ureteric bud induces the mesenchyme to differentiate into nephrons. If the ureteric bud does not reach/

signal properly to the surrounding mesenchyme, or vice versa, a kidney will not form (renal agenesis). If the ureteric bud bifurcates prematurely, a bifid ureter may result. Alternatively, if two ureteric buds develop an ectopic ureter may result.

The ureteric bud branches and gives rise to the collecting ducts and ureters; the metanephric blastema gives rise to the tubules, or nephrons.

The transcription factor and tumour suppressor gene, WT-1, is expressed in metanephric blastema, making it competent to receive signals from the ureteric bud that are essential for its induction. Mutations in the gene are associated with a cancer of the kidney in children known as Wilm's tumour.

The kidneys ascend from their original sacral location to a lumbar site. The mechanism responsible is not understood, but the differential growth of the lumbar and sacral regions of the embryo may play a role. Several anomalies can arise from variations in this process of ascent. A kidney may fail to ascend, remaining as a pelvic kidney. The inferior poles of the two metanephroi may fuse during ascent, forming a U-shaped horseshoe kidney. During ascent this kidney comes caught under the inferior mesenteric artery and therefore does not reach its normal site.

138E: It turns over approximately 4–5 times daily

Cerebrospinal fluid (CSF), situated within the ventricles and the subarachnoid space, bathes the surface of the brain and spinal cord, supplies nutrients to it, protects it and reduces its effective buoyancy. It also plays an important homeostatic role and is crucial for maintaining a constant external environment for neurones and glia. In humans the volume is about 150 mL and its rate of production is 0.5 mL/min (or approximately 30 mL/hour or 600 mL/day). Thus, the CSF turns over about four times daily.

Most of the CSF is produced by the choroid plexus, which is situated in the lateral, third and fourth ventricles. It flows between the lateral ventricles and third ventricle via the interventricular foramen (of Monro). The third and fourth ventricles communicate via the cerebral aqueduct (or Aqueduct of Sylvius). The fourth ventricle communicates with the spinal cord by way of the single median Foramen of Magendie and the two laterally placed Foramina of Luschka. CSF is absorbed directly into the cerebral venous sinuses through the arachnoid villi, or granulations, by a process known as 'mass or bulk flow'.

Occasionally the above physiology is disrupted and it becomes the centre of a pathological process. Hydrocephalus is an increase in the volume of CSF within the cerebral ventricles. It may arise from the oversecretion of CSF, impaired absorption of CSF, or obstruction of CSF pathways.

139D: Diversity is partly achieved through somatic hypermutation

Antibodies (immunoglobulins) are a heterogeneous group of proteins produced by plasma cells and B-lymphocytes that react with antigens. All have a similar structure with two heavy chains and two light chains. In addition, antibodies are made up of variable and constant regions. The antigen binding region is located in the variable region, whereas the complement fixing and antibody receptor binding activity is found in the constant region. The structure of the heavy-chain constant region determines the class of the antibody (i.e. IgG, IgM, IgA, IgE etc.). Although mast cells do not produce antibodies, they contain immunoglobulin receptors on their cell surfaces. As a result mast cells are able to bind pre-formed IgE on their cell surface which plays an important role in allergy and anaphylaxis (type I hypersensitivity reaction).

Any individual has about 10^{10} different antibodies. This astonishing degree of diversity arises through four main processes:

- pairing of different combinations of heavy and light chains
- recombination of V, D and J segments (VJ for light chains)
- variability in the joins of the recombined segments through imprecise joining by recombinatorial machinery and by the addition of extra random nucleotides by terminal deoxynucleotide transferase

- somatic hypermutation – a poorly understood mechanism for introducing mutations into V regions of activated B-cells (antigen driven).

A malignant tumour of plasma cells may result in the overproduction of a monoclonal population of immunoglobulins. This is known as multiple myeloma.

140B: Microcytic anaemia

Iron-deficiency anaemia is the most common cause of hypochromic, microcytic anaemia. Iron-deficiency anaemia occurs when the dietary intake or absorption of iron is insufficient and haemoglobin, which contains iron, cannot be formed. The principal cause of iron-deficiency anaemia in pre-menopausal women is blood lost during menses. Iron-deficiency anaemia is characterized by pallor, fatigue and weakness. Because it tends to develop slowly, adaptation occurs and the disease often goes unrecognized for some time. Hair loss and light-headedness can also be associated with iron-deficiency anaemia.

The blood smear of a patient with iron-deficiency shows many hypochromatic and rather small red blood cells (RBCs), and may also show poikilocytosis (variation in shape) and anisocytosis (variation in size). With more severe iron-deficiency anaemia the peripheral blood smear may show target cells, hypochromic pencil-shaped cells, and occasionally small numbers of nucleated RBCs (reticulocytes). The diagnosis of iron-deficiency anaemia will be suggested by appropriate history (e.g. anaemia in a menstruating woman) and by diagnostic tests such as a low serum ferritin, a low serum iron level, an elevated serum transferrin and a high total iron-binding capacity (TIBC). Serum ferritin is the most sensitive laboratory test for iron-deficiency anaemia.

If the cause is dietary iron deficiency, iron supplements, usually with ferrous sulphate or ferrous gluconate, will usually correct the anaemia.

141C: Bendroflumethiazide

Thiazide diuretics, which include bendroflumethiazide and metolazone, act mainly on the distal convoluted tubule where sodium reabsorption is inhibited. Water accompanies the sodium. Common side effects include hypokalaemia, hyperuricaemia and impaired glucose tolerance. Potassium loss arises from two distinct mechanisms that are not mutually exclusive. First, an increased sodium load in the collecting ducts stimulates sodium absorption in exchange for potassium secretion. Second, the high flow rate of filtrate produced by these diuretics will also favour potassium excretion by continually flushing it away, increasing the gradient from cell to lumen.

Acetazolamide is a carbonic anhydrase inhibitor, which acts by reducing bicarbonate reabsorption from the proximal tubule. Excretion of bicarbonate, sodium and water is therefore increased.

Furosemide is a loop diuretic which inhibits sodium and chloride reabsorption from the thick ascending Loop of Henle (acting on the $Na^+/K^+/2Cl^-$ transporter). As with thiazide diuretics, side-effects include hypokalaemia, hyperglycaemia and hyperuricaemia.

Vasopressin (ADH) acts by increasing the number of aquaporins, or water channels, in the collecting ducts, which increases the reabsorption of water.

Potassium-sparing diuretics (e.g. spironolactone, amiloride) also act on the distal convoluted tubule and collecting ducts to reduce sodium reabsorption and subsequently water reabsorption. Aldosterone stimulates sodium and subsequent water reabsorption from the distal convoluted tubule.

142C: The left pleuroperitoneal canal is larger and closes later compared with the right

The diaphragm is a composite musculotendinous structure formed in the embryo by the fusion of four separate elements:

- septum transversum (giving rise to the non-muscular central tendon)
- pleuroperitoneal membranes – closes the primitive communication between the pleural and peritoneal cavities (forms the bulk of the diaphragmatic muscle)

- a peripheral rim derived from the body wall (paraxial mesoderm)
- dorsal oesophageal mesenchyme (forms the left and right crura).

The septum transversum develops within the cervical region. This explains how the diaphragm derives its innervation from the phrenic nerve ('C3, C4, C5, keeps the diaphragm alive!'). Caudal translocation of the septum transversum is accompanied by elongation of the phrenic nerves and explains the long course of the phrenic nerves (from the cervical roots) through the thoracic cavity.

In a congenital diaphragmatic hernia, one of the pleuroperitoneal canals (which forms a communication between the pleural and peritoneal cavities, respectively) fails to close off through failure of pleuroperitoneal membrane development. This allows the developing abdominal viscera to bulge into the pleural cavity. If the mass of displaced viscera is large enough, it will stunt the growth of lung on that side, resulting in pulmonary hypoplasia and respiratory insufficiency, which may be fatal. The left side is involved four to eight times more often than the right, primarily because the left pleuroperitoneal canal is larger and closes later than the right, but also because of the liver on the right side.

143C: The protein content of cerebrospinal fluid is 0.5 per cent that of plasma

The constituents of the CSF are regulated by an active process that takes place within the choroid plexus. Thus the composition of CSF is different from that of plasma. Of importance to mention are the concentrations of K^+, Ca^{2+}, bicarbonate and protein that are lower in CSF than in plasma. This is to prevent high concentrations of these electrolytes inadvertently exciting neurones present within the brain substance. The potassium content of the CSF in this respect is particularly important. Further buffering of the K^+ content of CSF take place through astrocytes.

Likewise, the low protein content of the CSF (the CSF protein content is 0.5 per cent that of plasma) is deliberate to prevent some proteins and amino acids acting as 'false neurotransmitters'. The CSF is more acidic than plasma because pH of the CSF plays a critical role in the regulation of pulmonary ventilation and cerebral blood flow. Another reason why the CSF protein is kept deliberately low is to prevent proteins buffering pH. The result is that the pH of the CSF accurately reflects carbon dioxide levels of the blood. In this way changes in pH act as a powerful regulator of the respiratory system (through the action of pH on central chemoreceptors) and on cerebral blood flow.

144C: They can activate complement

IgM antibodies are usually pentameric, whereas IgG is monomeric and IgA is usually found as a dimer linked by a J-chain. IgM antibodies are characteristic of a primary immune response; IgG antibodies predominate in a secondary immune response. IgM is an effective activator of complement when it has bound specific antigen. IgA, rather than IgM, is found lining mucosal surfaces and is secreted into breast milk; IgA is therefore known as secretory immunoglobulin.

IgM cannot cross the placenta, whereas IgG can. The consequences of this are three-fold. First, if IgM antibodies directed against infectious organisms are found in the fetal blood, they are an indicator of intra-uterine infection. Second, antibodies to ordinary ABO blood groups (anti-A and anti-B) are usually of the IgM type and hence do not cross the placenta. Third, because IgG can cross the placenta, whereas IgM cannot, it explains why rhesus haemolytic disease of the newborn is uncommon with the first pregnancy (the initial exposure to rhesus antigen evokes the formation of IgM antibodies). Subsequent exposure during a second or third pregnancy generally leads to a brisk IgG antibody response.

145E: Increased lipolysis

Adrenaline acts mainly on beta-adrenoceptors (unlike noradrenaline which acts mainly on alpha-adrenoceptors) and has numerous metabolic effects. It has direct effects on adipose tissue inducing hormone sensitive lipases, thereby promoting lipolysis and releasing fatty acids into the bloodstream. Increased glycogenolysis in the liver releases large amounts of glucose into the

bloodstream. Glycogen synthesis in the liver and in muscles is inhibited. Glycogenolysis in muscles does not increase blood glucose as the glucose generated remains within the muscles for rapid metabolism.

146B: Erythromycin

Penicillins and cephalosporins (which includes cefuroxime, cefotaxime, ceftriaxone) inhibit bacterial cell wall synthesis through the inhibition of peptidoglycan cross-linking. This weakens the cell wall of bacteria and renders them susceptible to osmotic shock. Macrolides (such as erythromycin), tetracyclines, aminoglycosides and chloramphenicol act by interfering with bacterial protein synthesis. Sulphonamides (e.g. trimethoprim, co-trimoxazole) work by inhibiting the synthesis of nucleic acid (Table 3).

Table 3

Mechanism of action	Examples
Inhibition of cell wall synthesis	Penicillins, cephalosporins, vancomycin
Inhibition of protein synthesis	Macrolides, tetracyclines, aminoglycosides, chloramphenicol, clindamycin
Inhibition of nucleic acid synthesis	Sulphonamides, trimethoprim, quinolones, metronidazole, rifampicin
Inhibition of cell membrane synthesis	Lincomycins, polymyxins

147B: Alcohol is the most common cause of holoprosencephaly

The human face forms from the fusion of five facial swellings:

- median frontonasal prominence (in front of forebrain)
- bilateral maxillary swellings (first arch derivative)
- bilateral mandibular swellings (first arch derivative).

All appear by the end of the fourth week of development.

In the fifth week of development, a pair of ectodermal thickenings appear on the frontonasal process called the nasal placodes. In the sixth week, the nasal placode divides into medial and lateral nasal processes. The groove between the lateral nasal process and the adjacent maxillary swelling is called the nasolacrimal groove. This later forms the nasolacrimal duct that drains excess tears from the conjunctiva of the eye into the inferior meatus of the nasal cavity. The palate forms from medial extensions of the maxillary swellings, the palatine shelves, which fuse with one another in the midline. An appreciation of the five facial swellings helps to explain how the different parts of the face are separately innervated by the different branches of the trigeminal nerve.

In this remodelling process all the different parts must be in register to ensure perfect fusion. This is complex both temporally and spatially, so craniofacial development is highly sensitive to perturbations. Indeed craniofacial abnormalities account for a third of all human congenital defects. Anomalies in the fusion of the five facial swellings result in facial clefts: for example, cleft lip results when the maxillary swelling fails to fuse correctly with the medial nasal process, and cleft palate from incomplete fusion of the palatine shelves. These can be of variable severity, are sometimes bilateral and have a number of causes.

The term holoprosencephaly refers to a spectrum of malformations of the head midline, including abnormal development of the forebrain, medial nasal processes and associated midfacial structures (e.g. nasal bones and septum). In severe cases this may result in a single nostril (cebocephaly) with close-set eyes (hypotelorism), or even a single eye (cyclopia). It is most commonly caused by alcohol consumption during the first month of pregnancy, being the most disabling manifestation of fetal alcohol syndrome, and alcohol is now regarded as the commonest cause of congenital mental retardation in the western world.

148B: Increasing membrane capacitance

The speed of nerve conduction increases with:

- increasing axonal diameter which decreases axonal resistance
- myelination (insulation of axons) by Schwann cells in the peripheral nervous system, or oligodendrocytes in the central nervous system
- increasing temperature
- decreasing membrane capacitance.

Capacitance slows down passive conduction because some of the current has to be used to charge or discharge the capacitance before it can spread further.

The effect of temperature on axonal velocity is easily understood by remembering what happens to one's hands when playing in the snow on a cold day. Most will be able to recall that hands go numb, but retain the ability to feel pain. The reason is straightforward and is based on axonal velocity. Light touch is carried by myelinated, Aβ nerve fibres. As the temperature decreases, the velocity of impulse propagation decreases until a point comes at which the amplitude of impulse is insufficient to regenerate the action potential at the next Node of Ranvier. Cooling has the further effect of slowing sodium conductance at the Nodes of Ranvier. Saltatory conduction is therefore disrupted; the result being that the hands are numb. Pain, on the other hand, is carried by unmyelinated C fibres. The generation of action potentials is not therefore restricted to the Nodes of Ranvier and pain sensation is preserved until far lower temperatures are reached.

The myelin sheath increases velocity by three mechanisms: first, by insulating the axon; second, by decreasing membrane capacitance; and third, by restricting the generation of axon potentials to the Nodes of Ranvier. The importance of myelination in increasing the speed of nerve conduction is illustrated by certain disease states where the myelin sheath is absent or lacking. One example is the condition multiple sclerosis which is a chronic, inflammatory, demyelinating condition resulting in multifocal lesions within the white matter of the central nervous system. The equivalent disease process within the peripheral nervous system is known as Guillain–Barré syndrome. Both result in neurological deficits, such as motor weakness and sensory loss as a result of the decreased velocity of impulse propagation down nerve fibres.

149B: Is composed of six human leukocyte antigen (HLA) genes

The human MHC is situated on chromosome 6. There are six pairs of allelic genes (A, B, C, DP, DQ, DR). The human MHC will be identical only in monozygotic (identical) twins. There are two classes of MHC antigens: class I antigens are expressed on the surface of all nucleated cells; class II are expressed only on the surfaces of cells such as antigen-presenting cells.

150A: It commonly exhibits an autosomal dominant pattern of inheritance

Von Willebrand disease is the most common hereditary bleeding disorder. It is caused by an abnormality, either quantitative or qualitative, of the von Willebrand factor, which is a large multimeric glycoprotein that functions as the carrier protein for factor VIII. Von Willebrand factor is also required for normal platelet adhesion. Von Willebrand disease can be classified into three main types:

- Type 1 accounts for 70–80 per cent of cases. It is characterized by a partial quantitative decrease of qualitatively normal von Willebrand factor and factor VIII. An individual with type 1 disease generally has mild clinical symptoms, and this type is usually inherited as an autosomal dominant trait; however, penetrance may widely vary in a single family.
- Type 2 accounts for 15–20 per cent of cases. It is a variant with primarily qualitative defects of von Willebrand factor. It can be either autosomal dominant or autosomal recessive.
- Type 3 is the most severe form. In the homozygous patient, it is characterized by marked deficiencies of both von Willebrand factor and factor VIII in the plasma, and the absence of von

Willebrand factor from both platelets and endothelial cells. It is characterized by severe clinical bleeding and is inherited as an autosomal recessive trait.

Investigations commonly reveal a normal platelet count and prothrombin time, with a prolonged activated partial thromboplastin time (APTT) and bleeding time.

151D: Simvastatin

Statins reduce cholesterol by competitively inhibiting HMG CoA reductase, an enzyme involved in cholesterol biosynthesis. They are more effective at lowering both total and LDL cholesterol than other classes of drugs, but are less effective than fibrates in reducing triglycerides. Side effects include myopathy and deranged liver function.

Nicotinic acid acts by inhibiting the release of VLDL, lowering plasma triglycerides and cholesterol, and increasing HDL. Its side effects include dizziness and flushing, which limit its use.

Fibrates stimulate lipoprotein lipase activity and work mainly to decrease triglycerides as well as moderately decreasing LDL and increasing HDL cholesterol.

Colestyramine (and other anion exchange resins) act by increasing the excretion of bile acids, and thus more cholesterol is converted into bile acid.

152E: Midgut development involves herniation of bowel into the umbilicus

The gut is an endodermal derivative created from a midline gut tube through a complex series of rotations. The gut is divided into three distinct territories:

- foregut = mouth up to second part of duodenum
- midgut = second part of duodenum up to two-thirds along the transverse colon
- hindgut = two-thirds along the transverse colon up to the anus.

This distinction is important developmentally, anatomically and clinically.

One consequence of the midline development of the gut is that visceral pain arising from the intestine often refers to the midline in the adult. Thus, foregut pain typically refers to the epigastric region, midgut pain to the peri-umbilical region and hindgut pain to the suprapubic region.

The cranial end of the embryological gut tube is capped by the buccopharyngeal membrane and the caudal end by the cloacal membrane. Both later rupture, forming the orifices of the body (i.e. the mouth and anus, respectively).

The stomach forms the thoracic part of the foregut. The dorsal wall of the stomach grows faster than the ventral wall, resulting in a dorsal 'greater curvature' and a ventral 'lesser curvature'. Subsequently the stomach rotates 90 degrees about the craniocaudal axis. As a result the greater curvature lies to the left. This has the consequence that the two vagus nerves that initially flanked the stomach on the left and right now lie posterior and anterior in the region of the stomach (remembered by the mnemonic RIP, or right is posterior). An additional tilting caudally orients the greater curvature so that it lies inferiorly.

Excessive growth of the midgut results in its herniation into the umbilicus, forming the primary intestinal loop. This loop undergoes a 90-degree rotation counterclockwise. Subsequently the midgut is rapidly retracted into the abdomen. As it does so, it rotates counterclockwise a further 180 degrees. Finally the caecum moves inferiorly to give the definitive organization of the intestine. If the anterior abdominal wall does not close completely, loops of midgut may remain outside the abdominal cavity at birth, forming a condition known as omphalocele, or gastroschisis. Abnormal rotation of gut can cause a spectrum of anomalies; for example, there may be freely (malrotated) suspended coils of intestine that are prone to volvulus, causing constriction of its blood supply.

153E: They contain intracellular stores of calcium ions

A single motor neurone supplies a group of muscle fibres in what is known as a motor unit. The more precise the movement, the fewer the muscle fibres supplied by one motor neurone. However, each muscle fibre is innervated by only one motor neurone.

Mammalian skeletal muscle is optimally organized for rapid excitation of muscle contraction in a process known as 'excitation–contraction coupling'. Calcium is released from the intracellular stores (sarcotubular system) when skeletal muscle contracts. Calcium reuptake occurs through an active mechanism requiring a calcium pump. During contraction the actin and myosin filaments do not shorten but slide together over one another (sliding filament theory).

Decreasing extracellular calcium increases excitability and may lead to spontaneous contractions (tetany), possibly by increasing sodium permeability. In hypocalcaemia this may manifest clinically as Chvostek's sign (activation of the facial nerve and muscles by merely tapping the skin) or Trousseau's sign (carpopedal spasm producing the '*main d'accoucheur*'). Fatal spasm of the larynx and seizures may later ensue if calcium levels are not corrected. Hyperventilation (overbreathing) may cause a similar effect through the respiratory alkalosis that it generates. Amino acids buffer the change in pH by loosing protons to the plasma and in doing so become negatively charged. This negative charge binds free calcium in the plasma, resulting in hypocalcaemia.

154D: Class II MHC presents exogenous antigens

Two principal classes of MHC exist; both play as important role in antigen presentation and recognition by T-cells. Class I MHC molecules are made up of one heavy chain and a light chain called β_2-microglobulin. Class II molecules do not contain β_2-microglobulin and consist of two chains of similar size.

Almost all nucleated cells of the body express MHC class I molecules on their cell surfaces. Hepatocytes express relatively low levels of class I MHC. This may explain why infection by certain hepatitis viruses (namely hepatitis B and C) or Plasmodium protozoa (the cause of malaria) commonly leads to a chronic carrier state in the host. Non-nucleated cells such as erythrocytes express little or no class I MHC; infection in the interior of red cells (such as malaria) can therefore go undetected. Class II MHC molecules are constitutively expressed only by certain cells involved in immune responses, though they can be induced in a variety of cells. Class II MHC molecules are richly expressed on the surface of dendritic cells.

The two classes of MHC are specialized to present different sources of antigen. MHC class I molecules present endogenously synthesized antigens (e.g. viral proteins). MHC class II molecules present exogenously derived proteins (e.g. extracellular microbes) that are first internalized and processed in the endosomes or lysosomes. Class I MHC molecules present peptides generated in the cytosol to CD8 T-cells, whereas MHC class II molecules present peptides degraded in intracellular vesicles to CD4 T-cells.

155E: Neutrophil

The predominant cell type seen in acute inflammation is neutrophils. These generally infiltrate the area over 24 hours, and after 24–48 hours they are replaced by macrophages.

156C: Amiodarone

This question requires knowledge of the Vaughan Williams classification of antiarrhythmic drugs. Lignocaine is a class 1B drug and blocks sodium channels. Procainamide, a class 1A drug, and flecainide, a class 1C drug, also block sodium channels. All class I drugs have membrane stabilizing properties.

Class II drugs comprise the beta-blockers. They are believed to work by blocking the pro-arrhythmic effects of catecholamines and the sympathetic nervous system.

Class III drugs (e.g. amiodarone, sotalol) act through the blockade of potassium channels. They work by prolonging the action potential, thereby increasing the refractory period and hence suppressing ectopic and re-entrant activity. Note sotalol has both class II and class III actions.

Class IV includes drugs such as verapamil and diltiazem which act by blocking calcium channels.

157A: Apart from the first cleft, the other branchial clefts are normally obliterated by overgrowth of the second branchial arch

The pharyngeal, or branchial arches, are the mammalian equivalent of the gill arches in fish. In humans, there are five pairs of branchial arches that develop in a craniocaudal sequence (equivalent to gill arches 1, 2, 3, 4, 6). Note that the fifth branchial arch never forms in humans, or forms as a short-lived rudiment and promptly regresses. Each arch contains a central cartilaginous element, striated muscle, cranial nerve and aortic arch artery, surrounded by ectoderm on the outside and lined by endoderm. The arches are separated externally by ectodermally lined branchial clefts and internally by endodermally lined branchial pouches.

- The first arch gives muscles of mastication
- The second arch gives muscles of facial expression
- The third and fourth arches give muscles of vocalization and deglutition
- The sixth arch gives the intrinsic muscles of the larynx.

Certain key features concerning the branchial arches are worth remembering. First, the superior parathyroid glands develop from the fourth branchial pouch; the inferior parathyroids, along with the thymus, are third-pouch derivatives. Consequently, the inferior parathyroids may migrate with the thymus down into the mediastinum, hence its liability to end up in unusual positions.

The tongue is derived from several sources. The anterior two-thirds of the tongue mucosa is a first-arch derivative, whereas the posterior one-third is contributed to by the third and fourth arches. The tongue muscles, in contrast, are formed from occipital somite mesoderm. For this reason, the motor and sensory nerve fibres of the tongue are carried by separate sets of cranial nerves.

The thyroid gland arises from between the first and second arches as a diverticulum (thyroglossal duct) which grows downwards leaving the foramen caecum at its origin. Incomplete thyroid descent may give rise to a lingual thyroid, or a thyroglossal cyst.

Apart from the first branchial cleft (which forms the external ear), the other clefts are normally obliterated by overgrowth of the second pharyngeal arch, enclosing the remaining clefts in a transient, ectoderm-lined, lateral cervical sinus. This space normally disappears rapidly and completely. It may persist in adulthood as a branchial cyst or fistula.

158D: The equilibrium potential for an ion species depends on the ratio of the concentrations of the ion outside to inside of the cell

In axons, impulses can travel in both directions (orthodromic and antidromic) from a point of electrical stimulation. Antidromic activity explains certain clinical phenomena such as how infection of a dorsal root by herpes zoster virus causes the segmental cutaneous hyperaemia characteristic of shingles. The amplitude of the action potential generated by an excitatory stimulus is independent of the stimulus strength; this is known as the 'all or nothing' law. This means stimulus intensity is coded for by frequency rather than through the amplitude of action potential.

The resting membrane potential is dependent on the electrogenic sodium–potassium ATPase pump and the relative intracellular and extracellular concentrations of ions on each side of the nerve cell membrane, as well as their relative permeabilities across the membrane. This establishes both a concentration (chemical) gradient and an electrical gradient across the nerve cell membrane – an electrochemical gradient. The equilibrium potential for a given ion species depends on the ratio of the concentrations of the ion outside to that inside the cell (the Nernst potential or equation). The Goldman constant-field (or Goldman–Hodgkin–Katz) equation is a more general form of the Nernst equation which allows for different permeabilities. Resting nerve cell membranes are about 100 times more permeable to K^+ ions than to Na^+ ions.

If extracellular sodium is replaced by potassium it would follow from the Nernst equation

that this would depolarize the fibres completely. The resulting depolarization inactivates sodium channels and blocks the propagation of impulses down nerves. This is why hyperkalaemia is so dangerous. Cardiac muscle is especially sensitive to small changes in extracellular potassium concentrations and death often ensues from cardiac standstill.

159D: Is activated by IgM immune complexes

The complement system consists of a large number of distinct plasma proteins, triggering a cascade of reactions where the activation of one complement component results in the activation of another. This amplifies the effector molecules of the complement system. The main consequences of complement activation are opsonization of pathogens, the recruitment of inflammatory cells and direct killing of pathogens. There are two principal pathways of complement activation, the alternative and classical. The alternative pathway is the evolutionary older of the two pathways but the classical pathway was discovered first, hence the term classical pathway.

The alternative pathway is activated by the lipopolysaccharide of cell wall constituents, whereas the classical pathway is activated by IgM or IgG (but not IgA) which has bound to its specific antigen. Thus, in a transfusion reaction IgM from the recipient's blood binds to the incompatible donor red cells leading to complement activation, haemolysis and acute renal failure. The alternative pathway begins with the activation of the C3 component, but the classical pathway starts with the activation of the C1 component.

160A: Ingress of calcium ions

The cardiac action potential is divided into a number of phases (Figure 5):

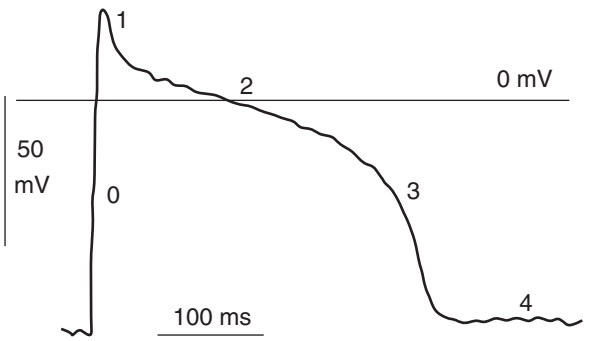

Figure 5 The cardiac plateau.

- 0 – rapid depolarization (caused by the rapid influx of sodium ions)
- 1 – early repolarization (caused by the inactivation of sodium channels and the outward passage of potassium ions)
- 2 – plateau phase (caused predominantly by the ingress of calcium ions and the efflux of potassium ions)
- 3 – late repolarization (caused predominantly by the efflux of potassium ions)
- 4 – diastolic phase.

161C: Entacapone

Parkinson's disease is a progressive neurodegenerative disorder characterized clinically by a triad of bradykinesia, rigidity and resting tremor. It results from the decreased production of dopamine from the substantia nigra of the basal ganglia. Direct replacement with dopamine is not possible since dopamine does not cross the blood–brain barrier.

L-Dopa (levodopa) is the amino-acid precursor of dopamine, and is able to cross the blood–brain barrier, where it is converted (decarboxylated) to dopamine. L-Dopa acts by directly

replenishing depleted striatal dopamine. It is given with a dopa-decarboxylase inhibitor (e.g. carbidopa), that does not cross the blood–brain barrier. This reduces the peripheral conversion of L-dopa to dopamine, thereby limiting side effects such as nausea, vomiting and cardiovascular effects (particularly hypotension).

Bromocriptine, cabergoline, ropinirole and pergolide are all dopamine agonists. They may be used alone, or in combination with L-dopa.

Selegiline inhibits the enzyme, MAO–B (monoamine oxidase B) for which dopamine is a substrate. It reduces the metabolism of dopamine in the brain and potentiates the action of L-dopa.

Entacapone inhibits the enzyme COMT (catechol-O-methyltransferase). By inhibiting this enzyme it slows the elimination of L-dopa. It prolongs the duration of a single dose, in addition to smoothing out any fluctuations in the plasma concentration of L-dopa.

Muscarinic antagonists, such as benzatropine, may play a role in the management of Parkinson's disease and are particularly useful when the resting tremor is the predominant symptom.

162A: Neural tube development requires signals from the underlying mesoderm

The nervous system arises from a special type of ectoderm that has been neurally induced to form neuroectoderm. The first stage in neurulation (i.e. development of the nervous system) is the establishment in the ectoderm of a region of cells that acquire neural competence (neural induction). The second stage is the morphogenetic process of neurulation that transforms the neuroepithelial sheet into the neural tube.

Neurulation involves communication between the mesoderm and the overlying ectoderm. The mesoderm primarily involved is the notochord, a dense rod of axial mesoderm that is very important in patterning the embryo early in development, but forms only the nucleus pulposus in the adult (in the centre of the intervertebral disc) and the apical ligament of the dens. Signals (specialized secreted proteins) are secreted by the notochord and induce the specialization of the overlying ectoderm cells to form the floor of the neural tube.

Closure of the neural tube proceeds bidirectionally, ending with closure of the cranial and caudal openings (neuropores). The cranial neuropore finally closes on day 24 and the caudal neuropore closes on day 26 of development. Closure of the neural tube is susceptible and a common cause of birth defects.

The neural crest, a migratory cell population, begins to emigrate from the dorsal half of the neural tube around the time of neural tube closure. They have a diverse and complex fate that include cartilage in the head, melanocytes, the medullary cells of the adrenal gland, glial Schwann cells, and neurones of both the peripheral and autonomic nervous systems. Aberrant neural crest migration may result in Hirschsprung's disease of the bowel (congenital megacolon or aganglionosis), but not neural tube defects.

A variety of malformations result from failure of part of the neural tube and overlying skeleton to close, usually at the cranial or caudal end of the nervous system. Such neural tube defects originate during the third week of development and are the commonest group of neurological malformations encountered in humans, occurring in 1 in 300 to 1 in 5000 births, depending on the geographical region. In spina bifida, the vertebral arch is defective dorsally, usually caudally in the lumbrosacral region (spina bifida occulta), and in severe cases the meninges protrudes from the vertebral canal (meningocele), sometimes including neural tissue (myelomeningocele) with associated neural impairment. Rarely, failure of cranial neural tube closure results in anencephaly where the forebrain is in contact with the amniotic fluid and degenerates (it is fatal). Approximately 50 per cent of neural tube defects may be prevented by women taking folic acid, even in the babies of mothers who have previously given birth to infants with neural tube defects. However, it must be taken during the first few weeks of pregnancy since this is when the neural tube is closing and hence susceptible to perturbations.

163A: Excitation depends more on the influx of extracellular calcium than release from internal stores

In smooth muscle, actin and myosin filaments occur but are less obvious on microscopy, giving it a non-striated appearance. Most smooth muscle has extensive electrically conducting gap junctions between cells which allows propagation of waves of electrical excitation through the tissue. Smooth muscle is usually under autonomic (involuntary nervous) or hormonal control, unlike skeletal muscle which is under somatic control. Unlike skeletal muscle, smooth muscle can generate active tension in the absence of any neural activity (latch bridge mechanism).

There is a vesicular sarcoplasmic reticulum close to the membrane (caveolae), but no T-tubular system. This is because the slow speed of smooth muscle does not require an elaborate mechanism for intracellular calcium release. For this reason, and because of the higher surface area to volume ratio of smooth muscle cells, excitation depends more on the influx of extracellular calcium than release from internal stores, since smooth muscle has a less well-developed sarcoplasmic reticulum.

The intrinsic myogenic response in smooth muscle opposes stretch. The result is that contraction may be generated by mechanical stretch of muscle fibres, for example in blood vessel walls. This is partly the basis for autoregulation of blood flow in the cerebral, coronary and renal vascular beds. It also plays a role in the peristaltic movements of material in the intestine.

164E: Cranial nerve VIII as it enters the internal acoustic meatus

The internal acoustic meatus (IAM) is contained in the posterior cranial fossa. It transmits cranial nerves VII and VIII. The abducens nerve in the cavernous sinus lies in the middle cranial fossa, along the body of the sphenoid bone. The mandibular division of the trigeminal nerve (Vc) exits the middle cranial fossa through the formamen ovale, the temporal lobe occupies the middle cranial fossa, and the temporomandibular joint (TMJ) is a joint between the head of the mandible and the mandibular fossa of the squamous part of the temporal bone.

165B: 15–40 days

Hepatitis A has a short incubation period of between 15 and 40 days. The infection is transmitted by the faecal–oral route and takes hold very quickly. The virus replicates in the gastrointestinal tract and is shed in the faeces during both the incubation and acute phases of the disease.

166C: β_2-adrenoceptor agonism

Asthma is an inflammatory (reactive) disorder of the airways characterized by reversible airway obstruction (or bronchospasm). It results from a type I hypersensitivity reaction, where the IgE-mediated degranulation of mast cells and release of inflammatory mediators is central to the pathogenesis.

Bronchial smooth muscle contains β_2-adrenoceptors. Throughout the body, β_2-adrenoceptors act to relax smooth muscle. Salbutamol stimulates these receptors (i.e. it is a selective β_2-adrenoceptor agonist), thereby relaxing the smooth muscle in the airways and increasing their calibre. Longer-acting β_2-adrenoceptor agonists (such as salmeterol) play a role in more severe asthma.

Bronchial smooth muscle also contains muscarinic receptors. Stimulating these receptors causes smooth muscle contraction. Therefore muscarinic antagonists (such as ipratropium) are useful adjuncts in the management of asthma.

Other drugs used in the management of asthma include steroids (oral or inhaled), leukotriene receptor antagonists (e.g. montelukast), xanthines (e.g. theophylline) and sodium cromoglycate.

167E: May contain ectopic tissue

A Meckel's diverticulum is the anatomical remnant of the vitello-intestinal duct. In the developing fetus the vitello-intestinal duct connects the primitive midgut to the yolk sac and also plays a

part in intestinal rotation. The urachus (a derivative of the allantois) is different and connects the bladder to the umbilicus in the fetus. After birth the urachus becomes known as the median umbilical ligament.

The vitello-intestinal duct normally regresses between the fifth and eighth weeks of development, but in 2 per cent of individuals it persists as a remnant of variable length and location, known as a Meckel's diverticulum – in honour of J. F. Meckel who first discussed the embryological basis of this anomaly in the nineteenth century. Most often it is observed as a 2-inch (5 cm) intestinal diverticulum projecting from the antimesenteric wall of the ileum, about 2 feet (60 cm) from the ileocaecal valve. It is about twice as common in males as in females. However, this useful mnemonic ('the rule of 2s') holds true in only two-thirds of cases; the length of the diverticulum is variable and its site may be more proximal.

It is estimated that 15–30 per cent of individuals with a Meckel's diverticulum develop symptoms from intestinal obstruction, gastrointestinal bleeding, acute inflammation (diverticulitis) or perforation. Its blind end may contain ectopic tissue, namely gastric mucosa (in 10 per cent of cases), liver, pancreatic tissue, carcinoid or lymphoid tissue. This is important because gastric mucosa bears HCl-secreting parietal cells and can therefore ulcerate within the diverticulum (like a stomach ulcer) causing bleeding. Bowel obstruction may be caused by the trapping of part of the small bowel by a fibrous band (that represents a remnant of the vitelline vessels) connecting the diverticulum to the umbilicus. Symptoms may closely mimic appendicitis. Therefore if a normal-looking appendix is found at laparoscopy, or during an open appendicectomy, it is important to exclude a Meckel's diverticulum as a cause of the patient's symptoms. Mortality in untreated cases is estimated to be 2.5–15 per cent.

168D: Specialized intercellular junctions exist between myocytes

The structure of cardiac muscle correlates beautifully with its function. Certain features concerning cardiac myocytes are worth remembering:

- They are shorter than skeletal muscle cells.
- They are branched.
- Cardiac myocytes typically contain a single, centrally placed nucleus (unlike skeletal muscle fibres that are multinucleate, with peripherally located nuclei).
- Intercalated discs with gap junctions results in a syncytium where adjacent cardiac cells are mechanically and electrically coupled to one another, optimizing cardiac contractility.
- They are rich in mitochondria.
- There is sarcoplasmic reticulum.
- There are transverse tubules at the Z-line. Note that in skeletal muscle the T-tubules are located at the junction of the A and I bands.
- There are unstable resting membrane potentials of pacemaker cells.
- Cardiac muscle contracts spontaneously (myogenic).

A property shared by skeletal and cardiac muscle is their striated microscopic appearance from the highly organized arrangement of actin and myosin filaments.

169A: Bacterial endotoxin induces the acute-phase response

The acute-phase response is part of the innate (natural) immune system. Macrophages are exquisitely sensitive to the lipopolysaccharide (LPS) present in certain bacteria. They respond by producing cytokines, notably TNFα, IL-1 and IL-6 (but not IL-10 which can generally be thought of as an inhibitory cytokine). The aforementioned cytokines act on the liver to increase the concentration of many key serum proteins to aid the host defence response (such as C-reactive protein, serum amyloid protein, mannose binding protein, fibrinogen, complement). C-reactive protein (CRP) concentrations form a useful marker for detecting the presence (or confirming the absence) of inflammation or infection; this is a readily available laboratory test in the hospital

setting. In addition, monitoring the trend in CRP values (as opposed to one-off values) provides the clinician with extremely valuable information as to whether the patient is getting better or worse.

Activation of the acute-phase response is responsible for a number of different effects. First, it is responsible for the fever that may accompany a variety of different inflammatory and infectious states, through the action of IL-1 on the thermosensory centres in the anterior hypothalamus. Second, hepatic protein synthesis is diminished and the level of serum albumin decreases. This is an attempt by the body to conserve protein and is responsible for the hypoalbuminaemia that often accompanies many disease states. Third, TNFα (cachectin) and IL-1 have catabolic effects and are responsible for the cachexia and anorexia seen in a variety of chronic inflammatory and infectious conditions. TNFα is also believed to be responsible for the cachexia seen in malignancy (cancer cachexia). In the latter, TNFα is produced by macrophages in response to the tumour, or by the tumour cells themselves. Finally, activation of the acute-phase response is central to the pathogenesis of septic shock where excessive activation of the acute-phase response leads to an overproduction of cytotoxic cytokines, resulting in a massive inflammatory reaction that may culminate in multiple organ failure and death.

170B: Limbic system

The limbic system is concerned with unconscious biological drives and emotions. It is considered the limbic lobe, hippocampus, anterior thalamic nucleus, hypothalamus and amygdala.

171C: Mitochondria can multiply independently

Smooth endoplasmic reticulum (ER) is involved in steroid hormone synthesis, whereas rough ER makes polypeptides. Mitochondria are the key organelles in aerobic respiration. Mitochondria are able to multiply independently. They are thought to have evolved millions of years ago from primitive bacteria (endosymbiotic theory), and therefore contain everything that is required to be self-sufficient, including DNA and ribosomes. Prokaryotic cells have no membrane-bound organelles; it is eukaryotic cells which have internal compartmentalization of organelles, hence division of labour (specialization). The Golgi apparatus has a role in the transportation and modification of proteins, such as the glycosylation to proteins. It is the lysosomes and proteasomes that are involved in the degradation of proteins.

172D: III

There are 12 pairs of cranial nerves that, together with the 31 pairs of spinal nerves, constitute the peripheral nervous system. The central nervous system comprises the brain and spinal cord. A peripheral nerve is a mixed nerve containing motor, sensory and autonomic (parasympathetic, sympathetic) elements. Parasympathetic outflow arises from the 'craniosacral' region; i.e. from certain cranial nerves and sacral roots S2–4. Cranial nerves III (occulomotor), VII (facial), IX (glossopharyngeal) and X (vagus) carry parasympathetic fibres whose function is primarily secretomotor (e.g. salivary secretions in the case of cranial nerve VII), ciliary motor (pupillary reflexes and accommodation in the case of cranial nerve III), while cranial nerves IX and X play an integral role in blood pressure regulation. Sympathetic outflow is principally 'thoracolumbar' (i.e. from spinal segments T1 through to L2). The sympathetic nervous system serves vasomotor (vascular tone), sudomotor (sweating) and pilomotor functions, in addition to controlling smooth muscle and sphincter tone and playing a key role in cardiovascular homeostasis.

Understanding the above makes it easy to predict the outcome of particular lesions in certain clinical settings. Take an occulomotor (3rd) cranial nerve palsy, for instance. Interruption of the parasympathetic fibres to the constrictor pupillae muscle results in a unilaterally dilated pupil (mydriasis) as an important hallmark of a 3rd-nerve palsy. This can thus easily be distinguished from a Horner's syndrome (sympathetic chain disruption), which causes a unilaterally constricted pupil (miosis).

173C: Excitation–contraction coupling requires calcium-induced calcium release

The most important source of activator calcium in cardiac muscle remains its release from the sarcoplasmic reticulum. Calcium, however, also enters from the extracellular space during the plateau phase of the action potential. This calcium entry provides the stimulus that induces calcium release from the sarcoplasmic reticulum (calcium-induced calcium release). The result is that tension generated in cardiac, but not in skeletal, muscle is profoundly influenced both by extracellular calcium levels and factors that affect the magnitude of the inward calcium current. This is of practical value in two key clinical situations: in heart failure where digoxin is used to increase cardiac contractility (by increasing the intracellular calcium concentration), and in hyperkalaemia where calcium gluconate is used to stabilize the myocardium.

The force of contraction of cardiac muscle is heavily dependent on its stretched fibre length. This is the basis of the Frank–Starling mechanism that adjusts the energy of cardiac contraction in response to diastolic stretch (filling). This autoregulatory mechanism makes the heart a self-regulating pump with respect both to demands from the peripheral circulation and in balancing the pumping by the right and left sides of the heart.

The plateau phase of the action potential in cardiac muscle (principally due to calcium influx) maintains the membrane at a depolarized potential for as long as 500 ms. The result is that the cell membrane is refractory throughout most of the mechanical response, largely due to the inactivation of fast sodium channels. This prevents tetany upon repetitive stimulation which would be detrimental to cardiac output. Furthermore, the prolonged refractory period in cardiac muscle allows the impulse that originates in the sinoatrial node to propagate throughout the entire myocardium just once, thereby preventing re-entry arrhythmias.

174B: It depends on the action of prostaglandins within the hypothalamus

Fever is brought about by toxins from microorganisms which act on cells of the immune system to produce cytokines (including IL-1, IL-6 and TNFα). It is the body's immune response to the invading microorganism, rather than a direct result of the microorganism *per se* that results in fever. The cytokines produced by the immune system act as endogenous pyrogens and act on the hypothalamus to generate fever, via the production of prostaglandins. Aspirin works as an antipyretic by blocking the enzyme (cyclo-oxygenase) that generates prostaglandins.

Fever also results from a variety of non-infectious causes, in addition to the infectious ones. Examples are various inflammatory conditions, connective tissue diseases, drug reactions and malignancies.

Fever is evolutionary advantageous; it inhibits the growth of some microorganisms (most organisms only grow well in narrow temperature range), increases the rate of production of antibodies, improves the efficiency of leukocyte killing, and decreases the mobility of the host (thereby aiding recovery of the host and preventing spread of infection to other individuals). However, in some situations fever becomes maladaptive resulting in hyperpyrexia, dehydration and death.

175D: Abnormal passive abduction of the extended knee

The medial collateral ligament of the knee prevents abduction of the leg at the knee. It extends from the medial femoral epicondyle to the shaft of the tibia. The oblique popliteal ligament resists lateral rotation during the final degree of extension. The posterior cruciate ligament prevents posterior displacement of the tibia. The anterior ligament helps lock the knee joint on full extension.

176B: Southern blotting

The polymerase chain reaction (PCR) is an amplification process used to amplify small amounts of DNA in order to perform analysis. It does not identify specific sequences. The DNA can then be analysed using Southern blotting. PCR involves synthesizing two oligonucleotide primers, that is short segments of RNA, that will bind to the DNA and when added to denatured DNA will bind to the DNA and amplify the DNA. The cycle is continually repeated 20–30 times, resulting

in an exponential increase in the quantity of DNA. Reverse transcription PCR uses RNA. RNA is too unstable to be used for PCR, so it must be converted to a complementary copy of DNA using reverse transcriptase. PCR is then performed.

Southern blotting involves digestion of DNA and are denatured in alkali making them single-stranded. A permanent copy of the single strands is made by placing the DNA on a nitrocellulose filter – i.e. the Southern blot. A target radioactively labelled DNA fragment is then added and will bind to its homologous DNA fragment (if present). The DNA is then washed to remove any unbound DNA. The hybridized DNA can then be visualized as a band using autoradiography.

Northern blotting is similar to Southern blotting but uses mRNA as the target nucleic acid, rather than DNA. The mRNA can be hybridized to a radiolabelled DNA probe.

Western blotting is used to analyse proteins that are separated by electrophoresis, transferred to nitrocellulose, and reacted with antibody for detection.

177A: The posterior crico-arytenoids are the only muscles that separate the vocal cords

The posterior crico-arytenoid muscles are perhaps the most important muscles in the body as they are the only intrinsic muscles of the larynx that open up the airway by separating the vocal cords. Without them asphyxiation would quickly ensue.

All the intrinsic muscles of the larynx are supplied by the recurrent laryngeal nerve of the vagus, with the exception of the important cricothyroid muscle, which is supplied by the external branch of the superior laryngeal nerve. Cricothyroid is the muscle which is principally concerned with altering voice pitch by altering the length of the vocal cords. Damage to the superior laryngeal or recurrent laryngeal nerves can occur during thyroid, oesophageal or aortic arch surgery, leading to changes in the character of the voice and even airway compromise (Semon's law).

The true vocal cords form the superior border of the cricothyroid membrane and are lined by stratified squamous mucosa, not the typical respiratory epithelium that lines the rest of the respiratory tract. This confers protective properties on the vocal cords, which are subject to 'wear and tear' from vocalization. The same is true of the epiglottis which is also lined by 'protective' stratified squamous epithelium. The epiglottis is largely composed of elastic cartilage, rather than hyaline cartilage.

The cricoid cartilage is the only complete ring of cartilage within the human body, in contrast to the tracheal rings which are C-shaped rings of hyaline cartilage which provide support to the trachea but are deficient posteriorly.

178D: The nucleus accumbens and substantia nigra are rich in dopamine

The nervous system can be arbitrarily divided into the somatic (or 'voluntary') and autonomic (or 'involuntary') parts. The autonomic nervous system consists of two arms, namely the sympathetic and parasympathetic nervous system. Both sympathetic and parasympathetic fibres consist of two neurones (first-order or preganglionic, and second-order or postganglionic, neurones) and two synapses (the synaptic cleft between the first- and second-order neurones and the synaptic cleft between the second-order neurone and the organ or effector). There are key differences between both the neurones and the synapses of the sympathetic and parasympathetic nervous systems.

First-order (preganglionic) sympathetic and parasympathetic neurones are myelinated, whereas second-order (postganglionic) sympathetic and parasympathetic neurones are small, unmyelinated fibres. In both the sympathetic and parasympathetic nervous system, preganglionic neurones release acetylcholine which acts on postsynaptic nicotinic cholinergic receptors. However, they differ at the second synapse (between second-order neurones and the effector) where noradrenaline is the principal chemical neurotransmitter used within the sympathetic nervous system (although this is not entirely true because the postganglionic sympathetic nerve fibres to the sweat glands, the piloerector muscles and a few blood vessels are cholinergic), but acetylcholine is the principal neurotransmitter used within the parasympathetic nervous system (but this time acting on muscarinic cholinergic receptors).

The neuromuscular junction (the synapse between somatic motor neurones and skeletal muscle) operates by way of acetylcholine acting through nicotinic acetylcholine receptors. The substantia nigra is a dense area of dopaminergic neurones which forms part of the basal ganglia; degeneration leads to Parkinson's disease. The periaqueductal grey is a region rich in endogenous opioids which is believed to play a pivotal role in attenuation of painful stimuli through descending inhibition from higher centres. The noradrenergic-rich locus coeruleus is believed to play a key role in attention. The nucleus accumbens is dopamine-rich and plays an important role in addiction and reward. The adrenal medulla is an endocrine gland, but is effectively a specialized second-order (postganglionic) sympathetic nerve terminal that secretes approximately 70 per cent adrenaline, 30 per cent noradrenaline. Excess catecholamines are secreted by the adrenal medulla in a condition known as a phaeochromocytoma, which is a rare tumour of the adrenal gland. A thorough grounding of the aforementioned chemical neurotransmitters is imperative if one is to understand certain disease states and how particular drugs act within the nervous system.

179B: Skin

Immunologically privileged sites are anatomical sites that are normally segregated from the immune system. Immunological privilege results from the effects of both physical barriers to cell and antigen migration and soluble immunosuppressive mediators such as certain cytokines. Such sites include:

- central nervous system
- eyes
- testes
- uterus (fetus)
- interior of red blood cells (one mechanism by which malaria evades the immune system).

Note that the skin is not an immunologically privileged site and is rich in Langerhans' dendritic cells.

By definition, immunologically privileged sites are sites in which immunocompetent hosts can maintain allogenic tissues without eliciting rejection. Thus HLA matching is not required for corneal transplants and the rarity with which such transplants reject has contributed to the considerable success rate of corneal transplants. In addition, the immunologically privileged environment of the uterus may help to explain the mysterious lack of rejection of the fetus which has puzzled generations of reproductive immunologists, but is obviously of compelling importance for the propagation of the species.

Damage to an immunologically privileged site can induce an autoimmune response, presumably because the adult immune system has never been exposed to the antigens sequestered in such sites. In other words, the immune system has not had the opportunity to become tolerant to such antigens. Thus a breakdown in the blood–brain barrier may lead to multiple sclerosis (a chronic inflammatory, demyelinating condition of the central nervous system, resulting in multifocal white matter lesions separated in time and space), damage to the blood–testis barrier may result in infertility (an autoimmune reaction to one's own spermatozoa) and a trauma to the eye may result in sympathetic ophthalmia (where rupturing one eye results in the release of antigens, which triggers an autoimmune attack on both eyes).

180D: Borrelia burgorferi – athropod vector-borne entry

Borrelia burgorferi is spread by ticks and is caused by Lyme disease. *Rickettsia rickettsii* also is usually spread by ticks. *Clostridium tetani* enters the body through wounds. *Neisseria meningitidis* and *Corynebacterium diphtheriae* both enter via the respiratory tract.

181D: RNA polymerase II gives rise to protein encoding mRNA

In prokaryotes, both transcription and translation occur in the cytoplasm; whereas in eukaryotes, transcription occurs in the nucleus and translation in the cytoplasm. Transcription is the process of

synthesizing messenger RNA (mRNA) from DNA; it is catalysed by the enzyme RNA polymerase II. RNA and DNA is always synthesized in a 5′ → 3′ direction.

The production of mature mRNA is a result of gene splicing. The introns which are non-coding sequences of DNA are removed and intervening exons are joined together. The exons are then coded into proteins during translation.

Amino acids are coded for by groups of three bases and these three bases together make up a codon. As there are four types of base, there is a potential for 4^3 (or 64) amino acids. Only 20 amino acids are used in protein synthesis, so in fact 44 codons are considered redundant.

182B: Embryologically starts out at the foramen caecum of the tongue

The thyroid gland is an endocrine gland that sits as the base of the neck like a bow-tie. It consists of two lateral lobes and an isthmus which is attached via Berry's ligament to the second to fourth tracheal rings (it is not attached to the thyroid cartilage, but sits lower down in the neck). The fact that the thyroid gland is attached to the trachea by Berry's ligament and also the fact that it is invested within pretracheal fascia explains why the thyroid gland moves up with swallowing. This is important clinically as it defines a swelling within the neck as being of thyroid origin.

The embryology is important. The thyroid gland descends from the foramen caecum between the anterior two-thirds and posterior one-third of the tongue via the thyroglossal duct. If the embryology is faulty it can lead to problems in later adult life. An incompletely descended thyroid gland may persist in adult life as a lingual thyroid or a thyroglossal cyst.

The blood supply to the thyroid is by way of the superior thyroid artery (which is a branch of the external thyroid artery), the inferior thyroid artery (which is a branch of the thyrocervical trunk of the first part of the subclavian artery) and, rarely, the small thyroidea ima which arises from the aorta to supply the isthmus. Venous drainage is through the superior and middle thyroid veins to the internal jugular veins and via the inferior thyroid veins to the brachiocephalic veins (usually on the left). The arterial supply and venous drainage is important to know about when considering thyroid surgery.

The thyroid gland is stimulated by TSH (which is produced from the anterior lobe of the pituitary gland) to produce T3 and T4 – hormones that play an important role in basal metabolic rate.

183D: Lead to tolerance

Opioids are mainly used in the hospital setting for their analgesic properties. They are now believed to act both peripherally (outside the central nervous system) and within the CNS itself. Unfortunately opioids exert most of their beneficial effects and side effects through the same opioid receptor (μ-receptors). It is therefore unlikely that we will ever be able to develop a synthetic opioid agent that has the analgesic properties of other opioids without their unpleasant side effects.

Opioids induce side effects through both excitatory and inhibitory mechanisms. Excitatory effects are:

- pinpoint pupils (direct effect of opioids on the Edinger–Westphal nucleus)
- nausea and vomiting (direct effect on the area postrema)
- pruritus (due to mast-cell degranulation and histamine release)
- dysphoria and euphoria (direct effect on the CNS).

Inhibitory effects are:

- cardiorespiratory depression
- sedation
- relaxation of smooth muscles – constipation, urinary retention.

Constipation and nausea/vomiting are common side effects of opioids. It is therefore always a good idea to co-prescribe laxatives and antiemetics whenever an opioid is prescribed.

Opioids cause tolerance, dependence and withdrawal with increasing use. Tolerance means increasing dosages of the drug need to be used in order to obtain the same effect.

It is important to know how to reverse the effects of opioids because opioid overdose may be fatal. Specific opioid antagonists include naloxone and naltrexone. Flumazenil antagonizes the effects of benzodiazepines.

184B: Results in mast-cell degranulation

Hypersensitivity is a condition in which undesirable tissue damage follows the development of humoral or cell-mediated immunity. Gell and Coombs classified hypersensitivity reactions into four types. However, some also include a fifth type, as shown below.

Gell and Coombs' classification of hypersensitivity reactions

- *Type I*. Mast-cell degranulation mediated by pre-formed IgE bound to mast cells. Immediate (within minutes). Anaphylaxis, atopic allergies.
- *Type II*. Antibodies directed towards antigens present on the surface of cells or tissue components. Humoral antibodies participate directly in injuring cells by predisposing them to phagocytosis or lysis. Good examples are transfusion reactions, autoimmune haemolytic anaemia and Goodpasture's syndrome. Initiates within several hours.
- *Type III*. Formation of antibody–antigen complexes (immune complex mediated). Good examples are the Arthus reaction, serum sickness, and SLE. Initiates in several hours.
- *Type IV*. Delayed type of hypersensitivity. Cell-mediated. T-lymphocytes involved. Granulomatous conditions. Contact dermatitis. Initiation time is 24–72 hours.
- *Type V*. Due to the formation of stimulatory autoantibodies in autoimmune conditions such as Graves' disease.

185A: Pain from the transverse colon is usually referred to the midline area below the umbilicus

Referred pain is not well understood. Somatic referred pain is very well localized and intense. Visceral pain is the opposite and conveyed by automatic fibres. Diaphragmatic pain is usually referred to the shoulder. Appendix pain is usually referred to the umbilicus.

186B: Mitosis always produces genetically identical daughter cells

Mitosis is the process of cell division in somatic cells and produces two genetically identical diploid cells. Meiosis occurs in gamete formation and differs from mitosis in two important respects: each daughter cell contains half the genetic information (haploid) and the resultant cells differ in their genetic material. There are two separate phases (or divisions) in meiosis. In the first division, two genetically different haploid cells are formed, and in the second each of the haploid cells divides.

The exchange of genetic material occurs in Prophase I. The cell cycle is controlled internally by gene products called cyclins which vary in concentration throughout the cell cycle. Cyclin-dependent kinases control the activity of cyclins by switching on cyclins through phosphorylation. p53 is an example of a tumour suppressor gene. It normally functions to inhibit the cell cycle. p53 is the most common mutated gene in cancers. It encodes a transcription factor which downregulates the cell cycle preventing the cell from undergoing mitosis. Oncogenes control cell growth and differentiation, examples of which include growth factors, growth factor receptors and nuclear transcription factors.

187D: Genioglossus muscle protrudes the tongue

Call it what you will, but the tongue is composed of striated, voluntary or skeletal muscle, not smooth muscle. The tongue assists in the formation of a food bolus and propagation towards the back of the mouth and thence into the oesophagus. The tongue also plays a key role in the suckling reflex in neonates, in the articulation of speech and the special sense of taste. Its epithelium is composed of stratified squamous (protective) epithelium as, like the skin, it is

subject to 'wear and tear'. Tumours arising from the tongue are therefore typically squamous cell carcinomas.

Special taste sensation is by way of the chorda tympani division of the facial nerve for the anterior two-thirds of the tongue and the glossopharyngeal nerve for the posterior one-third. Taste sensation on the anterior two-thirds of the tongue is therefore commonly lost in a facial nerve (or Bell's) palsy. Somatic sensation is by way of the mandibular division of the trigeminal nerve for the anterior two-thirds of the tongue (lingual nerve) and the glossopharyngeal nerve for the posterior one-third.

All the muscles of the tongue are supplied by the hypoglossal, or 12th cranial nerve, with the exception of the palatoglossus muscle which is supplied by the pharyngeal plexus of nerves (IX, X and sympathetics). The hypoglossal nerve may be injured in a carotid endarterectomy or submandibular gland procedures. The most important muscle to know about is the genioglossus muscle which serves to protrude the tongue. When genioglossal muscle tone is lost, as in someone with a decreased level of consciousness, or a fractured mandible (where the genioglossus muscle arises), the tongue falls back and obstructs the airway, rapidly resulting in hypoxia and death if basic life support measures are not quickly instigated.

188C: The Q-T interval gives a rough indication of the duration of ventricular systole

The nature of the electrocardiogram (ECG) is important to understand. As a junior doctor you will reading and interpreting ECGs every day at work.

- P-wave = atrial depolarization
- QRS complex = ventricular depolarization
- T-wave = ventricular repolarization.

(Electrical activity resulting from atrial repolarization is 'hidden' within the QRS complex.)

The Q-T interval gives a rough indication of the duration of ventricular systole. The first heart sound results from closure of the atrioventricular valves and occurs as the ventricles contract. It therefore coincides with the QRS complex. The second heart sound is due to closure of the aortic and pulmonary valves, respectively, and occurs at about the same time as the T-wave.

189D: May occur in systemic lupus erythematosus

Type III hypersensitivity reactions are mediated by antibodies. Type IV reactions are cell-mediated through specifically sensitized T-lymphocytes. Nickel sensitivity is a type IV hypersensitivity reaction.

Allergic rhinitis is a type I hypersensitivity reaction. Systemic lupus erythematosus (SLE) is a type III hypersensitivity reaction where large amounts of immune complexes form between nuclear antigens and antibodies.

Latex allergies can be one of three types:

- irritant contact dermatitis (non-immune)
- allergic contact dermatitis (type IV hypersensitivity reaction)
- immediate hypersensitivity (type I hypersensitivity reaction or anaphylaxis) – what everyone worries about!

190D: Transpeptidase

Antibiotics act by specifically binding to macromolecules only found in the parasite. Transpeptidase is the only penicillin-binding protein listed; it is inactivated when binding occurs.

191B: Cytosine always pairs with guanine

DNA consists of a right-handed double helix with 10 bases per turn. Adenine and guanine are purine bases; cytosine, thymine (and uracil) are pyrimidine bases (remembered by the 'y' in pyrimidine, thymine, cytosine). Adenine pairs with thymine in DNA via two hydrogen bonds. Adenine pairs with uracil in RNA. Guanine pairs with cytosine in DNA via three hydrogen bonds.

192D:They are all supplied by the inferior thyroid artery

The parathyroid glands are pinkish/brown glands usually found on the posterior aspect of the thyroid gland. There are usually four, two on each side (in 90 per cent of subjects), but this varies from two to six. Each weighs about 50 mg and measures $6 \times 3 \times 2$ mm. The superior parathyroid glands arise from the fourth branchial pouch, whereas the inferior parathyroids are third branchial pouch derivatives. The thymus gland, however, also derives from the third branchial pouch. Therefore, the inferior parathyroid glands may get dragged down with the thymus into the mediastinum, making the position of the inferior parathyroid glands highly variable. The superior glands are more constant in position.

The parathyroid glands are all usually supplied by the inferior thyroid artery. A consequence of this is that the inferior thyroid artery should always be preserved during a total thyroidectomy to prevent ischaemia of the parathyroid glands, which would render the patient hypocalcaemic and necessitate lifelong calcium supplementation.

The parathyroid glands secrete parathyroid hormone from chief (or principal) cells. Parathyroid hormone plays an essential role in calcium homeostasis. Calcitonin, however, is secreted by the parafollicular cells of the thyroid gland. A parathyroid adenoma is a benign tumour of usually one (but sometimes more than one) parathyroid gland that leads to the overproduction of parathyroid hormone and hypercalcaemia. Treatment consists of neck exploration and removal of the problematic parathyroid adenoma (parathyroidectomy). Care must be taken to avoid damaging the recurrent laryngeal nerves. Exposure of the thymus through a median sternotomy may rarely be necessary, given the liability of the inferior parathyroid glands to end up in unusual positions.

193A: In terminally differentiated squamous cells

Warts, caused by papilloma virus, are non-malignant tumours of squamous cells. Infectious papilloma viruses are most likely to be found in terminally differentiated squamous cells, and are not found in either the basal cells, in the surface layers of warts, in transformed cancer cells, or throughout the warts.

194E: May be minimized by blood-group matching

Hyperacute rejection is due to the formation of preformed antibodies against the donor organ. It occurs within minutes of transplantation so the surgeon can usually see the changes taking place as the anastomoses are completed.

The antibodies are usually directed against blood group antigens and it can therefore be minimized by blood-group matching. The blood groups and HLA antigens of autografts (tissue from the same individual) will be identical, so hyperacute rejection will never occur in such circumstances.

No drug treatment can reverse hyperacute rejection; the main treatment is removal of the transplanted organ.

Transplant rejections can be classified into the following types:

- *hyperacute* – preformed antibodies (minutes–hours)
- *accelerated acute* – reactivation of sensitized T-cells and secondary antibody response (days)
- *acute* – cytotoxic T-cell mediated with primary activation of T-cells (days to weeks)
- *chronic* – antibody-mediated vascular damage (months to years, controversial).

195B: Paired t-test

A paired *t*-test allows a comparison of mean potassium values before and after treatment by comparing each patient's initial serum level with his or her repeat value.

196B: Promoters

Transcription of genes is initiated by promoters. Enhancers and silencers are proteins that bind to the promoter region on the DNA and will influence gene transcription. Exons carry the coding sequences of DNA.

197D: Lateral rectus is supplied by the abducens nerve

The extra-ocular muscles are innervated by the 3rd (occulomotor), 4th (trochlear) and 6th (abducens) cranial nerves. The trochlear nerve supplies only one muscle and that is the superior oblique muscle. The abducens nerve also supplies only one muscle and that is the lateral rectus muscle. This may be remembered by 'S04, LR6'. All the remaining muscles are supplied by the occulomotor nerve – that is, the superior rectus, inferior rectus, inferior oblique and medial rectus are all supplied by the occulomotor, or 3rd, cranial nerve. Injury to any of these cranial nerves (3rd, 4th or 6th) may result in ophthalmoplegia and double vision (diplopia).

The recti muscles are easily understood as they move the eyeball in the respective directions indicated by their name. The superior and inferior obliques are more difficult to understand. The superior oblique muscle moves the cornea downwards and outwards, whereas the inferior oblique muscle moves the cornea upwards and inwards. The reason for this is that the oblique muscles pass posteriorly to attach behind the axis of movement and therefore impart movement opposite to their suggested names. Weakness of the extra-ocular muscles may occur in the autoimmune condition, myasthenia gravis.

The levator palpebrae superioris is the exception to the above. It elevates the eyelid but has a dual innervation from both the occulomotor nerve and sympathetic fibres. The latter innervate a small smooth muscle portion of the levator muscle known as Muller's muscle. The clinical significance of this dual innervation is that a 3rd cranial nerve (occulomotor) palsy, or sympathetic interruption (Horner's syndrome), may result in a droopy eyelid (ptosis). To distinguish the two it is essential to lift up the eyelid and inspect the pupil to see if it is enlarged (mydriasis, in an occulomotor nerve palsy) or constricted (miosis, in a Horner's syndrome). Furthermore, in an occulomotor palsy the eyeball points downwards and outwards from the unopposed action of superior oblique and lateral rectus, supplied by the 4th and 6th cranial nerves. Horner's syndrome is associated with hemifacial anhidrosis (absent sweating of the ipsilateral face), flushing symptoms (the so-called Harlequin syndrome or effect) and enophthalmos (a sunken eyeball), in addition to ptosis and miosis.

198B: Nitric oxide

The importance of endothelium in vascular responses was first noted when it was discovered that removing the endothelium from perfused arteries prevented the vasodilator action of acetylcholine on those vessels. The endothelium-derived relaxing factor has since been recognized as nitric oxide (a vasodilator). Vasopressin, angiotensin II, thromboxane A2 and noradrenaline are all vasoconstrictors.

Since its discovery, nitric oxide has been implicated in a diverse array of different biological processes, both physiological and pathological, besides vasodilatation, including:

- acting as a neurotransmitter
- the killing of microorganisms by phagocytes
- long-term potentiation (memory)
- male erection (Viagra enhances the effect of nitric oxide)
- sepsis
- excitotoxicity.

In addition, nitric oxide explains how glyceryl trinitrate exerts its beneficial effect in angina. More and more is being discovered about nitric oxide all the time.

199D: Result from a breakdown in immunological tolerance

Autoimmune diseases result from the direct attack by the host immune system against its own, or self, antigens (autoantigens), usually as a result of a breakdown in immunological tolerance. They are normally acquired, rather than congenital, and for some unknown reason they are more common in women than men. The female preponderance is often taken to imply that sex hormones are involved in the pathogenesis.

It is still unclear as to the exact nature of the stimulus that triggers an autoimmune reaction. The most plausible explanation is that certain exogenous agents (such as a dietary factors, drugs or microbial agents), that share epitopes with self-antigens, stimulate an immune response against both themselves and the host tissues, producing tissue-damaging reactions. This is known as 'molecular mimicry'. However, genetic factors undoubtedly also play a role. For instance, autoimmune diseases are often associated with specific HLA types.

Although in many cases the precise combination of pathogenic mechanisms is not understood, either antibody or T-cells can cause tissue damage in autoimmune disease.

200A: Reed–Sternberg cells

Reed–Sternberg cells are diagnostic for Hodgkin's lymphoma. The Philadelphia chromosome and decreased quantities of leucocytes alkaline phosphatase are commonly observed in chronic myelogenous leukaemia. Auer rods are most often seen in increased numbers in acute myelogenous or myelonocytic leukaemia. Pappenheimer bodies are abnormal iron granules found inside red blood cells. They are associated with sideroblastic anaemia, haemolytic anaemia, and sickle cell disease.

201C: Affects males and females equally

Autosomal dominant disorders affect males and females equally since there is no involvement of the sex chromosomes and autosomes are similar for males and females. Only one of the parents need carry the abnormality for it to be classified as an autosomal dominant disorder; if both parents were required to carry the abnormality it would be an autosomal recessive disorder.

Only half the children of an affected adult would inherit the condition since half would receive the normal autosome. Carriers of an autosomal dominant trait do not exist; carriers of a dominant character exhibit the disease.

Autosomal dominant conditions are commonly transmitted from one generation to the next, either because of their late onset (e.g. Huntington's disease), or because reproduction occurs before death ensues.

202D: Inflammation may cause referred pain to the ear

The palatine tonsils ('tonsils') are a large collection of lymphoid tissue that project into the oropharynx from the tonsillar fossa, between the palatoglossal arch (in front) and the palatopharyngeal arch (behind). They are most prominent in early life and regress in later years as the lymphoid tissue atrophies. The surface marking is medial to the lower masseter. The palatine, lingual, pharyngeal ('adenoids') and tubal tonsils collectively form an interrupted circle of protective lymphoid tissue at the upper end of the respiratory and alimentary tracts known as Waldeyer's ring. This area has a role in the priming of lymphocytes for antigens during the early years of life.

The floor of the tonsillar fossa (lateral wall) is the lower part of the superior constrictor, with styloglossus on its lateral side. The luminal surface of the tonsil is covered by non-keratinized stratified squamous epithelium which deeply invaginates the tonsil forming blind-ended tonsillar crypts. The tonsillar branch of the facial artery (in turn a branch of the external carotid artery) forms the main arterial supply. It enters the tonsil by piercing the superior constrictor.

The main function of the tonsils is immunological, especially within the early years of life. Since they harbour microbes, this makes them vulnerable to infection and inflammation (tonsillitis). Lymphatic channels pierce the superior constrictor to reach the deep cervical nodes, especially the jugulodigastric (or tonsillar) node below the angle of the mandible. This is the lymph node that is most commonly enlarged in tonsillitis (jugulodigastric lymphadenopathy). The mucous membrane overlying the tonsil is supplied mainly by the tonsillar branch of the glossopharyngeal nerve. The glossopharyngeal nerve also supplies the middle ear through its tympanic branch. This explains why tonsillitis commonly causes referred pain to the middle ear. Ear pain may also feature in the early postoperative period after tonsillectomy.

Tonsillectomy (removal of the tonsils) is indicated for recurrent episodes of tonsillitis or obstructive sleep apnoea. Removal does not appear to compromise immune function. The main complication after tonsillectomy is haemorrhage and the usual cause is venous, rather than arterial bleeding, from the external palatine, or paratonsillar, vein. The close proximity of the internal carotid artery (which lies 2.5 cm posterolateral) to the palatine tonsil must be borne in mind at tonsillectomy in order to prevent inadvertent injury.

203B: Local metabolic activity is the chief factor determining rate of blood flow to the heart

Given that there is a high myocardial oxygen demand at rest (around 20 times that of skeletal muscle), certain functional adaptations ensure that supply adequately meets demand.

- The heart receives 4–5 per cent of the cardiac output.
- There is a high capillary density.
- There is a high oxygen extraction ratio. The myocardium extracts around 70 per cent of the oxygen that is delivered to it from the coronary blood. In contrast, the body average is only 25 per cent.
- There is efficient metabolic hyperaemia, where local metabolism is the dominant controller of coronary flow. The extra oxygen required at high work rates is supplied chiefly by an increase in blood flow rather than an increase in the oxygen extraction ratio.

Unlike other vascular beds, the coronary flow to the left ventricle is greatest in diastole. This occurs because of the mechanical compression of the coronary vessels during systole, such that there is reversal of the transmural pressure gradient across the vessel wall, leading to momentary occlusion. Coronary perfusion is reduced in aortic stenosis (narrowing) because the coronary ostia lie distal to the aortic valve. This is why patients with aortic stenosis get angina.

In hypothermia there is a fall in metabolic rate and cardiac output. This reduces cardiac work, resulting in a decrease in the rate of production of vasodilator metabolites (adenosine, carbon dioxide etc.). The reduction in coronary artery perfusion pressure explains why angina is commonly triggered by exposure to the cold.

204B: Gram-positive bacteria retain an iodine purple dye complex

Microorganisms can be classified into bacteria, viruses, fungi, protozoa and parasites. Bacteria can be classified according to their:

- staining properties – Gram-positive, Gram-negative, acid-fast etc.
- morphology – round (cocci), rods (bacilli), spiral (spirochaetes), comma-shaped (vibrio), flagellated, possession of a capsule etc.
- oxygen requirements – aerobic or anaerobic; obligate or facultative
- ability to form spores – spore-forming or non-spore forming.

In Gram-positive bacteria, the peptidoglycan forms a thick (20–80 nm) layer external to the cell membrane. In Gram-negative species the peptidoglycan layer is thinner (only 5–10 nm) but is overlaid by an outer membrane. The principal molecules in the outer membrane of Gram-negative bacteria are lipopolysaccharides.

These structural differences form the basis of the Gram stain. Gram-positive bacteria are able to retain an iodine purple dye complex when exposed to a brief alcohol wash. Gram-negative bacteria have a smaller cell wall but a higher lipid content and as a result the alcohol washes away the purple dye. Gram-positive bacteria appear blue and Gram-negative bacteria are counter-stained with a pink dye.

As a general rule:

- all cocci are Gram-positive (except *Neisseria* which causes meningitis and gonorrhoea)
- all bacilli are Gram-negative (except *Clostridia*, Mycobacteria and the organisms that cause anthrax, listeria, diphtheria and actinomycosis).

The lipopolysaccharide (LPS) in the outer membrane of Gram-negative bacteria is a complex molecule found nowhere else in nature and is an important factor in bacterial survival in the mammalian host. It consists of three portions:

- A lipid portion (lipid A) embedded in the outer membrane (the damaging endotoxin). As it is embedded in the outer membrane it exerts its effects only when bacteria lyse.
- A conserved core polysaccharide.
- The highly variable O-polysaccharide (O-antigen), responsible for antigenic diversity. It has been hypothesized that such structural variability is an attempt by the bacterium to evade host defences.

Endotoxins are not in themselves toxic (unlike exotoxins) but they can induce toxic effects due to their potent activation of the complement cascade, coagulation cascade and stimulating the release of powerful cytokines (such as TNFα, IL-1 etc.) from leucocytes. In overwhelming infections, the patient is said to suffer from endotoxic shock.

205C: Inferior mesenteric artery

The artery to the hindgut and its derivatives is the inferior mesenteric artery. The coeliac artery supplies structures derived from the caudal foregut. In the fetus, the ductus arteriosus shunts blood from the pulmonary trunk to the aorta to bypass the lungs. The superior mesenteric artery supplies the structures derived from the midgut. In the fetus, the umbilical artery delivers blood to the placental circulation.

206E: Marfan's syndrome

As a general rule, disorders that affect metabolic pathways/enzymes are autosomal recessive, whereas diseases that affect structural proteins are autosomal dominant. Thus Marfan's syndrome, Huntington's disease and neurofibromatosis (Von Recklinghausen's disease) are examples of autosomal dominant conditions as they affect structural proteins. Cystic fibrosis and phenylketonuria are autosomal recessive since they affect metabolic pathways.

Haemophilia A, haemophilia B (or Christmas disease) and red/green colour-blindness are examples of sex-linked conditions.

207C: Trapezius

The spinal accessory nerve is a branch of the 11th cranial nerve. It has been given the name spinal accessory since it originates from the upper end of the spinal cord (spinal roots, C1–C5). It passes through the foramen magnum and 'hitches a ride' with the cranial accessory nerve originating from the nucleus ambiguus. It passes out of the skull again by way of the jugular foramen. Its function is to supply only two muscles in the neck – the sternocleidomastoid and trapezius muscles.

Stylopharyngeus is innervated by the glossopharyngeal nerve and palatoglossus is supplied by the pharyngeal plexus (IX, X, sympathetics). Buccinator, on the other hand, is regarded as a muscle of facial expression and is therefore innervated by the facial nerve. Consequently, in a facial nerve (Bell's) palsy, food may collect in the vestibule of the mouth.

The surface marking of the spinal accessory nerve is important. It traverses the posterior triangle of the neck from one-third of the way down the posterior border of the sternocleidomastoid muscle to one-third of the way up the anterior border of trapezius where it terminates (the 'rule of thirds'). It is vulnerable to iatrogenic injury in procedures that necessitate dissection within the posterior triangle of the neck, such as excision biopsy of a lymph node. In a radical en-bloc lymph node dissection of the neck for malignant disease, the spinal accessory nerve may have to be sacrificed deliberately in order to obtain satisfactory clearance.

Damage to the spinal accessory nerve in the posterior triangle of the neck leads to a predictive weakness of the trapezius muscle. This results in an inability to shrug the shoulder on the side in which the spinal accessory nerve is affected. The sternocleidomastoid muscle is typically spared

as the branch to sternocleidomastoid is given off prior to the spinal accessory nerve entering the posterior triangle of the neck. The trapezius muscle also plays a role in hyperabduction of the arm and so activities such as combing one's hair would become more difficult. In the long term, a trapezius palsy (with dropping of the shoulder) may result in a chronic, disabling neuralgia. This may occur as a result of pain from neurological dennervation, adhesive capsulitis of the shoulder joint, traction radiculitis of the brachial plexus or, more commonly, from fatigue.

208A: Purkinje fibres lead to contraction of the apex before the base of the heart

The group of cells that show the highest automaticity (that is, the cells with which the resting membrane potential drifts towards the threshold fastest) dictates the overall heart rate and is accordingly called the primary intrinsic pacemaker of the heart. These are normally the pacemaker cells from the sinoatrial (SA) node which discharge at about 60–80 times/min. The SA node is found in the right atrium near its junction with the superior vena cava. The SA node receives a rich innervation from both arms of the autonomic nervous system (sympathetic and parasympathetic). By this means they can exert a powerful extrinsic influence on the heart.

Atrial fibres conduct impulses from the SA node to the atrioventricular (AV) node. The AV node provides the only communication in the normal heart between the atria and ventricles. Conduction through this node is slower than the remaining myocardium; this synchronizes the sequential atrial and ventricular contraction. Purkinje fibres are confined to the ventricles.

Impulse generation is due to spontaneous diastolic depolarization of the cells. The SA node has intrinsic rhythmicity and can generate impulses independently, even when completely dennervated.

Purkinje fibres are larger than ventricular myocardial cells and this facilitates the rapid spread of depolarization over the entire ventricular myocardium. Purkinje fibres travel to the apex before proceeding to the base of the heart. This arrangement enables the activation wave to spread from the apex to the base of the ventricles. The resulting pattern of activation leads to a ventricular contraction from apex to base which optimizes the extrusion of blood from the chambers.

Problems with cardiac conduction are commonly encountered in clinical practice. Arrhythmias are the commonest cause of death following a myocardial infarction. In the event that the SA node function is abnormal, as in sick sinus syndrome, or following myocardial ischaemia, other sites with a slower intrinsic rate can substitute the role of the pacemaker, resulting in an escape rhythm.

209D: Neisseria meningitidis

The spleen plays an important role in the removal of dead and dying erythrocytes and in the defence against microbes. Removal of the spleen (splenectomy) leaves the host susceptible to a wide array of pathogens but especially to encapsulated organisms.

Certain bacteria have evolved ways of evading the human immune system. One way is through the production of a 'slimy' capsule on the outside of the bacterial cell wall. Such a capsule resists phagocytosis and ingestion by macrophages and neutrophils. This allows them not only to escape direct destruction by phagocytes but also to avoid stimulating T-cell responses through the presentation of bacterial peptides by macrophages. The only way that such organisms can be defeated is by making them more palatable by coating their capsular polysaccharide surfaces in opsonizing antibody.

The production of antibody against capsular polysaccharide primarily occurs through T-cell independent mechanisms. The spleen plays a central role in both the initiation of the antibody response and the phagocytosis of opsonized encapsulated bacteria from the bloodstream. This helps to explain why following a splenectomy the host is most susceptible to infection by encapsulated organisms, notably *Streptococcus pneumoniae* (Pneumococcus), *Neisseria meningitidis* (Meningococcus) and *Haemophilus influenzae*.

Understanding the above, one can quickly envisage what preventative strategies must be employed post-splenectomy. Patients are given relevant vaccinations and are advised to take

prophylactic penicillin, in most cases for the rest of their lives. In addition, they are advised to wear a Medic Alert bracelet to warn other healthcare professionals of their condition.

210C: Right hepatic artery

The cystic artery most commonly arises form the right hepatic artery. In decreasing order of occurrence, it can also arise from the left hepatic artery, gastro-duodenal artery, or hepatic artery proper. The superior pancreatico-duodenal artery is located too inferiorly to contribute to the blood supply to the gall bladder.

211C: Fifty per cent

The key to this question is to understand that, in order to have a child with an autosomal recessive disease, both parents must carry the gene; so although the mother may have the disease, the father has to be a carrier. The question fails to inform you that he has the disease, so you can safely assume that he carries only one abnormal gene. To be a carrier for an autosomal recessive disease, you will have one normal and one abnormal copy of the gene. As his mother carries both abnormal genes, and his father carries one abnormal gene and one normal gene, there is a 50 per cent chance that the teenager has the disease and a 50 per cent chance that he is a carrier.

Phenylketonuria (PKU) is an inborn error of metabolism. As a result of a specific enzyme deficiency, phenylalanine accumulates. The enzyme block leads to a deficiency of tyrosine, leading to a reduction in melanin; thus children often have blue eyes and blonde hair. Pigmented areas of the brain are affected, such as the substantia nigra. PKU is tested for at birth in children using the Guthrie test. PKU can be treated by removing phenylalanine from the diet. If PKU is detected early enough in childhood, mental retardation can be prevented.

212C: Secreto-motor innervation is via the glossopharyngeal and auriculotemporal nerves

The parotid gland is the largest of the major salivary glands. It is mainly a serous gland, with only a few scattered mucinous acini. This in part explains why salivary stones (calculi) are rarely encountered in the parotid gland and are found more often in the submandibular gland, where the secretion is more mucinous and where the gland lies below the opening of the duct (which impedes drainage and encourages stasis).

Anteriorly, the gland overlaps the masseter. The parotid duct (of Stensen), not to be confused with Wharton's duct (which is the submandibular duct), passes forward over the masseter and turns around its anterior border to pierce the buccinator (not masseter) muscle. The buccinator muscle acts like a sphincter at this point and plays an extremely important role in preventing the reflux of air into the parotid (and hence its insufflation) when the intraoral pressure is raised, as when playing a trumpet. The duct opens on the mucous membrane of the cheek opposite the second upper molar tooth.

The parotid gland consists of two lobes, superficial and deep. Hence the importance of looking in the mouth in cases where a parotid swelling is present, to look for, or exclude, involvement of the deep lobe. There is no middle lobe, although there may be an accessory lobe. The parotid is surrounded by a tough fascial capsule, derived from the investing layer of deep cervical fascia, that is richly innervated. It is the acute swelling of this fibrous envelope that produces the pain of mumps parotitis, a virus infection of the gland.

From superficial to the deep within the parotid lie the following:

- five terminal branches of the facial nerve (also known as the pes anserinus, or 'goose's foot')
- retromandibular vein
- external carotid artery.

The branches of the facial nerve lie most superficially within the parotid gland and hence are extremely vulnerable to damage in parotid surgery. Thus, if the retromandibular vein comes into view, it is too late; the facial nerve has already been severed! It is important to identify and protect

the various branches of the facial nerve, which may be remembered by the mnemonic 'ten Zulus baited my cat' (from top to bottom):

- ten = **t**emporal branch
- Zulus = **z**ygomatic branch
- baited = **b**uccal branch
- my = **m**arginal mandibular branch
- cat = **c**ervical branch.

The branches of the facial nerve are also likely to be injured by a malignant tumour of the parotid which is usually highly invasive and quickly involves the facial nerve, causing a facial paralysis.

The secreto-motor supply to the parotid (for secretion of saliva) is by way of parasympathetic fibres of the glossopharyngeal nerve, synapsing in the otic ganglion and relaying onwards to the parotid gland through the auriculotemporal nerve. The importance of knowing this lies in a phenomenon known as Frey's syndrome which may occur, not infrequently, following parotid surgery, or penetrating trauma to the parotid gland. It is caused by misdirected reinnervation of the auriculotemporal nerve fibres to the sweat glands in the facial skin following its injury. The patient may complain of gustatory sweating (i.e. a stimulus intended for saliva production produces sweating instead).

213D: They lack nuclei and mitochondria

Erythrocytes do not contain nuclei (they are anucleate) or mitochondria. This maximizes the haemoglobin-carrying capacity of red cells. The absence of mitochondria precludes aerobic energy production; hence they are very efficient oxygen transporters because they do not consume any O_2 directly. Erythrocytes are thus totally dependent on the anaerobic metabolism of glucose to generate the energy needed to maintain electrochemical gradients across their cell membranes.

Without nuclei, erythrocytes are unable to replace deteriorating enzymes and membrane proteins; this shortens their life expectancy. The average lifespan of a normal erythrocyte is 120 days (or 16–18 weeks). Lifespan may be reduced further as a result of the premature destruction of red cells. This is a feature of haemolysis. Aged red cells are removed from the circulation by the spleen and liver.

Erythrocytes contain the enzyme carbonic anhydrase that catalyses the reaction $CO_2 + H_2O = H^+ + HCO^{3-}$ and requires zinc as a cofactor. This plays an important role in carbon dioxide transport and in the buffering of pH.

Erythrocytes do not burst when placed in 0.9% (normal) saline, since this is isotonic with their contents.

214B: It is a known carcinogen

Helicobacter pylori is a Gram-negative, micro-aerophilic, motile, spiral-shaped bacterium which selectively colonizes the mucous layer of the stomach and duodenum. Around 50 per cent of all humans worldwide are infected with the organism. However, it seems to cause disease only in a small proportion of all those infected. It is still unclear at present as to why this is the case but it probably reflects differences in virulence among different strains, along with differences in the background genetics of the host that affects their susceptibility to the organism.

It is now firmly established that *H. pylori* causes more than 90 per cent of duodenal ulcers and up to 80 per cent of gastric ulcers. The link between *H. pylori* infection and subsequent gastritis and peptic ulcer disease has been established through studies of human volunteers, antibiotic treatment studies and epidemiological studies. *H. pylori* is also a known risk factor for gastric adenocarcinoma and lymphoma. Indeed, *H. pylori* has been classified as a class 1 (definite) carcinogen for malignancy.

H. pylori is unique among bacteria in being able to survive within the acidic environment of the stomach. It achieves this by producing a urease enzyme which produces ammonia from

endogenous urea, thereby buffering gastric acid in the immediate vicinity of the organism. The elaboration of urease by *H. pylori* forms the basis of the urea breath test that may be used in the diagnosis of *H. pylori* infection.

H. pylori is treated with antibiotic therapy. *H. pylori* eradication therapy (also known as triple therapy) usually consists of a proton pump inhibitor in conjunction with two antibiotics. At present, there is no known vaccination against *H. pylori*. However, development of a vaccine against *H. pylori* would have the potential to prevent peptic ulcer disease and perhaps even gastric carcinoma.

215A: A- and B-cells

In the pancreas, A- and B-cells of the Islets of Langerhans secrete glucagons and insulin, respectively. Pancreatic D1 cells release a product similar to vasoactive intestinal polypeptide (VIP). Pancreatic polypeptide cells secrete pancreatic polypeptide and D-cells secrete somatostatin. Acinar cells are part of the exocrine, not endocrine, pancreas and are involved in the release of enzymes and digestive juices, rather than hormones.

216A: 45XO

This is Turner's syndrome. It is a chromosome disorder caused by the lack of the Y chromosome (45XO). Features include widely spaced nipples, short stature, webbed neck, a kinked aorta (coarctation of aorta), primary amenorrhoea, high arched palate. 47XXY is Klinefelter's syndrome which is associated with tall stature.

217C: The pituitary and sphenoidal air sinus lie in its medial wall

The cavernous sinus is one of those tricky areas that is difficult to get one's head around. It consists of a plexus of veins that lies alongside the sphenoid in the middle cranial fossa. Blood can flow in either direction in the cavernous sinus, depending on local venous pressures. In addition, there are no valves in the cavernous sinus or its connected veins.

The function of the cavernous sinus is unclear. However, since it surrounds the internal carotid artery, which forms the main blood supply to the brain, some have suggested that the cavernous sinus may have evolved to act as a cooling system for the brain. A sort of counter-current mechanism is set up whereby the venous blood contained within the cavernous sinus may actually draw out heat from the internal carotid artery at its centre. However, rupture of the internal carotid artery within the cavernous sinus (usually a result of an internal carotid artery aneurysm, or following trauma) may result in a carotico-cavernous fistula.

The walls of the cavernous sinus may be summarized as follows:

- Roof – anterior and posterior clinoid processes with uncus of temporal lobe and internal carotid artery on it, cranial nerves III and IV
- Floor – greater wing of sphenoid
- Anterior wall (narrow) – medial end of superior orbital fissure, ophthalmic veins, orbit
- Posterior wall (narrow) – dura of posterior fossa, superior and inferior petrosal sinuses, peduncle of brain
- Medial wall – dura over sphenoid, sella turica, pituitary, sphenoidal air sinus
- Lateral wall – dura, temporal lobe, cranial nerves III, IV, Va, Vb in wall (from top to bottom)
- Contents – internal carotid artery (with its associated sympathetic plexus), cranial nerve VI, blood.

Note that the optic nerve is not contained within the cavernous sinus.

The area of facial skin bounded by the upper lip, nose, medial part of cheek and the eye is a potentially dangerous area to have an infection (the so-called 'danger area of the face'). An infection in this area may result in thrombosis of the facial vein, with spread of organisms through the inferior ophthalmic vein to the cavernous sinus. This may result in a cavernous sinus thrombosis. By the superficial middle cerebral vein, such thrombosis may spread to the cerebral hemisphere, which may be fatal unless adequately treated with antibiotics.

218E: They deform as they pass through the capillaries

Unstressed erythrocytes normally appear as biconcave discs. This provides a 20–30 per cent greater surface area than a sphere relative to cell volume, thus significantly enhancing gaseous exchange. This shape, with the fluidity of the plasma membrane, allows the erythrocyte to deform easily thus making them able to pass through the smallest capillaries. Erythrocytes appear spherical in a genetic condition known as hereditary spherocytosis.

Normal red blood cells are around 7 microns in diameter, whereas the diameter of capillaries is only around 5 microns. Red cells possess deformable walls and therefore become bullet-shaped as they pass through capillaries. This enables 'bolus flow' or 'plug flow' which eliminates some of the internal friction associated with lamina sliding over one another (Fahraeus–Lindqvist effect). The reduction in apparent viscosity means that capillaries have a lower resistance to flow than they would do if the blood were a uniform fluid containing the same amounts of protein without the red cell membrane to parcel it up. The efficiency of bolus flow depends critically on the deformability of the red cell, and this is impaired in many clinical conditions. The most dramatic of these is sickle cell anaemia.

Erythrocytes make a major contribution to the buffering capacity of the blood through the action of carbonic anhydrase and haemoglobin contained within the red cells. Indeed, red cells are responsible for most of the buffering power of whole blood.

Erythropoiesis (the production of red cells) is stimulated by the hormone erythropoietin, but the main source of erythropoietin is the kidney, not erythrocytes.

The capillary bed has a greater cross-sectional area than the venular bed. Blood therefore travels more slowly in capillaries compared to venules. This prolongs the time available for gaseous exchange. Red cells are not evenly distributed across the bloodstream in large blood vessels, but form an axial stream away from the vessel wall, leaving a cell-deficient layer of plasma at the margins. This marginal layer helps to ease the blood along.

219D: Is caused by a toxin which increases adenylate cyclase activity

Cholera is caused by *Vibrio cholerae*, a Gram-negative, comma-shaped, flagellated bacterium. It is usually transmitted by contaminated water supplies, as deduced from the famous epidemiological work of John Snow in the 1850s, who was able to trace a cholera outbreak in London to a single water pump that had become contaminated with sewage. Removing the handle of the water pump led to a dramatic reduction in the number of new cases of cholera.

The diarrhoea of cholera is caused by the action of an exotoxin or enterotoxin (not endotoxin) called cholera toxin. The toxin increases the activity of adenylate cyclase resulting in the massive secretion of chloride, sodium and water (so-called 'rice-water diarrhoea'). The watery diarrhoea may be so extreme that death may occur from dehydration and electrolyte imbalance. The mucosa is not invaded by the bacteria (in contrast to *Salmonella*, *Shigella* and *Campylobacter*) so that mucosal inflammation is only slight and there is no ulceration.

Overall absorption from the gut remains intact so that oral rehydration therapy can replace massive fluid and electrolyte losses, reducing the mortality from 50 per cent to less than 1 per cent. Antibiotics (such as tetracyclines) are used as an adjunct to fluid therapy. Antibiotics diminish the duration and volume of the fluid loss and hasten clearance of the organism from the stool.

220C: Parotid salivary gland

The glossopharyngeal nerve provides parasympathetic innervation for the parotid salivary gland, via the auriculotemporal nerve. The facial nerve supplies the parasympathetic innervation of the lacrimal, nasal, sublingual and submandibular glands.

221D: The risk of having a child with Down's syndrome is approximately 1 in 1000 if the mother is 30 years old

Down's syndrome is trisomy 21. It arises in approximately 1 in 700 births, but there is a strong association between the incidence and advancing maternal age. When the mother is 30 years old, her

risk of having a child with Down's syndrome is 1 in 1000. Affected children have a lower intelligence quotient (IQ). Classical features include epicanthic folds, a protruding tongue, a single palmar crease, a wide gap between the first and second toe, cardiac anomalies including atrial and ventricular septal defects. Early death occurs in 15–20 per cent of cases and is usually cardiac-related.

A large proportion of (but not all) individuals will develop Alzheimer's disease in later life. This is believed to occur through a gene dosage effect and the accumulation of amyloid precursor protein (APP, the protein linked to Alzheimer's) which is coded for by chromosome 21.

The extra chromosome arises in 94 per cent of cases from non-dysjunction at maternal Meiosis I. Robertsonian translocations account for 5 per cent of cases. One per cent of cases occur due to mosaicism.

222B: Buccinator

There are four muscles of mastication: temporalis, masseter, medial pterygoid and lateral pterygoid. They are all first branchial arch derivatives and are therefore all innervated by the same nerve (mandibular division of trigeminal, or Vc).

The buccinator muscle is regarded as a muscle of facial expression and is therefore a second branchial arch derivative innervated by the facial, or 7th, cranial nerve. This is one of many situations in which a good knowledge of embryology and especially the branchial arches may help to predict the anatomy.

223D: It is reversed by plasmin (fibrinolysin)

One of the drawbacks of having a high-pressure circulation is that even slight damage to blood vessels, especially on the arterial side, can lead to a rapid loss of circulatory blood volume. To prevent bleeding we have developed quite complicated responses to vessel damage designed to stop bleeding. Three key physiological events occur upon the onset of bleeding:

- vasoconstriction
- platelet aggregation to form the primary haemostatic plug
- activation of the clotting cascade to form a fibrin plug (secondary or stable haemostatic plug).

The balance of all components – vessel wall, platelets, adhesive and coagulation proteins and regulatory mechanisms – determines the effectiveness of the haemostatic plug in maintaining the structural and functional integrity of the circulatory system.

Blood platelets are formed from megakaryocytes in the bone marrow. They are anucleate, but the cytoplasm contains electron-dense granules, lysosomes and mitochondria. Each megakaryocyte is responsible for the production of around 4000 platelets. The half-life of platelets in the blood is about 8–12 days.

The clotting cascade involves a series of several highly specific serine proteases which activate each other in a stepwise manner. In this way a rapid response is achieved because at each step the signal is amplified. Clotting factors are produced in the liver so that liver failure results in a tendency to bleed (anticoagulant state). The final stage of the clotting cascade involves the conversion of fibrinogen to fibrin; this is catalysed by thrombin, not prothrombin, which is the inactive precursor of thrombin.

Plasmin acts as a regulatory mechanism to keep the clotting cascade in check and to prevent the over-clotting of blood which could have disastrous consequences (such as the occlusion of blood vessels). It degrades both fibrin and fibrinogen to products that can inhibit thrombin. Fibrinolytic agents are widely used in clinical practice, a good example being the use of thrombolytics in acute myocardial infarction.

224C: It is the second commonest human carcinogen worldwide

A third of the world's population are currently infected with the hepatitis B virus. Hepatitis B is a double-stranded DNA virus, usually transmitted haematogenously, by sexual intercourse, or vertically from mother to baby. Hepatitis A (not hepatitis B) is acquired by the faeco-oral route.

Infection during childhood leads to a high rate of chronic carriage of the virus, with only 10 per cent of children clearing the virus. This chronic carrier state is associated with long-term complications in later life. Ninety per cent of adults, on the other hand, clear the virus, with only 10 per cent of adults becoming chronic carriers of the virus.

Hepatic complications of hepatitis B infections include:

- acute viral hepatitis
- fulminant hepatic failure
- chronic active and chronic persistent viral hepatitis
- cirrhosis
- hepatocellular carcinoma.

Chronic carriage of the virus is facilitated by the ability of the hepatitis B virus to integrate into the DNA and to infect hepatocytes which normally express low levels of MHC class I on their cell surface. Both these strategies help the virus to evade the host's defence mechanisms. Damage to the liver usually results from the host's immune response in an attempt to clear the virus (so-called immune pathology).

It is now well recognized that hepatitis B is a risk factor for the development of primary liver cancer (hepatocellular carcinoma). Indeed, after tobacco smoking, hepatitis B is the second most common human carcinogen worldwide.

Hepatitis B is effectively prevented (not treated) by hepatitis B vaccination. Vaccination is mandatory for all healthcare professionals who regularly come into contact with blood products. Hepatitis B is treated with serum immunoglobulin and antiviral agents (α-interferon, lamivudine).

225E: 23 years of age

Fusion of the ilium, ischium and pubis at the acetabulum is usually complete by the age of 23. From birth to the early twenties, the three bones are held together by Y-shaped cartilage.

226E: Exhibits a genetic phenomenon known as 'anticipation'

Huntington's disease is a late-onset, autosomal dominant disorder characterized by CAG trinucleotide repeat sequences within the *huntingtin* gene on chromosome 4 (myotonic dystrophy is a CTG trinucleotide repeat disorder). This translates into poly-glutamine repeats within the huntingtin protein (not the fibrillin protein which forms the basis of Marfan's syndrome).

Huntington's disease is characterized clinically by a triad of choreiform (dance-like) movements, cognitive changes and psychiatric disturbances. It is Parkinson's disease that is characterized clinically by a triad of bradykinesia, rigidity (which may be of the lead-pipe or cog-wheel variety) and resting tremor. Histologically, Huntington's disease is characterized by atrophy and loss of neurones in the caudate nucleus and putamen.

It is also important to appreciate that Huntington's disease exhibits a genetic phenomenon known as 'anticipation'. This simply means that both the age of onset and severity of the disease phenotype alters with successive generations as a result of the unstable trinucleotide repeat sequence.

227B: The anterior communicating artery joins the two anterior cerebral arteries

The internal carotid and vertebral systems anastomose with each other around the optic chiasm and infundibulum of the pituitary stalk at the base of the brain, forming the arterial Circle of Willis. The circle is formed in the following way:

- *Posteriorly*. At the lower border of the pons, two vertebral arteries combine to form the basilar artery. At the upper border of the pons, the basilar artery terminates as right and left posterior cerebral arteries.
- *Anteriorly*. Each internal carotid artery gives off an anterior and middle cerebral artery.

The circle is completed anteriorly by the single, anterior communicating artery which connects the two anterior cerebral arteries. The circle is completed posteriorly by the two posterior

communicating arteries that connect the posterior cerebral arteries with the internal carotid arteries.

The communicating vessels allow equalization of blood flow between the two sides of the brain and can allow anastomotic compensation if parts are occluded. However, compensation is not always effective owing to the small size of the blood vessels and a stroke (or cerebrovascular accident) may result.

Congenital berry aneurysms are abnormal dilatations of blood vessels, usually located around the Circle of Willis (because here the tunica media is weakest). Rupture of an aneurysm of the arterial circle accounts for 90 per cent of subarachnoid haemorrhages.

228D: Interstitial fluid hydrostatic pressure is normally negative

Four primary forces determine the movement of fluid across the capillary membrane (Starling's forces):

- capillary hydrostatic pressure – 'forces fluid out'
- plasma colloid osmotic pressure – 'pulls fluid in'
- interstitial fluid hydrostatic pressure – 'pushes fluid in'
- interstitial fluid colloid osmotic pressure – 'pulls fluid out'.

At the arterial end of the capillary, the capillary hydrostatic pressure exceeds the plasma colloid osmotic pressure and fluid is drawn out of the capillary into the interstitium. By this means transport of nutrients to the tissues occurs. However, as one moves along the capillary the capillary hydrostatic pressure falls such that, at the venous end of the capillary, the plasma colloid osmotic pressure exceeds the capillary hydrostatic pressure and fluid moves back into the capillary, removing cellular excreta. In this way, about 90 per cent of the fluid that has filtered out of the arterial ends of capillaries is reabsorbed at the venous ends. Only the remainder flows into the lymph vessels.

Interstitial fluid hydrostatic pressure is normally subatmospheric (negative). This results from the suction effect of the lymphatics returning fluid to the circulation. This maintains the structural integrity of the tissues, keeps the interstitial spaces small and reduces distances for diffusion.

Movement of lymph in one direction along the lymphatics depends on:

- filtration pressure from capillaries
- action of local muscles
- action of local arterial pulsation
- respiratory movement (thoraco-abdominal pump) with intermittent negative pressures in the brachiocephalic veins
- smooth muscle in the walls of larger lymphatics (sympathetically controlled)
- valves within.

Oedema (excess fluid accumulation in the extracellular spaces) results from:

- elevated capillary pressure
- decreased plasma colloid osmotic pressure
- increased interstitial fluid protein
- increased capillary permeability
- blockage of lymph return (lymphoedema).

Diffusion distances are greatly increased as a result of oedema and this can interfere with cell nutrition.

229D: Establishes persistence through antigenic variation

HIV is an enveloped RNA retrovirus containing two copies of genomic RNA and three viral enzymes (reverse transcriptase, protease and integrase). HIV RNA is transcribed by viral reverse

transcriptase into DNA that integrates into the host-cell genome. HIV is transmitted by three routes: sexual contact, blood-borne transmission (transfusions or contaminated needles), or vertically from mother to baby (transplacental or via breast milk).

The CD4 antigen on helper T-cells is the receptor for the gp120 viral envelope protein, allowing HIV to infect CD4 T-cells (helper T-cells). The destruction of CD4 cells is central to the pathogenesis of HIV infection. CD4 cells play a pivotal role in the orchestration of both humoral and cell-mediated immune responses. Therefore, by directly infecting and eliminating CD4 cells, the HIV virus leads to a slow and progressive decline in immune function. The end result is AIDS (acquired immunodeficiency syndrome) where the body opens up a whole range of opportunistic infections, the consequences of which are often fatal.

There are several ways in which the HIV evades the host immune system and establishes persistence. For example:

- by directly infecting cells of the immune system, thereby enabling the virus to 'hide' from the immune system
- by infecting macrophages and dendritic cells in addition to CD4 cells, thereby establishing an important reservoir of infection in lymphoid tissues and forming a site for continued viral replication
- by directly integrating into the host cell DNA
- by constantly mutating in a process known as antigenic variation.

The generation of new antigenic variants is primarily a function of the high intrinsic error rate present in the reverse transcriptase enzyme (1 in 1000 base-pair error rate). The huge number of variants of HIV in a single infected patient during the course of infection eventually swamps the immune system, leading to its collapse.

230E: Tremor

Hyperthyroidism is associated with tremor, tachycardia, low serum cholesterol and hyperreflexia. All the other options are classical findings of hypothyroidism.

231C: It is the most common inherited disease in Caucasians

Cystic fibrosis (also known as mucoviscidosis) is an autosomal recessive condition, caused by a genetic mutation in the cystic fibrosis transmembrane regulator (CFTR) on chromosome 7. It is the most common inherited disease in Caucasians, affecting 1 in 2500 children. Cystic fibrosis carriers are believed to offer a selective advantage to the population by being relatively more resistant to cholera. This may explain the fact that, on the basis of the frequency of affected homozygotes in the white population, 2–4 per cent must be heterozygote carriers (using the Hardy–Weinberg equation).

Clinical manifestations relate mainly to the lungs (chronic lung infections, especially caused by *Pseudomonas aeruginosa*, bronchiectasis) and the digestive system (meconium ileus, pancreatic insufficiency, failure to thrive). There is no cure for cystic fibrosis. Treatment is mainly supportive, through a multidisciplinary approach, consisting of vigorous chest physiotherapy, mucolytics, antibiotics to treat chest infections, pancreatic enzyme replacement (Creon), and in some cases heart–lung transplantation may be an option in the final stages of the disease. Life expectancy is markedly reduced with a median survival of around 35 years. End-stage lung disease is the principal cause of death.

Gene therapy is not a well-established treatment option and is still best confined to clinical trials. The main problems that have been encountered in the application of gene therapy to clinical practice concern the targeting of vectors to specific sites and integration into the genome.

232C: A subdural haematoma lies in the plane between the dura and arachnoid mater

The pia mater is to brain as periosteum is to bone. The pia mater is therefore the innermost layer of the meninges and invests the central nervous system to the depths of the deepest fissures and sulci.

The dura mater is the outermost layer of the meninges closest to the bone. It consists of two layers, an outer endosteal layer and inner meningeal layer. The two layers separate to enclose the venous sinuses and folds of the inner layer project into the cranial cavity and are responsible for the formation of the four fibrous flanges, or septa, that minimize rotatory displacement of the brain (the falx cerebri, the falx cerebelli, tentorium cerebelli, diaphragma sellae). The dura mater is richly innervated and therefore dural stretch causes pain that is commonly experienced as a headache. Two good examples are the headache of meningitis which is caused by inflammation of the meninges, and a post-lumbar puncture headache where a headache results from the stimulation of sensory nerve endings in the dura after removal of cerebrospinal fluid.

The arachnoid mater is a delicate membrane that sits in between the dura and pia mater. It is connected to the pia mater by many fine filamentous processes (hence the name arachnoid, or spider-like). The region between the pia and arachnoid mater is the subarachnoid space, filled with cerebrospinal fluid. The term 'leptomeninges' refers to the arachnoid and pia mater.
A good understanding of the various meningeal layers is necessary in order to understand the various types of intracranial haemorrhage that may occur.

An extradural haematoma occurs between the endosteal layer of the dura mater and the skull. It is commonly the result of trauma with bleeding from the middle meningeal artery. It is often associated with an underlying fracture (commonly in the region of the pterion which is the surface marking for the anterior branch of the middle meningeal artery that is commonly implicated). Containment of the arterial bleed may lead to a lucid interval until the pressure builds up to such a point that compression of the brain occurs with resulting coma.

A subdural haematoma is often a result of venous bleeding in the space between the dura and arachnoid mater. It commonly occurs in the elderly, demented, or alcoholics where shrinkage of the brain occurs. This stretches the bridging veins that run across the surface of the brain and makes them vulnerable to tearing. Since the bleed is venous rather than arterial, lower pressures result in a more gradual accumulation of blood than an arterial bleed. The result is a gradual deterioration in cognitive function and patients often present with confusion (chronic subdural haematoma).

A subarachnoid haematoma is an arterial bleed that occurs in the subarachnoid space, between the pia and arachnoid layers. This usually follows rupture of a berry aneurysm in the region of the Circle of Willis. This causes blood to contaminate the cerebrospinal fluid, which is visible at lumbar puncture.

Finally, an intracerebral bleed occurs within the brain parenchyma itself and is therefore unrelated to the cranial meninges.

233B: Cerebral blood flow is very sensitive to changes in the pCO_2 of the perfusing blood

The cerebral circulation does not consist of functional end-arteries. Rather, a rich vascular anastomosis known as the Circle of Willis surrounds the base of the brain, into which all the main arteries to the brain connect so that if one artery should block, the brain can still be supplied by the other arteries in this anastomotic arrangement.

Cerebral blood flow is little affected by cardiovascular reflexes (i.e. the autonomic nervous system). Carbon dioxide is the most important determinant of cerebral blood flow, via its local vasodilator action (in underperfused areas carbon dioxide accumulates and this leads to vasodilatation and restoration of normal cerebral perfusion). Hyperventilation leads to washout of carbon dioxide from the blood and constriction of cerebral blood vessels. This may result in syncope following a panic attack. In addition, it explains why hyperventilating prior to diving into water can result in syncope underwater and drowning. The local effect of carbon dioxide on the cerebral vasculature is deliberately utilized in the management of head injury where hyperventilation is used to reduce raised intracranial pressure.

The rate of cerebral blood flow remains essentially stable, up to a point, with changing blood pressure owing to local autoregulation of flow. Autoregulation is very well developed in the brain;

a fall in blood pressure causes the resistance vessels to dilate and thereby maintain flow. Cerebral autoregulation seems to involve both myogenic and metabolic mechanisms.

The important relationship between the cerebral perfusion, mean arterial blood pressure and intracranial pressure is as follows:

CPP = MABP – ICP

where CPP is cerebral perfusion pressure, MABP is mean arterial blood pressure and ICP is intracranial pressure. It stems from the fact that the adult brain is enclosed in a rigid, incompressible box, with the result that the volume inside it must remain constant (Monro–Kelly doctrine). A rise in intracranial pressure therefore decreases cerebral perfusion pressure (and hence cerebral blood flow). In raised intracranial pressure, as the brainstem becomes compressed, local neuronal activity causes a rise in sympathetic vasomotor drive and thus a rise in blood pressure. This is known as the Cushing's reflex. This elevated blood pressure evokes a bradycardia via the baroreceptor reflex. The Cushing's reflex helps to maintain cerebral blood flow and protect the vital centres of the brain from loss of nutrition if the intracranial pressure rises high enough to compress the cerebral arteries.

234D: Mutations in the haemagglutinin molecule are responsible for antigenic drift

Viruses can be classified according to:

- particle structure (i.e. virus family)
- genomic type – RNA or DNA, single-stranded or double-stranded.

In addition, single-stranded RNA viruses can be divided into positive-stranded (coding) and negative-stranded (non-coding) RNA.

Influenza is a member of the Orthomyxoviridae family of viruses and has a negative single-stranded RNA genome. The spherical surface of the virus is a lipid bilayer (envelope) containing the viral haemagglutinin (HA) and neuramidase (NA) which determine the subtype of the virus. The HA molecule mediates the entry of the virus into host cells. The NA molecule may be important in the release of viruses from host cells.

Epidemics of influenza occur through mutations, resulting in amino acid substitutions of the HA and NA that allow the virus to escape most host antibodies (antigenic drift). Pandemics, which tend to be longer and more widespread then epidemics, may occur when both the HA and NA are replaced through recombination of RNA segments with those of animal viruses, making all individuals susceptible to the new influenza virus (antigenic shift). The most notable influenza pandemics occurred in 1918, 1957 and 1968, resulting in millions of deaths worldwide. The virus that caused the last pandemic (H3N2) has been drifting ever since and we have no idea when the next pandemic will occur.

Transmission of influenza occurs by droplet inhalation. The initial symptoms of influenza are due to direct viral damage and associated inflammatory responses. Life-threatening influenza is often due to secondary bacterial infection as a result of the destruction of the respiratory epithelium by the influenza virus.

Influenza may be prevented by a vaccine that consists of inactivated preparations of the virus. It provides protection in up to 70 per cent of individuals for about one year. It is recommended for those only at high risk of acquiring the virus. The vaccines in use contain the HA and NA components in relation to the prevalent strain or strains of influenza circulating the previous year. Each year the World Health Organization recommends which strains should be included.

235B: Low calcium intake

High dietary intake of calcium promotes calcium absorption, suppresses PTH release and bone dissolution and thus protects against osteoporosis. Excess alcohol intake, sedentary lifestyle, early menopause and a thin body habitus all promote bone loss.

236E: Affects the intrinsic, rather than the extrinsic, pathway for blood coagulation

Haemophilia A is a sex-linked (X-linked recessive) disorder that results in a reduction in the amount or activity of the clotting factor, factor VIII, a member of the intrinsic pathway. Since the inheritance pattern is X-linked the disorder primarily affects males, since female individuals who carry the affected gene usually do not have bleeding manifestations. Clinically there is a tendency toward easy bruising and haemorrhage after trauma or operative procedures. In addition, spontaneous haemorrhages are frequently encountered in regions of the body normally subject to trauma, particularly the joints (haemarthroses).

Factor IX deficiency is known as haemophilia B (or Christmas disease) and is clinically indistinguishable from haemophilia A. Treatment of haemophilia A includes clotting factor replacement with recombinant factor VIII. The continued presence of this devastating disease throughout history may be explained by the protective effect against ischaemic heart disease in haemophilia carriers (by reducing the 'stickiness' of the blood; a similar effect to aspirin).

237C: It is secreto-motor to the lacrimal gland

The facial, or 7th cranial, nerve has a variety of different functions and is important clinically. Its functions may be summarized as follows:

- is associated developmentally with the second branchial arch
- supplies the muscles of facial expression
- gives special taste sensation to the anterior two-thirds of the tongue via the chorda tympani nerve
- carries secreto-motor fibres to the lacrimal gland through the greater petrosal nerve
- is secreto-motor to the submandibular and sublingual glands
- gives somatic sensation to the external auditory meatus.

Special taste from the posterior third of the tongue is carried by the glossopharyngeal nerve. The levator palpebrae superioris muscle, responsible for elevating the eyelid, is not a muscle of facial expression – it is innervated by the occulomotor nerve and sympathetics. The orbicularis oculi muscle, responsible for blinking and for screwing the eye tight, is regarded as a muscle of facial expression and is supplied by the facial nerve.

The four principal muscles of mastication (temporalis, medial and lateral pterygoids, masseter) are all supplied by the mandibular division of the trigeminal nerve. Note buccinator is not a muscle of mastication and is innervated by the facial nerve.

Understanding the above helps to explain what happens when things go wrong. A facial nerve (Bell's) palsy results in weakness of the muscles of facial expression down one side of the face, leading to a droop. Note that this is a lower motor neurone palsy and that all the muscles down the side of the face are affected including the forehead muscles. This is in sharp contrast to a cerebrovascular accident, or upper motor neurone facial palsy, where the upper (forehead) muscles are spared since they are bilaterally innervated from both cerebral cortices.

Beside a droopy face, however, a Bell's palsy also results in loss of sensation to the anterior two-thirds of the tongue and hyperacusis (sensitivity to sounds) as a result of denervation of the stapedius muscle, which normally serves to dampen down sounds in the middle ear. Dry eyes occur as a result of the loss of the secreto-motor supply to the lacrimal gland (and hence the need to protect the eye to prevent keratitis and corneal ulceration in a facial nerve palsy). This is exacerbated by the denervation of the orbicularis oculi muscle which normally functions to spread the tear film over the surface of the cornea with the blinking reflex.

Although it may not seem very important, the small somatic sensory branch of the facial nerve (that supplies the external auditory meatus) may explain why in Ramsey–Hunt syndrome (herpes zoster infection of the geniculate ganglion) herpes vesicles are found around the external auditory meatus.

This question illustrates nicely how a good understanding of anatomy may help the student in future clinical practice.

238B: The vital capacity is the sum of the inspiratory reserve volume, the expiratory reserve volume and the tidal volume

Spirometry traces are easy to understand if you remember the following two rules:

- There are four lung volumes and five capacities that you need to remember.
- A capacity is made up of two or more lung volumes.

The *four lung volumes* are:

- *Tidal volume* = volume of air inspired or expired with each normal breath in quiet breathing – approximately 500 mL
- *Residual volume* = the volume of air that remains in the lung after forced expiration
- *Inspiratory reserve volume* = extra volume of air that can be inspired over and above the normal tidal volume
- *Expiratory reserve volume* = extra volume of air that can be expired by forceful expiration after the end of a normal tidal expiration.

The *five lung capacities* are:

- *Functional residual capacity* = the volume of air that remains in the lung at the end of quiet expiration – equal to the sum of the residual volume and the expiratory reserve volume
- *Inspiratory capacity* = inspiratory reserve volume + tidal volume
- *Expiratory capacity* = expiratory reserve volume + tidal volume
- *Vital capacity* = inspiratory reserve volume + tidal volume + expiratory reserve volume (or total lung capacity minus residual volume)
- *Total lung capacity* = vital capacity + residual volume.

The residual volume (and therefore functional residual capacity and total lung capacity) cannot be measured directly by spirometry. They are measured by either whole-body plethysmography, or by using the helium dilution or nitrogen washout techniques.

239B: Delayed hypersensitivity reaction against the bacteria

Mycobacteria stimulate a specific T-cell response of cell-mediated immunity resulting in granuloma formation. While this is effective in reducing the infection, the delayed hypersensitivity (type IV) reaction also damages the host tissues. Damage therefore primarily results from the host's immune response in an attempt to clear the body of infection – so-called immune pathology. The formation of granulomas is the host's attempt to wall off the mycobacteria from the rest of the body, thereby preventing dissemination. When an individual is immunosuppressed (in HIV for example), dissemination therefore occurs more readily with disastrous consequences.

The tubercle bacilli can survive within macrophages and this may account for latent infections and reactivation of tuberculosis in later life. There is no significant humoral response to mycobacteria. Necrosis does occur in tuberculosis, but it is usually within the granuloma (caseous necrosis). *M. tuberculosis* causes little or no direct or toxin-mediated damage.

240D: Ptosis of the left eye

This patient has Horner's syndrome. Unilateral loss of sympathetic innervation of the face results in ptosis, pupil constriction (miosis), anhidrosis, facial flushing and enophthalmos. Lateral deviation of the eye would suggest damage to the 3rd cranial nerve.

241D: It is more common in regions of the world in which malaria is endemic

Sickle cell anaemia is an autosomal recessive condition, caused by a single base change in the DNA coding for the amino acid in the 6th position of the beta-haemoglobin chain (adenine is replaced by thymine). This leads to an amino acid change from glutamic acid to valine. The resultant haemoglobin, HbS, has abnormal physiochemical properties that leads to sickling of red

bloods cells and sickle cell disease. Homozygosity at the sickle cell locus is known as sickle cell anaemia, while heterozygosity at the same locus is known as the sickle cell trait. Where malaria is endemic, as many as 30 per cent of black Africans are heterozygous. This frequency may be related in part to the slight protection against *Plasmodium falciparum* afforded by HbS.

Clinical manifestations do not occur until around 3–6 months after birth when the main switch from fetal to adult haemoglobin occurs (fetal haemoglobin does not contain β-haemoglobin chains). Clinical manifestations relate to the sickling of red blood cells as a result of the production of a structurally abnormal haemoglobin. This includes haemolysis (the average red cell survival is shortened from the normal 120 days to approximately 20 days) and occlusion of small blood vessels resulting in ischaemic tissue damage (so-called painful vaso-occlusive crises). The latter crises are precipitated by factors such as infection, acidosis, dehydration or hypoxia. Homozygotes sickle at PO_2 levels of 5–6 kPa (i.e. normal venous blood) and thus sickling takes place all the time. Heterozygotes sickle at PO_2 levels of 2.5–4 kPa and therefore only sickle at extremely low oxygen tensions.

The spleen is enlarged in infancy and childhood, as a result of extramedullary haematopoiesis, but later is often reduced in size (autosplenectomy) as a result of erythrostasis within the spleen leading to thrombosis, autoinfarction or at least to marked tissue hypoxia. Therefore one should not expect to find a palpable spleen on examining an adult with sickle cell anaemia.

242B: The intervertebral joints are secondary cartilaginous joints

The spinal cord terminates at the level of L1/L2. Below this only nerve roots exist within the vertebral canal (cauda equina). It is therefore safe to perform a lumbar puncture at the level of L3/4 or L4/5. Fortunately for the purpose of a lumbar puncture, the dural sac containing the cerebrospinal fluid does not terminate until the level of S2.

The intervertebral joints are secondary cartilaginous joints. Between each vertebral body lies an intervertebral disc which is predominantly created from an annulus fibrosus of fibrocartilage with an internal nucleus pulposus, a bubble of semiliquid gelatinous substance derived from the embryonic notochord. With age the fibrocartilaginous annulus does deteriorate and may weaken, often in the lower lumbar region, giving rise to a slipped, or prolapsed, disc. In such cases the nucleus pulposus is typically extruded posterolaterally.

The relationship of the nerve roots to intervertebral discs is of great importance. At the level of the L4/5 disc, the 4th lumbar nerve roots within their dural sheath have already emerged from the intervertebral foramen and so are not lying low enough to come into contact with the disc. The roots that lie behind the posterolateral part of this disc are those of the 5th lumbar nerve and these are the ones likely to be irritated by the prolapse. Thus the general rule throughout the vertebral column is that when a disc herniates (usually posterolaterally, rather than in the midline) it may irritate the nerve roots numbered one below the disc.

The spinal cord is supplied by the single, anterior spinal artery and two (right and left) posterior spinal arteries. Since there is only one anterior spinal artery, the spinal cord is vulnerable to anterior ischaemia (the anterior spinal artery syndrome). The posterior columns (mediating light touch and proprioception) remain intact, but most of the rest of the cord below the level of the lesion is affected, leading to weakness (corticospinal tract involvement) and loss of pain/temperature sensation (anterolateral, or spinothalamic, tract involvement).

The richly supplied red marrow of the vertebral body drains through its posterior surface by large basivertebral veins into Batson's internal vertebral venous plexus, which lies inside the vertebral canal, but outside the dura (in the extradural space). It drains into the external vertebral venous plexus and thence into regional segmental veins. These veins are valveless and often act as a subsidiary route for blood flow when the inferior vena cava cannot cope with a sudden flush of blood resulting from a sudden increase of intra-abdominal pressure (e.g. straining, coughing, sneezing). A rise in pressure on the abdominal and pelvic veins would tend to force the blood backward out of the abdominal and pelvic cavities into the valveless veins within the vertebral

canal. This existence of this venous plexus may explain how carcinoma of the prostate, kidney, breast, bronchus and thyroid may metastasize to the vertebral column.

243E: It helps to prevent the formation of pulmonary oedema

Surfactant is formed in and secreted by type II pneumocytes. The active ingredient is dipalmitoyl phosphatidylcholine. It helps prevent alveolar collapse by lowering the surface tension between water molecules in the surface layer. In this way it helps to reduce the work of breathing (makes the lungs more compliant) and permits the lung to be more easily inflated.

Since the surfactant remains at the water-air interface, the space between surfactant molecules decreases as the surface area is reduced; this is equivalent to raising its concentration which lowers surface tension. This prevents alveolar collapse. Likewise, the decreasing effect of surfactant as the lungs inflate helps to prevent overinflation. This unique property of surfactant helps to stabilize different sizes of alveoli (otherwise the smaller alveoli would empty into the larger alveoli by LaPlace's law).

Surfactant is not produced in any significant quantity until the 32nd week of gestation and it then builds up to a high concentration by the 35th week (the normal gestation period is 39 weeks). Premature delivery may therefore result in inadequate surfactant production and respiratory distress syndrome of the newborn (hyaline membrane disease).

Surfactant also plays an important role in keeping the alveoli dry. Just as the surface tension forces tend to collapse alveoli, they also tend to suck fluid into the alveolar spaces from the capillaries. By reducing these surface forces, surfactant prevents the transudation of fluid. In this way surfactant acts as an important safety mechanism against the formation of pulmonary oedema.

244C: Typically affects the apical lung in post-primary TB

One-third of the world's population are infected with *Mycobacterium tuberculosis*. It is a major cause of death worldwide and is rapidly increasing in prevalence, in part because of the sharp increase in the number of individuals infected with HIV and because of the recent emergence of multi-drug resistant TB. Mycobacteria are obligate aerobic, rod-shaped, non-spore forming, non-motile bacilli with a waxy coat that causes them to retain certain stains after being treated with acid and alcohol; they are therefore known as acid–alcohol-fast bacilli (AAFB). Mycobacteria do not readily take up the Gram stain but they would be Gram-positive if the Gram stain could penetrate their waxy walls. The Ziehl–Neelsen stain is used instead to visualize the organisms, which stain pinkish red.

The pattern of host response depends on whether the infection represents a primary first exposure to the organism (primary TB) or secondary reactivation or reinfection (post-primary or secondary TB). Primary TB is most often subpleural, most often in the periphery of one lung, in the mid-zone. The residuum of the primary infection is a calcified scar in the lung parenchyma (Ghon focus) along with hilar lymph node enlargement, together referred to as the Ghon complex. Secondary TB most often occurs at the lung apex (Assman lesion) of one or both lungs which may cavitate and heal by dense fibrosis. The apex of the lung is more highly oxygenated, allowing the aerobic mycobacteria to multiply more rapidly. Involvement of extrapulmonary sites (kidney, meninges, bone etc.) is not uncommon.

M. tuberculosis is resistant to penicillin and requires multimodal antibiotic therapy (which may be remembered by RIPE) to prevent the emergence of resistance:

- rifampicin (main side-effect, liver toxicity)
- isoniazid (main side-effect, peripheral neuropathy)
- pyrazinamide (main side-effect, liver toxicity)
- ethambutol (main side-effect, optic neuropathy with visual disturbances).

Several months of combination treatment are required to treat *M. tuberculosis*. Pyridoxine (vitamin B_6) should be given with isoniazid to prevent isoniazid neuropathy.

M. tuberculosis can be prevented by immunization with BCG, a vaccine made from non-virulent tubercle bacilli. However, the protective efficacy of the vaccine is variable, ranging from 0 to 80 per cent depending on the part of the world in which it is administered.

245C: 500–1000 mL

Fluid balance is maintained by water intake that is equal to losses in urine, stool, sweat and insensible losses (through skin and lungs).

246C: Defective haem synthesis results in porphyria

- Sickle cell disease is due to the production of abnormal globin.
- Thalassaemia is due to the decreased production of normal globin.

Both sickle cell and thalassaemia seemingly developed as a form of carrier resistance against malaria, and as such are widespread in areas profoundly affected by malaria, predominantly Africa, South East Asia, the Mediterranean, and the Middle East.

The porphyrias are a group of genetic diseases resulting from errors in the pathway of haem biosynthesis, resulting in the toxic accumulation of porphyrin precursors. Interestingly, porphyria has been suggested as an explanation for the origin of vampire and werewolf legends and is believed to have accounted for the insanity exhibited by King George III that may have cost Britain the American War of Independence.

Carbon monoxide binds 250 times more avidly to haemoglobin than oxygen, resulting in the formation of carboxyhaemoglobin. The result is a decrease in the oxygen-carrying capacity of the blood. Carbon monoxide is a colourless, odourless and tasteless gas, so poisoning often occurs unnoticed. Levels of carboxyhaemoglobin >50–60 per cent result in death. The treatment is 100% oxygen which competitively displaces carbon monoxide from the haemoglobin, thereby decreasing the half-life of carboxyhaemoglobin from around 4 hours to 30 minutes.

Cyanide binds more strongly than oxygen to the iron atom present in the enzyme, cytochrome oxidase. This deactivates the enzyme and the final transport of electrons from cytochrome oxidase to oxygen cannot be completed. As a result, oxidative phosphorylation is disrupted, meaning that the cell can no longer produce ATP for energy. Tissues that mainly depend on aerobic respiration, such as the central nervous system and heart, are particularly affected, rapidly resulting in death.

247D: Lymphatics of the breast have connections with those of the opposite breast

The base of the breast is fairly constant. From the sternal edge to the midaxillary line and from the 2nd to 6th ribs, two-thirds of its base overlies pectoralis major and one-third overlaps on to serratus anterior. Contraction of the underlying pectoralis major muscle (by putting one's hands on their hips and pushing in) exacerbates any asymmetry between the breasts (e.g. as a result of a breast cancer) and is a clinically useful manoeuvre.

The breast's main purpose is lactation. The organ enlarges in pregnancy in preparation for lactation. After the menopause, involution (atrophy) occurs. Hence mammograms are less useful in the young (when the breast tissue is dense and cancers do not show up as well), but are more useful at the time of the menopause and beyond, when the breast tissue is composed of mainly fat (less dense on mammography) enabling cancers to show up more clearly.

Blood supply to the breast is mainly derived from the lateral thoracic artery (a branch of the second part of the axillary artery). However, the internal thoracic, thoracoacromial and posterior intercostal arteries also send branches to the breast.

The lymph drainage is of considerable anatomical and clinical importance because of the frequent development of cancer in the gland and the subsequent dissemination of malignant cells along the lymphatics to the lymph nodes. Around 75 per cent of the lymphatic drainage of the breast passes to 20–30, or so, axillary lymph nodes. They are usually described as lying in the following groups, which can be remembered by the mnemonic, APICAL:

- A = **a**nterior (or pectoral) group
- P = **p**osterior (or subscapular) group
- I = **i**nfraclavicular (or deltopectoral) group
- C = **c**entral group
- A = **a**pical group
- L = **l**ateral (or brachial) group.

The medial quadrants of the breast (where fortunately cancer is less common) enter the thorax to drain into the internal mammary lymph nodes alongside the internal thoracic artery. Thoracic lymph nodes are difficult or impossible to treat, but lymph nodes of the axilla can be removed surgically.

The superficial lymphatics of the breast have connections with those of the opposite breast, anterior abdominal wall and supraclavicular lymph nodes. These tend to convey lymph from the breast when the other channels are obstructed by malignant disease, or following their destruction after radiotherapy or surgery.

248C: During exercise, blood flow to the upper portion of the lung increases

Systolic and diastolic pressures in the pulmonary artery are about one-sixth those in the aorta and so is the pulse pressure. This is because the pulmonary vascular resistance is about one-sixth of the systemic vascular resistance. The blood flow is the same in both circulations, otherwise blood would accumulate in one or other bed.

In a standing subject, blood flow is less in the upper parts of the lung than the lower regions, but this is not matched by the differences in ventilation, so that the ventilation/perfusion ratio is not the same in all parts of the lung. A standing subject has a higher ventilation/perfusion ratio at the apex than the base.

During exercise, recruitment of the apical vessels occurs to accommodate the increase in cardiac output and pulmonary blood flow that occurs with exercise. This has the effect of increasing the area of capillaries available for gas exchange.

The pulmonary vasculature exhibits a peculiar property found nowhere else in the circulation, known as hypoxic pulmonary vasoconstriction. It consists of contraction of smooth muscle in the walls of the small arterioles in response to hypoxia – the opposite effect to that normally observed in the systemic circulation. The mechanism remains obscure. It has the effect of directing blood flow away from hypoxic regions of the lung (e.g. poorly ventilated areas of the diseased lung in adults) and in this way helps to optimize the local ventilation/perfusion ratios.

249C: It results from the secretion of exotoxin

All members of the *Clostridia* group of organisms have the following properties:

- Gram-positive bacilli
- obligate anaerobes
- spore-forming
- saprophytic (i.e. live in the soil)
- motile (but non-invasive)
- exotoxin-producing.

Clostridia are responsible for causing several diseases in man: *C. tetani* (tetanus), *C. botulinum* (botulism), *C. perfringens*, formerly known as *C. welchii* (gas gangrene and food poisoning) and *C. difficile* (pseudomembranous colitis).

Tetanus is typically a disease of soldiers, farmers or gardeners. It is caused by deep penetrating wounds caused by objects contaminated with soil, which introduces spores into the tissue. As soon as the wound becomes anaerobic, the tetanus spores germinate to produce vegetative cells, which then multiply and release a potent neurotoxin called tetanospasmin. Only the tiniest quantities of exotoxin are required for the disease to develop. The bacteria producing the exotoxin are entirely

non-invasive and lack all other virulence factors apart from the capacity to produce toxin. The exotoxin binds to local nerve endings, travels up the axon to the spinal cord, traverses a synpatic junction and finally gains entry to the cytoplasm of inhibitory neurones. Within these cells the toxin exerts a highly specific proteolytic activity on one of the proteins (synpatobrevin) present in the vesicles that is responsible for the normal trafficking of inhibitory neurotransmitter to the synaptic junction. As a result the inhibitory neurone cannot transmit its impulse and there is unopposed stimulation of skeletal muscles by motor neurones. Death is normally due to muscular spasm (spastic paralysis) extending to involve the muscles of the chest so that the patient is unable to breathe.

As in other diseases caused entirely by an exotoxin, tetanus can be treated by passive immunization with antitoxin, and prevented by vaccination with toxoid. However, antitoxin cannot neutralize any toxin that has already entered neurones. Antibiotics are of limited value against anaerobic bacteria like *Clostridia* because they cannot penetrate the necrotic infected area in sufficient concentrations to be effective; surgical debridement of wounds is far superior.

250E : Arginine

Nitric oxide (NO) is generated from arginine in a reaction catalysed by NO synthase. The other product of the reaction is citrulline.

251D: Blood group O is recessive to A and B

ABO blood groups are inherited in the following manner. Blood group O is recessive to both A and B, but A and B exhibit co-dominance. Thus AO or AA = blood group A; BO or BB = blood group B; OO = blood group O; AB = blood group AB. Blood group O is the most common blood group in the UK population. There is no known evolutionary advantage of being one ABO blood group over another, although people with blood group O are more susceptible to duodenal ulceration than other blood groups, and patients with blood group A are at higher risk of developing gastric carcinoma. Duffy blood-group–negative individuals are resistant to *Plasmodium vivax*, since the Duffy antigen acts as a receptor for invasion by the human parasite.

Since individuals with blood group AB have no antibodies present in their serum it follows that they are universal recipients. However, they can only donate to other AB individuals. Individuals of blood group O have antibodies present in their serum against blood groups A and B. It follows that they can only receive from other group O individuals. However, they are universal donors since the antibodies are rapidly diluted in the recipient's blood. Since blood group O is the universal donor it is used in emergency situations where there is not enough time to determine the exact blood grouping of the patient.

252B: The direction of fibres of the external intercostal muscle is downwards and medial

The intercostal neurovascular bundle lies in a groove on the undersurface of each rib, running in the plane between the internal and innermost intercostal muscles.

The vein, artery and nerve lie in that order, from above downwards, under cover of the lower border of the rib. This may be remembered by VAN:

- V = **v**ein
- A = **a**rtery
- N = **n**erve.

Thus, a needle or trocar for drainage, or aspiration, of fluid from the pleural cavity is inserted just above the rib in order to avoid the main vessels and nerves.

The fibres of the external intercostal muscle pass obliquely downwards and forwards from the sharp lower border of the rib above to the smooth upper border of the rib below. This may be remembered because it follows the same direction as having one's hands in pockets. Although important for the mechanics of respiration, the diaphragm is the main muscle of respiration.

253D: Carotid bodies primarily respond to hypoxia

A chemoreceptor is a receptor that responds to a change in the chemical composition of the blood. They are the most important receptors involved in the minute-to-minute control of ventilation. There are both central and peripheral chemoreceptors.

Central chemoreceptors lie within the medulla of the brainstem. They primarily respond to hypercapnia by increasing the ventilatory rate and depth of ventilation.

Peripheral chemoreceptors lie in the carotid bodies (at the origin of the internal carotid artery) and in the aortic arch. Carotid bodies are not to be confused with the nearby carotid sinus baroreceptors which comprise stretch receptors in the wall of internal carotid arteries. Carotid bodies primarily respond to hypoxia by increasing the ventilatory rate and depth of ventilation.

Eighty per cent of the hypercapnic response driving ventilation arises from the central chemoreceptors; 20 per cent arises from the peripheral chemoreceptors. The response of the central chemoreceptors to arterial PCO_2 is therefore more important than that of the peripheral chemoreceptors. The hypoxic response driving ventilation almost all comes from the peripheral chemoreceptors.

Each carotid body is only a few millimetres in size and has the distinction of having the highest blood flow per tissue weight of any organ in the body (20 mL/g per minute). This high flow is consistent with the prompt physiological reflex functions of the carotid body. Carotid bodies sample the partial pressure of oxygen in the blood, not its oxygen content. Anaemia, when the oxygen content is low but the PCO_2 is normal, does not stimulate them.

254D: It may cause blackwater fever

Malaria is a worldwide infection that affects 500 million people and kills 3 million people (mostly children) per year; it is therefore the major parasitic cause of death and is the most deadly vector-borne disease in the world. Malaria is caused by protozoan parasites of the genus *Plasmodium*. There are four main strains that infect humans: *P. falciparum*, *vivax*, *malariae* and *ovale*.

Of these, *P. falciparum* is the most virulent, most widespread, most drug-resistant and causes the most morbidity and mortality through its ability to cause cerebral malaria, severe anaemia, hypoglycaemia, lactic acidosis, renal failure, pulmonary oedema and shock ('algid malaria'). Blackwater fever is characterized by intravascular haemolysis, haemoglobinuria and kidney failure.

P. falciparum is the most pathogenic strain for two principal reasons:

- It can develop in red cells of all ages; the other less pathogenic species are limited to growing in subpopulations of cells – either very young or very mature cells. *P. falciparum* can therefore cause higher levels of parasitaemia.
- The distinctive behaviour of *P. falciparum*-infected red cells – namely cytoadherence to vascular endothelium and sequestration – minimizes removal of infected erythrocytes by the spleen.

Plasmodia is transmitted to humans by more than a dozen species of female *Anopheles* mosquito which require a blood meal before they can breed (the *Aedes* mosquito acts as a vector for yellow fever and Dengue fever, not malaria). The male mosquitoes feed harmlessly on plant sap. The *Anopheles* mosquito vector is also the definitive host in which sexual reproduction occurs; thus fertilization occurs in the insect, not in the human!

Malaria is treated with supportive management and chemotherapy. Preventative strategies include chemoprophylaxis (which is by no means 100 per cent effective!), vector control (such as insecticides) and bite prevention (insect repellents, mosquito nets, covering up exposed areas especially at dawn and dusk). Unfortunately, at present no effective vaccination exists for the prevention of malaria. The quest to develop a malaria vaccine is currently an active area of research.

255A: Tyrosine

Tyrosine is the precursor of each of these neurotransmitters. Tyrosine hydroxylase converts tyrosine to DOPA, which is in turn converted to dopamine, then to noradrenaline and finally adrenaline.

256C: Is associated with berry aneurysms of the Circle of Willis

Adult polycystic kidney disease is one of the most common inherited disorders in humans, affecting approximately 1 in 1000 individuals and accounting for 10 per cent of cases of end-stage renal failure. It is inherited as an autosomal dominant condition with a late-onset mode of presentation. Eighty-five per cent of cases have been localized to a gene on the short arm of chromosome 16 (*PKD1* gene). A second gene (*PKD2*), responsible for around 15 per cent of cases, has been localized to the long arm of chromosome 4. The corresponding gene products have been named polycystin-1 and polycystin-2, although their exact function is unknown.

Both kidneys are progressively replaced by enlarging cysts which compress and replace the functioning renal parenchyma, leading to renal failure. The condition usually presents in adult life (typically around 40 years of age). When renal failure occurs it usually progresses to end-stage renal failure at between 40–60 years of age.

Adult polycystic kidney disease is associated with cerebral berry aneurysms (so that death may occur due to subarachnoid haemorrhage). Other extrarenal manifestations include liver, pancreatic and splenic cysts.

257D: It lacks a true serosal surface

The oesophagus is a segmental muscular tube running from the cricoid ring, at the level of C6, to the cardia of the stomach. It is 25 cm long (with the distance from the upper incisor teeth to the lower oesophageal sphincter being approximately 40 cm). These distances are useful to learn for the purposes of endoscopy. The upper third of the oesophagus consists of skeletal muscle (voluntary muscle which initiates swallowing) but then there is a progressive change to smooth muscle, such that the lower third of the oesophagus consists only of smooth muscle.

Blood supply and lymphatic drainage is segmental. The upper third of the oesophagus is supplied by the inferior thyroid artery and lymphatics drain to the deep cervical group of lymph nodes. The middle third of the oesophagus is supplied directly by branches from the descending thoracic aorta and lymphatics drain to the pre-aortic and para-aortic lymph nodes. The lower third of the oesophagus is supplied by the left gastric artery and lymphatics drain to the coeliac group of lymph nodes. However, within the oesophageal walls there are lymphatic channels which enable lymph to pass for long distances within the viscus so that drainage from any given area does not strictly follow the above pattern.

The surface epithelium is largely non-keratinizing stratified squamous epithelium. This is normally replaced by columnar epithelium at the gastro-oesophageal junction, but columnar epithelium may line the lower oesophagus. An oesophagus that has the squamocolumnar junction 3 cm or more above the gastro-oesophageal junction is abnormal and called Barrett's oesophagus. This is a metaplastic change taking place in response to acid reflux and is a premalignant condition.

Except for the short intra-abdominal segment of the oesophagus there is no serosal surface. This is important to know about for two reasons. First, it makes the oesophagus vulnerable to anastomotic leakage in the postoperative period. Second, because the oesophagus lacks a serosal covering, oesophageal carcinoma encounters few anatomic barriers to local invasion.

258C: The Haldane effect describes changes in the affinity of the blood for CO_2 with variations in the PaO_2

Carbon dioxide is transported in the blood in three ways:

- bicarbonate accounts for about 80–90 per cent of the total CO_2 in the blood
- carbamino compounds (5–10 per cent)
- physically dissolved in solution (only 5 per cent).

Carbon dioxide is carried on the haemoglobin molecule as carbamino-haemoglobin; carboxyhaemoglobin is the combination of haemoglobin with carbon monoxide.

Venous blood contains a higher pCO_2 than arterial blood and is therefore more acidic (through the formation of carbonic acid), with a lower pH.

Carbon dioxide is approximately 20 times more soluble in plasma than is O_2. This means that CO_2 diffuses about 20 times more rapidly than does O_2. This rapid diffusion of CO_2 through aqueous solutions means that the elimination of CO_2 is much less of a problem than is O_2 delivery, so O_2 is likely to be the factor affected first in disorders of respiration.

Binding of oxygen with haemoglobin tends to displace carbon dioxide from the blood; this is known as the Haldane effect. In the capillaries, the Haldane effect causes increased pick up of CO_2 because of O_2 removed from the haemoglobin, while in the lungs it causes increased release of CO_2 because of O_2 pick up by the haemoglobin.

259B: Parasites may remain dormant in the liver as hypnozoites

The malaria parasite has a complex life cycle. In their definitive host (the mosquito), the parasites undergo a cycle of sexual and asexual development. In their intermediate host (the human), the parasites undergo two cycles of asexual development (in the liver and in red blood cells). In addition there are alternating and extracellular stages. The genetic recombination allowed by the sexual stage is one element in the remarkable antigenic diversity seen within malaria parasite populations that enables it to evade the immune response. The malaria life cycle is easiest to understand if it is broken down into three stages.

The intermediate host (humans) – hepatic stage

Human infection begins when sporozoites are introduced into an individual's bloodstream as an infected mosquito takes a blood meal. Within 30 minutes, they disappear from the blood as they infect hepatocytes. Here they undergo the first round of asexual reproduction (exoerythrocytic shizogeny) and develop into exoerythrocytic schizonts. These exoerythrocytic schizonts may contain many thousands of merozoites. On invasion of the hepatocyte by *Plasmodium vivax* and *P. ovale*, the development of the schizont is retarded, and a 'dormant' stage of the parasite, the hypnozoite, is formed. This is responsible for disease relapse months to years after supposed chemotherapeutic cure and clearance of bloodstream forms of the parasite.

The intermediate host (humans) – erythrocytic stage

The released merozoites infect red cells where they undergo another round of asexual reproduction (erythocytic schizogeny) changing from merozoite, to trophozoite (feeding stage), to schizont. Eventually the cell ruptures and releases new merozoites (usually between 8 and 32), which go on to infect more red cells. Generally the parasite's life cycle stages are highly synchronized, such that at any one time all the parasites are at the trophozoite stage, or all are at the schizont stage. Fever in malaria is either tertian (every 48 hours in *Plasmodium falciparum*, *vivax* and *ovale*) or quartan (every 72 hours in *P. malariae*) and is due to the synchronized release of merozoites from red cells. Malignant tertian fever is due to P. falciparum. In addition, on infection of new blood cells, instead of forming trophozoites the parasites may grow into the immature gametocytes. These are not released from the red cell until taken up by a feeding mosquito.

The determinate host (mosquito)

The female *Anopheles* mosquitoes ingest blood as part of their life cycle. Here the normal asexually dividing bloodstream forms die, but the gametocytes are stimulated to mature to microgametes (male) and macrogametes (female). Fertilization occurs in the mosquito midgut resulting in the formation of a zygote. This then goes on to produce a wormlike form, the ookinete, which penetrates the midgut wall of the mosquito, forming an oocyst, located between the epithelium and the basement membrane. Note that the zygote is the sole diploid stage of malaria parasites; the only meiosis event during this life cycle occurs within a few hours of zygote formation. Within the oocyst a cycle of asexual reproduction (sporogeny) then takes place, with the formation of numerous sporozoites. When mature, the oocyst bursts open releasing these

sporozoites, which then migrate to the insect's salivary glands. From here they may enter the bloodstream of a new host, thus completing the parasite's life cycle.

260C: Decrease in serum IgM

A deficiency in the production of J-chains for immunoglobulins could result in a decrease in serum IgA and IgM levels. These antibodies are dimers and pentamers of the basic immunoglobulin molecule and require a J-chain to join the immunoglobulin chains.

261A: Better sanitation

The reduced incidence of serious infections (e.g. typhoid, cholera, tuberculosis, smallpox) is mainly the result of improved sanitation. Indeed, sanitation, particularly sewage systems and the provision of fresh water supplies, has had a much greater impact on the incidence of these diseases than have advances in medical science. Thus for tuberculosis most of the decline in mortality came before the introduction of chemotherapy and the BCG vaccination. Having said that, mortality from bacterial infections had been much reduced by the advent of antibiotics and vaccinations have led to a considerable reduction in incidence of many viral infections. One such success story has been the worldwide eradication of smallpox through a mass vaccination programme. After successful vaccination campaigns the World Health Organization officially declared the total eradication of smallpox in 1979.

262C: The narrowest part of the oesophagus is at the level of cricopharyngeus

There are four classical points along the oesophagus where constrictions take place:

- Point 1 – cricopharyngeus sphincter, 15 cm from the incisor teeth, which is the narrowest part of the oesophagus. Its function is to prevent air entering the oesophagus and stomach. The cricopharyngeus sphincter relaxes with the swallowing reflex.
- Point 2 – where the oesophagus is crossed by the aortic arch, 22 cm from the incisor teeth.
- Point 3 – where the oesophagus is crossed by the left principal bronchus, 27 cm from the incisor teeth.
- Point 4 – where the oesophagus passes through the opening in the diaphragm, 38 cm from the incisor teeth.

Although the left atrium is in front of the lower part of the oesophagus below the left bronchus, it is only when enlarged (e.g. in mitral valve disease) that the left atrium causes an indentation in the oesophagus, resulting in difficulty swallowing, or dysphagia.

These constrictions are of considerable clinical importance since they are sites where swallowed foreign bodies can lodge, or through which it may be difficult to pass an oesophagoscope. Since a slight delay in the passage of food or fluid occurs at these levels, strictures commonly develop here following the drinking of caustic fluids. These constrictions are also common sites of carcinoma of the oesophagus.

The lower oesophageal sphincter is not a true anatomical sphincter, but rather a functional one. Maintenance of the lower oesophageal sphincter is largely brought about through the following features:

- the effect of the right crus of the diaphragm forming a 'sling' around the lower oesophagus
- the oblique angle the oesophagus takes on entering the gastric cardia (Angle of His) acting as a flap-valve mechanism
- greater intra-abdominal pressure than intra-gastric pressure acting to compress the abdominal part of the oesophagus
- mucosal rosette (prominent folds at the gastro-oesophageal junction)
- phrenico-oesophageal ligament (fold of connective tissue)
- the effect of gastrin in increasing lower oesophageal sphincter tone
- unidirectional peristalsis.

A problematic lower oesophageal sphincter may lead to problems, such as gastro-oesophageal reflux disease, hiatus hernia, or a condition known as achalasia.

263E: The shape of the curve is explained by the physico-chemical properties of haemoglobin

The haemoglobin oxygen dissociation curve is sigmoidal in shape. The sigmoid response reflects the underlying biochemical properties of haemoglobin and results from cooperativity. That is, the protein cannot be considered in terms of four independently oxygen-binding subunits. As haemoglobin binds successive oxygens, the oxygen affinity of the subunits increases. Hyperbolic curves are exhibited by monomeric molecules such as myoglobin. The significance of the sigmoidal curve is that it means that haemoglobin becomes highly saturated at high oxygen partial pressures (and is therefore highly efficient at collecting oxygen), and releases a significant amount of oxygen at pressures which are fairly low, but not extremely so (with the result that haemoglobin is highly effective at supplying oxygen where it is needed).

The effect of things that shift the curve to the right (raised CO_2, lowered pH, increased temperature, increase in 2,3-DPG) is to increase oxygen availability in the tissues. The effect of CO_2/H^+ on O_2 carriage is known as the Bohr shift or effect. This is exactly what is needed in metabolizing tissues; release of acids or CO_2 thus liberates O_2 to fulfil the metabolic needs of the tissue. Do not confuse this with the effect of changes in O_2 on CO_2 carriage, which is called the Haldane effect.

A shift of the oxygen dissociation curve to the left is characteristic of fetal haemoglobin. When compared with adult haemoglobin, it is composed of two alpha and two gamma chains, instead of the usual two alpha and two beta chains of adult haemoglobin. This arrangement assists in the transfer of oxygen across the placenta from the maternal to the fetal circulation. The corollary of this is that fetal tissue oxygen levels have to be low to permit the release of oxygen from the haemoglobin.

264D: Disease results from the immune response to schistosome eggs

Parasitic infections may be caused by protozoa or metazoa. Parasitic protozoa (e.g. *Plasmodium falciparum*) are single-celled nucleate organisms that possess all processes necessary for reproduction. A metazoon is a multicellular organism. Examples of infective metazoa include helminths (parasitic worms) which can be subdivided into three classes: nematodes (roundworms), cestodes (flatworms) and trematodes (flukes). Schistosomiasis is the most important helminth disease infecting 200 million people worldwide. Three major species of schistosome parasite can infect humans: *Schistosoma mansoni*, *japonicum* and *haematobium*. All are trematodes (flukes).

The life cycle of the flatworms that cause human schistosomiasis involves a sexual stage in the human (the definitive host) and an asexual stage in the freshwater snail host, which acts as a vector or intermediate host. Schistosome eggs excreted in the faeces or urine hatch out in fresh water and release miracidia that invade snails; free-swimming cercaria are released from the snail and invade human skin, losing their tails and becoming known as schistosomulae. The larvae migrate through the bloodstream via the lungs and liver to the veins of the bladder (*Schistosoma haematobium*) or bowel (*Schistosoma mansoni* and *japonicum*) where they develop into adult males and females. The adults lay eggs, which are excreted by the host, thus completing the cycle.

The pathophysiology of schistosomiasis is mainly due to the immune response against the schistosome eggs. In the liver this may result in granuloma formation, extensive fibrosis (pipe-stem portal fibrosis) and portal hypertension (hepatosplenic schistosomiasis). *Schistosoma haematobium* is responsible for urinary schistosomiasis, where granulomatous inflammation and fibrosis in the bladder may result in haematuria, obstructive uropathy, and squamous cell carcinoma of the bladder.

Schistosomiasis is treated with praziquantel which removes the flukes, but in advanced cases the pathology is irreversible. Intense inflammatory reactions are provoked when the worms killed by treatment are carried back into the liver.

265E: Coxsackie B

Myocarditis is most commonly caused by Coxsackie group B virus and may be preceded by gastrointestinal or respiratory symptoms. Rhinoviruses, coronaviruses and adenoviruses are associated with the common cold, influenza-like illnesses and gastrointestinal disturbances. Mumps causes orchitis and parotitis/parotidomegaly.

266E: The death rate from gastric carcinoma has fallen

The death rate from lung cancer in women has shown a steep rise since 1955 with no decline in the rate of increase. This may be attributable to the increasing smoking habits of women in modern society. In males the death rate from lung cancer peaked in the mid-1980s and has shown a slight fall since then. Suicide rates in all countries fall during wartime and was low in the 1950s. Since then it has shown a steady increase in both sexes.

In 1980 the terms HIV and AIDS did not even exist. However, as of January 2006, just over 25 years after its recognition, the World Health Organization has estimated that 38.6 million people worldwide are HIV-positive and more than 25 million people have died of AIDS-related deaths since its recognition, making it one of the most destructive pandemics in recorded history.

Much more mysterious is the downward trend in deaths from stomach carcinoma over the past 50 years. Such trends provide us with valuable information regarding the aetiology of stomach cancer. This downward trend may be due to a decrease in some dietary carcinogens. However, the more recent decline may in part be due to *Helicobacter pylori* eradication therapy since it is now believed that *H. pylori* plays a pivotal role in the development of gastric carcinoma.

267C: It forms the main muscle of respiration at rest

The diaphragm is a musculo-tendinous structure composed of outer skeletal muscle fibres and a central tendinous region. It partitions the thoracic from the abdominal cavity and is the main muscle of respiration at rest (accounting for 70 per cent of inspiration at rest). Upon inspiration, the diaphragm contracts, which lowers the diaphragm. This decreases pressure within the thoracic cavity and air moves into the lungs, resulting in lung inflation. Upon expiration, the diaphragm relaxes and the diaphragm moves up.

The diaphragm receives motor innervation from the phrenic nerve (C3, C4, C5). ('C3, C4, C5, keeps the diaphragm alive!'). The diaphragm has no other motor supply other than the phrenic nerve. This is why cervical spine injuries with injury to the cervical spinal cord can be so disastrous – and hence the importance of proper cervical spine immobilization in trauma victims.

The phrenic nerve is two-thirds motor and one-third sensory. The sensory nerve supply to the diaphragmatic parietal pleura and diaphragmatic peritoneum covering the central surfaces of the diaphragm is from the phrenic nerve. The sensory supply to the periphery of the diaphragm is from the lower six intercostal nerves.

268E: Increased blood viscosity

At high altitude, a decreased atmospheric pressure results in decreased ambient oxygen concentrations and therefore a decrease in arterial PO_2. In the short term, an increase in pulmonary ventilation occurs due to stimulation of peripheral chemoreceptors by an oxygen lack. Hyperventilation causes a respiratory alkalosis (rise in arterial pH) by blowing off CO_2. This inhibits the central chemoreceptors and thereby opposes the effect of low PO_2 to stimulate the peripheral chemoreceptors (braking effect). Hypoxia leads to pulmonary vasoconstriction and pulmonary hypertension.

Acclimatization (i.e. adaptive responses to sustained and gradually increasing hypoxia) occurs in the longer term through a variety of different mechanisms:

- Removal of the braking effect – by changes in the composition of the cerebrospinal fluid (a reduction in the bicarbonate concentration of the cerebrospinal fluid) and increasing the renal excretion of bicarbonate – results in increased pulmonary ventilation.

- Erythropoiesis – through the effect of hypoxia stimulating erythropoietin secretion from the kidney – increases the oxygen carrying capacity of the blood, but in doing so raises blood haematocrit and blood viscosity, the effects of which can be deleterious.
- There is increased cardiac output.
- There is increased capillarity (increased number of capillaries in tissues).
- An increase in the concentration of 2,3-DPG causes a rightward shift of the oxygen dissociation curve that results in better unloading of oxygen.
- There is cellular acclimatization – changes occur in the mitochondria and oxidative enzymes inside cells.

If a person ascends to a high altitude too quickly (without giving enough time for these acclimatization mechanisms to develop), or remains at high altitude for too long, high-altitude or mountain sickness may result. There is only one treatment for high-altitude sickness and that is immediate descent from the mountain.

269E: Are responsible for causing Kuru in humans

Prions are a novel, infectious agent composed of protein only. They differ from all known pathogens. They lack nucleic acid and cannot be considered microorganisms. They are highly resistant to decontamination methods such as standard autoclaving (heat), disinfectants (chemicals) and ionizing radiation.

If abnormal prion protein is inoculated into a normal host, conformational changes are induced in the normal host prions resulting in their conversion to abnormal host prions. These abnormal host proteins then induce further conformational changes in remaining normal host prions. Thus, the original inoculated protein is able to catalyse a chain reaction in which host proteins become conformationally abnormal. This is unaccompanied by inflammation, immune reaction or cytokine release.

Well-known prion diseases include Kuru, scrapie, bovine spongiform encephalopathy (BSE) and Creutzfeldt–Jakob disease (CJD). Kuru is probably one of the most fascinating stories to have emerged from any epidemiological investigation. It occurred in villages occupied by the Fore tribes in the highlands of New Guinea who practised ritual cannibalism as a rite of mourning for their dead. The first cases occurred in the 1950s and involved progressive loss of voluntary control, followed by death within a year of the onset of symptoms. Interestingly, Kuru occurred only in individuals who participated in cannibalistic feasts. Such cannibalism was believed to be responsible for the transmission of prions in Kuru.

There is still much work to be done in determining the exact modes of transmission of prions and in enhancing our understanding of the molecular biology of prions. In addition the exact interrelations between the different prion-related diseases (e.g. BSE and new-variant CJD) needs to be clarified.

270A: C5a

C5a is a component of complement. Activation of complement by endotoxin or antigen-antibody complexes produces C5a, which is a neutrophil and macrophage chemotactant. *HLA-A* and *HLA-B* are genes for the human leucocyte antigens and they control the synthesis of class I major histocompatibility complex. The J-chain of IgM and IgA does not possess chemotactant properties. The variable region of the heavy chain of IgG is not known as a best neutrophil or macrophage chemotactant.

271C: Lung cancer

Currently lung cancer is the most common cause of death from cancer in women, followed by breast cancer and then colorectal cancer. Breast cancer is the commonest cancer (in terms of incidence) in women, followed by lung cancer and then colorectal cancer.

The most common cause of death from cancer in men is lung cancer followed by prostate cancer and then colorectal cancer. In men the commonest cancer (in terms of incidence) is prostate cancer, followed by lung and then colorectal cancer.

272E: The sympathetic trunks pass posterior to the medial arcuate ligament.

See Table 4. The left phrenic nerve pierces the muscle of the left dome of the diaphragm.

Table 4

Vena cava opening (T8)	Inferior vena cava Right phrenic nerve
Oesophageal opening (T10)	Oesophagus Left and right vagus nerves (RIP = right is posterior) Oesophageal branches of left gastric vessels Lymphatics from lower 1/3 oesophagus
Aortic opening (T12)	Aorta Azygous and hemiazygous veins Thoracic duct
Crura (T12)	Greater, lesser and least splanchnic nerves
Behind medial arcuate ligament	Sympathetic trunks
Behind lateral arcuate ligament	Subcostal (T12) neurovascular bundle

The inferior vena cava passes through the central tendinous portion of the diaphragm and not the muscular portion of the diaphragm at the T8 level. The reason for this is clear: if the vena cava passed through the muscular part of the diaphragm, each time the diaphragm contracted with respiration it would obstruct venous return causing syncope.

273B: Under resting conditions, equilibration between alveoli Po_2 and red blood cell Po_2 occurs one-third of the way along the pulmonary capillary

Gas exchange within the lung takes place at the level of the alveoli. It obeys Fick's law, which states that the rate of transfer of a gas through a sheet of tissue is directly proportional to the tissue surface area and the difference in partial pressure between the two sides and inversely proportional to the tissue thickness. The area of the blood gas barrier in the lung is enormous (50–100 m^2, about the size of a tennis court) and the thickness is only 0.3 μm in some places, so the dimensions of the barrier are ideal for diffusion.

Any disruption to the factors that affect the rate of gas transfer through the respiratory membrane may result in disease states. For example, the thickness of the respiratory membrane increases significantly in interstitial fibrosis, pulmonary oedema and pneumonia interfering with the normal respiratory exchange of gases. Likewise, the surface area may be greatly decreased in emphysema, to name just a few examples.

The capillaries form a dense network in the walls of the alveoli. The diameter of a capillary is just large enough for a red blood cell; this further increases the efficacy of gaseous exchange by reducing the distance required for diffusion to take place. At rest, each red blood cell spends, on average, about 0.75 s in the capillary network, and during this time probably traverses two or three alveoli. Under typical resting conditions, the capillary Po_2 virtually reaches that of the alveolar gas (i.e. equilibration occurs) when the red cell is about one-third of the way along the capillary. This acts as a safety factor so that, during exercise, when the time spent in the capillary by the red cell decreases, it does not compromise oxygenation.

Carbon monoxide (rather than chlorine gas), is the gas of choice for measuring the transfer factor (i.e. the effectiveness of the diffusing surface). Carbon monoxide is used in the test because its great avidity for haemoglobin means that its concentration in the blood can be assumed zero and does not need to be measured.

274D: Anaplasia is almost a complete lack of differentiation

There are certain definitions regarding tumours that need to be remembered and understood:

- *Tumour* simply means 'swelling', which can be benign or malignant.
- *Neoplasm* simply means a 'new growth'. It is synonymous with tumour and can be benign or malignant. Malignant neoplasms can be primary or secondary. The latter are also known as metastases.
- *Hypertrophy* is an increase in tissue growth through an increase in cell size.
- *Hyperplasia* is an increase in tissue growth through an increase in cell numbers.
- *Metaplasia* is an adaptive response resulting in the replacement of one differentiated cell type with another.
- *Dysplasia* literally means 'disordered growth'. It is the disordered development of cells resulting in an alteration in their size, shape and organization.
- *Carcinoma-in-situ* is an epithelial tumour with features of malignancy but it has not invaded through the basement membrane.
- *Carcinoma* is a malignant tumour of epithelial derivation. By definition, because it is malignant, the basement membrane has been breached.
- *Anaplasia* is the almost complete lack of differentiation (i.e. poorly differentiated).

A more formal definition of a neoplasm is 'an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change'. The latter part of this definition is to distinguish a true neoplasm from the endometrial growth that normally accompanies the menstrual cycle; endometrial tissue is normally responsive to sex hormones and regresses upon its cessation; a true neoplasm would persist.

275D: Leucocytes, erythrocytes and fibrin filling of the alveolar spaces

Lobar pneumonia may progress through four stages:

- congestion (in the first 24 hours) – inflammatory exudate
- red hepatization
- grey hepatization
- resolution (complete recovery).

Red hepatization is characterized by a firm consistency to the lung due to filling of the alveolar spaces by extravasated erythrocytes, fibrin and leucocytes. A fibrin meshwork and degenerating erythrocytes defines grey hepatization.

276B: Cholera

Infections, in general, can be transmitted horizontally or vertically, through direct contact or indirect contact. Vertical transmission occurs when the mother is the source of infection for the fetus.

Examples of horizontal routes of transmission are:

- air-borne diseases (e.g. tuberculosis), via droplet inhalation/aerosol
- water-borne diseases (e.g. cholera)
- food-borne diseases (e.g. dysentery) – also known as faecal–oral spread
- blood-borne (e.g. hepatitis C)
- sexual contact (e.g. HIV)
- oral contact/salivary transfer (e.g. Epstein–Barr virus)
- vector-borne diseases carried, for example, by rats or mosquitoes (e.g. plague, malaria)
- infected/contaminated inert objects, or fomites (e.g. tetanus).

Vertical routes of transmission include:

- transplacental (e.g. rubella)
- parturition/puerperal (e.g. ophthalmia neonatorum)
- breast milk (e.g. CMV).

277C: It crosses the midline at the level of T5

The thoracic duct is 45 cm long and commences at T12 from the cisterna chyli which lies to the right of the aorta. It drains all lymph below the diaphragm, left thorax and left head and neck regions. Valves are present along the duct and encourage the propagation of chyle along the duct.

It ascends behind the right crus and to the right of the aorta and oesophagus. It crosses the midline to the left, posterior to the oesophagus, at the level of T5. It passes over the dome of the left pleura, anterior to the left vertebral and subclavian arteries and enters the confluence of the left subclavian and internal jugular veins.

The equivalent to the thoracic duct on the right is the right lymphatic trunk. This drains on the right into the confluence of the right subclavian and internal jugular veins.

Injury to the thoracic duct may occur following trauma, or during insertion of a central venous catheter on the left-hand side. This may result in a chylothorax (a collection of lymph within the thoracic cavity). A haemothorax is a collection of blood.

278E: Emphysema results in increased lung compliance

Compliance is expressed as volume change per unit change in pressure. Elastance is the reciprocal of compliance. Compliance is extremely small in infants compared to adults. The pressure/volume curve of the lung is nonlinear with the lungs becoming stiffer at high volumes. The curves that the lungs follow in inflation and deflation are different. This behaviour is known as 'hysteresis'. The lung volume at any given pressure during deflation is larger than during inflation. This behaviour depends on structural proteins (collagen, elastin), surface tension and the properties of surfactant.

A sigh or yawn is a reflexly generated single deep breath which occurs after a period of quiet breathing. The purpose of the lung inflation, which stretches and unfolds the alveolar surface area, is to spread out the surfactant molecules, returning the alveolar surface tension to its normal value.

Various disease states are associated with either a decrease or increase in the lung compliance. Fibrosis, atelectasis and pulmonary oedema all result in a decrease in lung compliance (stiffer lungs). An increased lung compliance occurs in emphysema where an alteration in elastic tissue is probably responsible (secondary to the long-term effects of smoking). The lung effectively behaves like a 'soggy bag' so that a given pressure change results in a large change in volume (i.e. the lungs are more compliant). However, during expiration the airways are less readily supported and collapse at higher lung volumes resulting in gas trapping and hyperinflation. Reduced gas transfer results from a loss of interstitial tissue causing loss of available active alveolar area.

279E: Liposarcoma is a malignant tumour of adipose tissue

In general, benign tumours are designated by attaching a suffix – oma – to the cell of origin. Thus an adenoma is a benign tumour of glandular epithelial cells. However, there are exceptions to this rule. For example a lymphoma is a malignant lymphoreticular tumour.

Malignant tumours arising from connective tissue are called sarcomas. Thus a liposarcoma is a malignant tumour of adipose tissue, leiomyosarcoma is a malignant tumour of smooth muscle, and rhabdomyosarcoma is a malignant tumour of skeletal muscle. Malignant tumours of epithelial origin are called carcinomas. Thus an adenocarcinoma is a malignant neoplasm of glandular epithelium, and squamous cell carcinomas are malignant neoplasms arising from squamous epithelium.

280D: Occlusion of the hepatic venous drainage

Budd–Chiari syndrome is due to extensive occlusive fibrosis of the hepatic venous drainage. Patients present with ascites, hepatomegaly and portal hypertension.

281B: Prospective studies allow direct determination of incidence rates

In a prospective (or cohort) study, exposed and non-exposed individuals are identified and followed up over time to determine the incidence of a specific clinical disease, or event. For example, a population of smokers and non-smokers are followed up to provide comparison rates for lung cancer or heart disease. The incidence of a disease is the number of new cases per unit population per unit time.

Cross-sectional studies are like a snapshot in time and measure both exposure and outcome at one time point. They provide information on disease prevalence in a population. Prevalence of a disease is the proportion of a population that exhibits the disease at any one time.

Retrospective (or case–control) studies compare individuals with and without a disease to determine possible associations or risk factors for the disease in question. However, bias may influence the recall of exposure in these studies, especially if possible associations are known (recall bias). In addition, selection bias may impact on the study. A case–control study, on the other hand, is relatively easy and inexpensive to conduct because long-term follow up is not required and this type of study is therefore suitable for studying rare diseases.

282E: The lungs receive a dual blood supply

The right and left lungs are not mirror images of each other. While the right lung is composed of three lobes, the left lung possesses only two. Each of the lobes, in turn, are separated by fissures or interlobar clefts. Thus, on the right, there must be two fissures separating three separate lobes (these are the oblique and the horizontal fissures, respectively). On the left there is only one fissure separating the two lobes and that is the oblique fissure. Thus the horizontal fissure exists only on the right.

There are typically ten anatomically definable bronchopulmonary segments within each lung, each containing a segmental (tertiary) bronchus, a segmental artery, a segmental vein, lymphatics and autonomic nerves and separated from their adjacent segments by connective tissue. Each is pyramidal in shape with its apex towards the lung root and its base towards the surface of the lung, and each is anatomically and functionally separate from the rest. The importance of understanding bronchopulmonary segments is that diseased segments, since they are structural units, can be selectively removed surgically (segmentectomy). Nowadays this can be performed by video-assisted thoracoscopic surgery (VATS).

The right bronchus is shorter, wider and more vertical than the left bronchus so that foreign bodies that fall down the trachea are more likely to enter the right bronchus. Furthermore, material aspirated by a supine, comatose or anaesthetised patient would tend to gravitate into the apical segment of the right lower lobe, which is consequently a common site for aspiration pneumonia and abscess formation.

The lungs receive a dual blood supply by way of the pulmonary artery and the bronchial arteries. Thus obstruction of a small pulmonary arteriole by a pulmonary embolus has no effect in an otherwise healthy individual with an intact bronchial circulation. In such circumstances, pulmonary embolism usually results in infarction only when the circulation is already inadequate, as in patients with heart or lung disease. A large embolus that impacts in the main pulmonary artery, or that lodges at the bifurcation (as a saddle embolus), results in sudden death.

283C: Each haemoglobimolecule combines with eight oxygen atoms

The formation of haemoglobin is:

- four pyrrole rings $\rightarrow$ protoporphyrin IX
- protoporphyrin IX + Fe^{2+} $\rightarrow$ haem
- haem + polypeptide (globin) $\rightarrow$ haemoglobin chain (alpha or beta)
- two alpha chains + two beta chains $\rightarrow$ haemoglobin A (normal adult Hb).

In normal adult haemoglobin, iron exists in the reduced, or ferrous (Fe^{2+}) state, rather than the ferric (Fe^{3+}) state. Oxygen combines with the ferrous iron that is present within the haem molecules and not with the globin chains. The globin molecules that surround the haem molecule serve two key functions; they form a microenvironment in which the Fe^{2+} is protected from oxidation and also contribute to the unique oxygen binding properties of haemoglobin (allosterism and cooperativity). When iron exists in the ferric state, instead of the normal ferrous state, the haemoglobin is known as methaemoglobin. This is abnormal and has a reduced oxygen-carrying capacity, resulting in cyanosis.

Haemoglobin consisting of two alpha and two gamma chains is fetal haemoglobin. Normal adult haemoglobin contains two alpha and two beta chains. Since each haemoglobin chain has a haem prosthetic group, there are four iron atoms in each haemoglobin molecule. Each of these can bind with one molecule of oxygen, making a total of four molecules of oxygen (or eight oxygen atoms) that can be transported by each haemoglobin molecule.

Why do we have red blood cells?

- Primarily for the transport of haemoglobin and oxygen. If haemoglobin molecules were free in the plasma (and not wrapped up inside red cells) they would get filtered through the capillary membrane into the tissue spaces, or through the glomerular membrane and would escape into the urine. For haemoglobin to remain in the bloodstream, it must exist inside red blood cells.
- There are enzyme systems in the red cell that help to prevent haemoglobin breakdown. For example, methaemoglobin reductase converts ferric (Fe^{3+}) methaemoglobin back to ferrous (Fe^{2+}) haemoglobin.
- Carbonic anhydrase is restricted to the red cells and is crucial in CO_2 transport.
- The chemical environment in the cell, especially the presence of DPG, displaces the dissociation curve to the right so that oxygen unloads readily in active tissues.
- If haemoglobin were free in plasma, the viscosity of blood would rise to intolerable levels and colloid osmotic pressure would increase considerably. The viscosity effect is especially important in capillaries where the presence of red cells in blood gives it an anomalously low viscosity (Fahraeus–Lindqvist effect).

284C: Metaplasia in the bronchus involves a change from columnar to stratified squamous epithelium

Metaplasia is the reversible change of one fully differentiated cell type into another fully differentiated cell type, in response to injury. It often represents an adaptive response to environmental stress. Squamous metaplasia is by far the commonest. Its significance lies in the fact that it can become dysplastic if the agent that caused the metaplasia persists and is capable of inducing dysplasia.

Important sites of metaplasia

- *Lower end of the oesophagus* – in response to acid reflux (Barrett's oesophagus). The normal stratified squamous epithelium is replaced by gastric-type columnar epithelium which is able to produce mucus and protect the epithelium from acid reflux.
- *Bronchi* – where the normal respiratory (ciliated columnar) epithelium is replaced by stratified squamous epithelium under the influence of chronic irritation by cigarette smoke (squamous metaplasia).
- *Transformation zone of the cervix* – in response to environmental changes during the reproductive cycle and in response to human papilloma virus. The normal columnar endocervical epithelium is replaced by stratified squamous epithelium.
- *Bladder* – squamous metaplasia in response to chronic inflammation, infection and irritation (schistosomiasis, calculi etc.).

285C: Phaeochromocytoma

Phaeochromocytoma is a neoplasm of the adrenal medulla. It presents with a triad of hypertension, adrenal mass and elevated catecholamines.

286D: Randomized controlled trial

Randomized controlled trials form the gold standard in epidemiological research. They resemble cohort studies in many respects, but include the randomization of participants to exposures. Randomization is an important part of the study design because it eliminates the effects of selection and confounding biases. Double-blinding (keeping trial participants and investigators oblivious to the assigned intervention) adds to the value of a randomized controlled trial by eliminating the effects of information bias.

Case reports are unreliable as they represent only single cases and do not have a comparison group to allow assessment of associations. However, they are often the first foray into a new disease or area of enquiry. Case–control studies are prone to bias. Cross-sectional studies measure both exposure and outcome simultaneously, so the temporal relationship between the two may be unclear.

287B: It extends above the clavicle superiorly

The pleura clothes each lung and lines the thoracic cavity. It is composed of two layers. The visceral layer on the lung surface is in contact with parietal pleura that lines the thoracic wall (rib cage, vertebra, diaphragm), the surfaces being lubricated by a thin film of fluid. The space in between the two layers is known as the pleural space, or cavity.

The parietal pleura (along with the apex of the lung) projects 2.5 cm above the medial third of the clavicle superiorly. A penetrating wound above the medial end of the clavicle may therefore involve the apex of the lung, resulting in a pneumothorax or a collapsed lung. This is most commonly seen as an iatrogenic complication during the insertion of a subclavian (central) venous line. Owing to the obliquity of the thoracic inlet, the pleura does not extend above the neck of the first rib, which lies well above the clavicle.

It is also important to remember that the lower limit of the pleural reflection, as seen from the back, lies below the medial border of the 12th rib, behind the upper border of the kidney. It is vulnerable to damage here during removal of the kidney (nephrectomy) through an incision in the loin. Proper identification of the 12th rib is essential to avoid entering the pleural cavity.

The visceral pleura is poorly innervated, has an autonomic nerve supply and is insensitive to ordinary stimuli. The parietal pleura, on the other hand, receives a rich innervation from the intercostal nerves and the phrenic nerve and is sensitive to pain. Thus, in tuberculosis or pneumonia pain may never be experienced. However, once lung disease crosses the visceral pleura to involve the parietal pleura, pain becomes a prominent feature. Lobar pneumonia with pleurisy is a good example. Since the lower part of the costal parietal pleura receives its innervation from the lower five intercostal nerves, which also innervate the skin of the lower anterior abdominal wall, pleurisy in this area commonly produces pain that is referred to the abdomen. This has sometimes resulted in a mistaken diagnosis of an acute abdominal lesion. In a similar manner, pleurisy of the central part of the diaphragmatic pleura, which receives sensory innervation from the phrenic nerve (C3, 4, 5), can lead to referred pain over the shoulder, since the skin of this region is supplied by the supraclavicular nerves (C3, 4).

The reflections (and therefore the surface anatomy) of the pleural linings and lungs may be remembered by the '2, 4, 6, 8, 10, 12 rule':

Pleura

- Starts 2.5 cm above the mid-point of the medial third of clavicle
- Meet in midline at rib **2**
- Left side diverges at rib **4** (to make room for the heart)

- Right side continues parasternally to rib **6**
- Both cross rib **8** in mid-clavicular line
- Both cross rib **10** in mid-axillary line
- Both reach posterior chest just below rib **12**

Lung

- Below rib **6**, the lungs extend to **2** rib spaces less than pleura (i.e. opposite rib **6** mid-clavicular line, rib **8** mid-axillary line and rib **10** posteriorly).
- The parietal pleura extends a further **2** rib spaces inferiorly than the inferior lung edge to allow space for lung expansion.

Note how the right and left reflections are not identical to one another. On the left it is displaced by the central position of the heart.

288D: It acts via a secondary messenger

Erythropoietin is a glycoprotein hormone, produced mainly by the juxtaglomerular apparatus of the kidney in adults. In the fetus, it is almost solely produced by the liver.

Once released, it acts on specific receptors which leads to activation of tyrosine kinase, which in turn promotes transcription towards the manufacture of more red cells from bone marrow.

The major factor causing erythropoietin release is local hypoxia in the kidney which may be derived from anaemia or systemic hypoxia. Erythropoietin secretion is a prominent feature of acclimatization to high altitude. A deficiency of erythropoietin partly explains the anaemia seen in individuals with chronic renal failure. Recombinant erythropoietin is now available, revolutionizing their treatment.

289D: Invasion beyond the basement membrane

The defining and most reliable characteristic differentiating a benign from a malignant tumour is the ability of the latter to invade through the basement membrane into the surrounding tissues and metastasize to distant sites.

Both benign and malignant tumours increase in size with time. However, malignant tumours tend to grow more rapidly and aggressively than benign tumours. The result is that malignant tumours tend to outstrip their blood supply, leading to necrosis. Haemorrhage occurs as a result of the fragile new vasculature that forms in an attempt to increase blood supply to the tumour.

Chromosomal abnormalities do not define a tumour as malignant as this may be a feature of both benign and malignant tumours. The presence of a pseudo-capsule is typically a feature of benign lesions and results from the neoplasm expanding symmetrically and compressing the surrounding stroma. Such encapsulation tends to contain the benign neoplasm as a discrete, readily palpable and easily movable mass that can be surgically enucleated since a well-defined cleavage plane exists around the tumour.

In general, benign tumours are well-differentiated, meaning the tumour cells resemble the normal mature cells of the tissue of origin of the neoplasm and display well-ordered maturation. Malignant tumours, in contrast, range from well-differentiated to undifferentiated, or poorly differentiated. Malignant tumours composed of undifferentiated cells are said to be anaplastic.

290B: Liver necrosis

Overdoses of paracetamol overwhelm the liver's glutathione reductase capacity. The toxic metabolites accumulate and produce hepatic necrosis.

291C: Ninety-five per cent of the subjects will have a blood glucose between 6.7 and 12.3

The blood glucose values follow a normal (Gaussian) distribution since the mean and median values are equal. Ninety-five per cent fall between two standard deviations (and not two standard errors!) of the mean, that is between 6.7 and 12.3. Another 2.5 per cent of subjects will have a

blood glucose greater than 12.3, and 2.5 per cent will have a blood glucose of less than 6.7. It is sometimes easier to physically draw the bell-shaped distribution and mark out the values on it: 68 per cent of values lie one standard deviation away from the mean. 99 per cent of values lie within 2.6 standard deviations away from the mean.

292C: It is responsible for the formation of the transverse and oblique sinuses

The pericardium refers to the sac that encloses the heart. It comprises three layers: an outer fibrous pericardium and an inner serous pericardium (which comprises both an outer parietal layer and an inner visceral layer). There is a small amount of pericardial fluid between the visceral and parietal layers of the serous pericardium. This allows the heart to move freely within the pericardial sac.

The pericardium serves two main functions. First, it protects and lubricates the heart. Second, it contributes to diastolic coupling of the left and right ventricles. However, cardiac contractility functions normally (although maybe not optimally) in the absence of a pericardium. Indeed, after coronary artery bypass grafting surgery the pericardium is often left open (pericardiotomy) to prevent the build-up of fluid in the postoperative period causing a tamponade effect.

Between the parietal and visceral layers there are two pericardial sinuses. The transverse sinus lies in between the pulmonary artery and aorta in front and the pulmonary veins and superior vena cava behind. The oblique sinus is a space behind the heart between the left atrium in front and the fibrous pericardium behind, posterior to which lies the oesophagus. The transverse sinus is especially important in cardiac surgery. A digit and ligature can be passed through the transverse sinus and, by tightening the ligature, the surgeon can stop the blood flow through the aorta or pulmonary trunk while cardiac surgery is performed.

The fibrous pericardium and the parietal layer of the serous pericardium receive a rich innervation from the phrenic nerve. However, the visceral layer is insensitive. The pain of pericardial inflammation (pericarditis) is pronounced, originates in the parietal layer and is transmitted by way of the phrenic nerve.

If extensive fluid collects within the pericardial cavity it interferes with the action of the heart since the fibrous pericardium is inelastic. The pericardial cavity, in this way, behaves like a rigid box with only a finite amount of space. Thus, if the pressure builds up within the compartment, something else has to give and this usually results in compression of the heart. Such a situation is most commonly encountered in the case of penetrating trauma where the build-up of blood within the pericardial space often results in a cardiac tamponade, manifesting as a precipitous fall in cardiac output. Pericardiocentesis (removal, by needle, of pericardial fluid) may be a life-saving manoeuvre in such circumstances.

293B: Production is decreased by angiotensin-converting enzyme inhibitors

Aldosterone is a steroid hormone secreted by the zona glomerulosa layer of the adrenal cortex. Secretion continues following the removal of the kidneys and their juxtaglomerular cells because other factors other than the renin–angiotensin system result in the secretion of aldosterone (e.g. hyperkalaemia).

Angiotensin-converting enzyme (ACE) inhibitors tend to reduce the level of angiotensin II which normally stimulates the adrenal cortex to produce aldosterone. The reduction of angiotensin II and aldosterone, in part, explains the antihypertensive effect of angiotensin-converting enzyme inhibitors.

Aldosterone increases the excretion of both potassium and hydrogen ions from the distal convoluted tubule and collecting ducts. This results in a potassium diuresis and an acidic urine of low pH.

294A: Hyperchromatism

Both cytology and histology involve the study of cells at the microscopic level. Cytology studies individual cells and cell morphology. Histology studies cells within the context of tissues and

provides information about tissue architecture. Only histology can provide definitive diagnosis of invasion.

The cytological features of malignancy include:

- increased nuclear to cytoplasmic ratio
- hyperchromatism (darkly staining nuclei due to increased amounts of DNA)
- prominent nucleoli
- variability in cellular and nuclear size and shape (cellular and nuclear pleomorphism)
- high mitotic index (increased mitotic rate)
- abnormal mitotic figures
- lack of differentiation (anaplasia).

The histological features of malignancy include all of the above, plus:

- loss of normal tissue architecture
- infiltrative borders, with a disordered growth pattern
- invasion beyond the basement membrane
- lymphovascular involvement
- excessive necrosis and haemorrhage
- loss of cell-to-cell cohesion, resulting in shedding.

Pyknosis, karyorrhexis and karyolysis are cytological features of cell death (necrosis and apoptosis), rather than malignancy.

295E: Amyloid

Amyloid is an acellular material that is eosinophilic. After Congo red staining, there is apple-green birefringence under plane polarized light. Calcium salts tend to be deeply basophilic, not eosinophilic with routine stains. Cholesterol deposits tend to dissolve out of tissues with routine processing agents and only empty outlines are seen of where the crystals were once present. Myocyte fibrinoid necrosis would be moderately cellular and eosinophilic.

296E: The mean and standard deviation of a random sample will generally be different from the mean and standard deviation of the true population

The standard error of the mean (SE) measures the variability of a sample statistic (i.e. mean or proportion) in relation to the true population characteristic (i.e. how accurate the sample mean is an estimate of the true population mean). The standard deviation (SD) is a measure of the variability of observations around the mean.

The SE is equal to the SD divided by the square-root of the sample size. The SE is therefore generally smaller than the SD. In addition, the SE is smaller when the sample size is larger.

- The mean is the arithmetic average.
- The median is the middle value when the values are ranked.
- The mode is the value that occurs most often.

In a normal (Gaussian) distribution, the mean = median = mode. In skewed distributions the following three rules apply:

- The median always lies between the mean and the mode.
- The mode occurs at the maximum point in a frequency distribution curve.
- The mean is affected by outliers.

Thus:

- In a positively skewed distribution: mean>median>mode.
- In a negatively skewed distribution: mode>median>mean.

297D: Occlusion of the anterior interventricular artery (left anterior descending artery) results in an anterior myocardial infarction

The heart is composed of cardiac muscle. This cardiac muscle receives the oxygen and nutrients that it requires to pump effectively through the coronary arteries. There are two principal coronary arteries, the right and the left. The right coronary originates from the anterior aortic sinus, whereas the left coronary artery originates from the left posterior aortic sinus. The left coronary artery divides into an anterior interventricular (or left anterior descending) artery and circumflex branches. The right coronary gives off the posterior interventricular (posterior descending) artery. The right coronary supplies the right atrium and part of the left atrium, the sinoatrial node in 60 per cent of cases, the right ventricle, the posterior part of the interventricular septum and the atrioventricular node in 80 per cent of cases. The left coronary artery supplies the left atrium, left ventricle, anterior interventricular septum, sinoatrial node in 40 per cent of cases and the atrioventricular node in 20 per cent of cases.

Understanding the above, one is able to predict the consequences of a blockage within a particular coronary artery. Thus a lesion within the anterior interventricular artery (of the left coronary artery) leads to an anterior myocardial infarct and death of the left ventricular muscle, resulting in congestive cardiac failure. A lesion within the right coronary artery would be expected to produce arrhythmias since the dominant arterial supply to the sinoatrial and atrioventricular nodes is through the right coronary artery.

Angina pectoris originates in the muscle or the vessels and is transmitted by sympathetic nerves. The pain of angina is often referred to the left arm and shoulder, but also frequently to the neck, throat and even to the side of the face. The reason for this is that the heart originates during embryonic life in the neck, as do the arms. Therefore both these structures receive pain fibres from the same spinal segments. Angina is usually a result of the laying down of fatty deposits within the coronary arteries (atherosclerosis). However, angina may also occur in the absence of atherosclerosis, in cases such as aortic stenosis, cocaine misuse, vasculitis, and variant (Prinzmetal's) angina; the latter being due to vasospasm of the coronary arteries.

298C: Activation results in the stimulation of aldosterone release

Angiotensinogen is synthesized by the liver. Renin catalyses the production of angiotensin I (a decapeptide) from angiotensinogen. Angiotensin I is further cleaved to an octapeptide, angiotensin II, by ACE found mainly in the capillaries of the lungs. Collectively, this is known as the renin–angiotensin system:

angiotensinogen → (renin) → angiotensin I → (ACE in lungs) → angiotensin II

The effects of activation of the renin–angiotensin system are several:

- stimulation of aldosterone release from the adrenal cortex; this increases sodium and water retention, helping to maintain the arterial pressure
- enhanced NaCl and water reabsorption from the proximal convoluted tubule
- angiotensin causing widespread vasoconstriction, increasing the systemic vascular resistance and so the arterial pressure (the resulting vasoconstriction also reduces the GFR at a time when water has to be conserved)
- stimulation of ADH secretion from the posterior pituitary, leading to an increased solute-free water reabsorption
- stimulation of thirst (dipsogenic effect).

299B: Lymphatics

Metastasis is the seeding of tumour cells to sites distant and detached from the primary tumour. This is different from invasion which is spread in continuity.

As a general rule, carcinomas (malignant tumours of epithelial origin) most often metastasize

via the lymph; sarcomas (malignant tumours of connective tissue origin) most often metastasize via the bloodstream.

Thus, breast carcinomas often spread to local lymph nodes (axillary and internal mammary), whereas osteosarcomas typically spread via the bloodstream, forming cannonball metastases in the lungs. However, this rule is slightly misleading because ultimately there are numerous interconnections between the vascular and lymphatic systems. In addition, every rule has exceptions (e.g. follicular carcinoma of the thyroid spreads by the haematogenous route).

Neoplasms, in general, may metastasize by several routes:

- local invasion (direct spread)
- via the bloodstream (haematogenous route)
- via the lymphatics
- trans-coelomic spread (e.g. across the peritoneal or pleural cavities)
- via the cerebrospinal fluid (for central nervous system tumours)
- peri-neural spread (e.g. adenoid cystic carcinoma of the parotid)
- implantation/accidental seeding during surgery – iatrogenic.

300C: Hepatic angiosarcoma

Environmental exposure to vinyl chloride is associated with the later development of hepatic angiosarcoma. Focal nodular hyperplasia and hepatic fibroma are not linked to any defined underlying carcinogen exposure. Hepatic adenomas occur sporadically in the setting of exogenous steroid hormone use. Hepatocellular carcinoma is associated with cirrhosis, chronic viral hepatitis and aflatoxin exposure.

301B: This difference would have arisen by chance alone less than one time in 200

Do not confuse the terms standard error and standard deviation. The standard deviation gives a measure of the spread of the distribution. The smaller the standard deviation (or variance), the more tightly grouped the values are. If the values are normally distributed, approximately 95 per cent of values lie within two standard deviations of the mean (not standard errors!).

The standard error is a measure of how precisely the sample mean reflects the population mean. The standard error can be used to construct confidence intervals. Typically a 95 per cent confidence interval is quoted, which means that we are 95 per cent certain that the true population mean lies within the interval given by mean ± 1.96 standard errors. In this case the 95 per cent confidence interval is approximately 0.5 ± 0.4, or 0.1–0.9. There is therefore a 5 per cent chance that the true population mean lies outside the range 0.1–0.9.

The *p*-value is a probability that derives from statistical significance tests. It takes a value between 0 and 1. Values close to zero suggest that the null hypothesis is unlikely to be true. The smaller the *p*-value, the more significant the result. A significant result is normally taken as a *p*-value <0.05 (or 5 per cent), meaning that the difference would have arisen by chance alone in less than 1 time in 20. A *p*-value <0.005 (or 0.5 per cent) is highly significant, meaning that the difference would have arisen by chance alone less than 1 time in 200.

302D: The posterior wall of the canal is bounded by transversalis fascia and the conjoint tendon medially

Many students are troubled by the anatomy and significance of the inguinal canal. Its boundaries are:

- *Anterior wall:* skin, superficial fascia, external oblique (for whole length), internal oblique for lateral one-third
- *Posterior wall:* transversalis fascia (for whole length), conjoint tendon and pectineal (Cooper's) ligament medially
- *Floor:* inguinal ligament (Poupart's ligament)

- *Roof:* arching fibres of internal oblique and transversus abdominus which fuse to form the conjoint tendon on the posteromedial aspect of the canal.

The inguinal canal is an oblique passage that runs from the deep to the superficial inguinal rings and serves to transmit the testis (in the developing male) and spermatic cord in adulthood. It therefore functions to exteriorize the testis so that an optimal temperature can be obtained in order for spermatogenesis to proceed. In the female the inguinal canal transmits the round ligament of the uterus and by this means helps to maintain and support the uterus in its typical anteverted, anteflexed position.

The deep inguinal ring is a hole in the transversalis fascia and lies a finger-breadth above the mid-point of the inguinal ligament (i.e. half way between the anterior superior iliac spine and pubic tubercle). The superficial inguinal ring is a hole in the external oblique aponeurosis. The key to understanding the inguinal canal is to concentrate on the internal oblique layer which laterally forms the anterior wall of the inguinal canal. The internal oblique then arches over the top of the canal forming its roof and then blends with the transversus abdominus layer posteriorly and medially to form the conjoint tendon.

A hernia is simply a protrusion of a viscus, or part of a viscus, outwith its normal position. A femoral hernia can be distinguished from an inguinal hernia by its position. An inguinal hernia lies above and medial to the pubic tubercle, while a femoral hernia lies below and lateral to the pubic tubercle. The pubic tubercle is thus an important landmark in differentiating a femoral from an inguinal hernia. In addition, an inguinal hernia may be either direct or indirect. A direct hernia passes straight through a weakness in the anterior abdominal wall and passes through the superficial ring only. An indirect hernia, in contrast, passes through both the deep and superficial inguinal rings and thereby passes along the entire length of the inguinal canal.

303D: A fall in pressure in the afferent arteriole promotes renin secretion

The juxtaglomerular apparatus is a specialization of the glomerular afferent arteriole and the distal convoluted tubule of the corresponding nephron and is involved in the regulation of extracellular volume and blood pressure via the renin–angiotensin system.

The juxtaglomerular apparatus has three components:

- macula densa – specialized epithelial cells lining the distal convoluted tubule
- juxtaglomerular cells (also known as granular cells) of the afferent arterioles – modified smooth muscle cells that are renin-secreting
- extraglomerular mesangial cells (also known as Lacis cells or Goormaghtigh cells) – their function remains obscure.

The extraglomerular mesangial cells contain contractile proteins that are instrumental in the fine tuning of glomerular filtration. They have phagocytic properties and may act as antigen-presenting cells. They may also be the site of secretion of the hormone erythropoietin.

The renin–angiotensin system is triggered to release renin under three circumstances:

- fall in the renal perfusion pressure detected by baroreceptors in the afferent arterioles
- activation of the sympathetic nervous system – this occurs when there is a fall in arterial blood pressure
- reduced sodium delivery to the macula densa (as detected by osmoreceptors) – this occurs when there is also a fall in renal perfusion pressure.

An unknown paracrine factor is believed to act between the macula densa and juxtaglomerular cells to stimulate renin release (a prostaglandin or nitric oxide has been postulated).

The renin–angiotensin system is strongly implicated in the pathogenesis of hypertension secondary to renal artery stenosis. The juxtaglomerular apparatus of the affected kidney responds to decreased perfusion pressure by increasing renin secretion (Goldblatt hypertension).

304C: Astrocytomas

It is estimated that 50 per cent of bronchial carcinomas have metastasized by the time of clinical presentation. Breast carcinoma metastasizes readily to sites such as the lung, bone and brain. Melanoma is an aggressive tumour that can metastasize to virtually any site within the body. It therefore carries an extremely poor prognosis. Renal cell carcinomas characteristically invade the renal veins and extend into the inferior vena cava (sometimes reaching as far up as the right atrium), so that blood-borne metastases are common, especially to the lungs, liver and bone.

Astrocytomas (and even the poorly differentiated form, glioblastoma multiforme), rarely metastasize to sites outside of the central nervous system since they are contained by the blood–brain barrier. They usually metastasize outside the central nervous system *only* if there is a breach in the blood–brain barrier, or if there is an artificial connection (such as a ventriculoperitoneal shunt) connecting the central nervous system with another part of the body.

305C: Neuroendocrine cells

Small-cell undifferentiated pulmonary carcinoma (oat-cell carcinoma) is closely linked to smoking. This malignancy is thought to arise from neuroendocrine cells of the bronchial mucosa. Clara cells may give rise to certain pulmonary adenocarcinomas, and metaplastic bronchial epithelium is a likely source of squamous cell carcinomas. Alveolar pneumocytes rarely undergo malignant transformation.

306D: The negative predictive value is 0.99

The *sensitivity* indicates how sensitive the test is at picking up those people who have the disease. It is equal to the number of people who are both disease-positive and test-positive divided by the number who are disease-positive. In this example, it is 4/5. The *specificity* indicates how good the test is at picking up those people who do not have the disease. It is equal to the number of people who are both disease-negative and test-negative divided by the number of people who are disease-negative. In this example it is 90/95.

The *positive predictive value* estimates the probability that a subject, who has a positive test, truly has the disease. In this example, it is 4/9. The *negative predictive value* estimates the probability that a subject who has a negative test truly does not have the disease. Here it is 90/91. The sensitivity and specificity are independent of disease prevalence.

307E: It forms the entrance to the lesser sac

The greater and lesser sacs of the peritoneal cavity communicate with each other by way of the epiploic foramen (of Winslow). This is therefore a key landmark within the abdomen both anatomically and clinically. The boundaries of the epiploic foramen are as follows:

- anteriorly – the lesser omentum with the common bile duct, portal vein and common hepatic artery in its free edge
- posteriorly – inferior vena cava
- superiorly – the caudate (not quadrate) lobe of the liver
- inferiorly – first part of duodenum
- medially – lesser sac (posterior to stomach)
- laterally – greater sac.

From a clinical standpoint, the epiploic foramen is important for two reasons. First, it may be the site of internal herniation of bowel. Second, compression of the common hepatic artery in the free edge of the lesser omentum by a carefully placed hand in the epiploic foramen may be a life-saving manoeuvre at laparotomy to control bleeding from the liver (Pringle's manoeuvre).

308A: It increases in response to a loss of circulating volume of at least 10 per cent

ADH synthesis occurs in the cell bodies of the magnocellular neurones in the supraoptic (5/6) and paraventricular nuclei (1/6) of the hypothalamus. From there, ADH is transported down the

axons of these neurones to their endings in the posterior pituitary (neurohypophysis or pars nervosa) where they are stored as secretory granules prior to release. Release is controlled directly by nerve impulses passing down the axons from the hypothalamus; this process is known as neurosecretion.

Increased secretion of ADH occurs in response to two main stimuli: an increase in plasma osmolality and a decrease in effective circulating volume. Significant changes in secretion occur when osmolality is changed as little as 1 per cent. Such a change is detected by osmoreceptors that lie outside the blood–brain barrier and appear to be located in the circumventricular organs, particularly the organum vasculosum of the lamina terminalis. In this way, the osmoreceptors rapidly respond to changes in plasma osmolality and in normal individuals plasma osmolality is maintained very close to 285 mOsm/L. ADH secretion is considerably more sensitive to small changes in osmolality than to similar changes in blood volume. Plasma ADH levels do not increase appreciably until blood volume is reduced by about 10 per cent, when ADH plays a significant role in the response to haemorrhage.

ADH has two main actions: it increases free-water absorption from the collecting ducts of the kidney (thereby conserving water), and it is a potent vasoconstrictor. The mechanism by which ADH exerts its antidiuretic effect is through the action on V2 receptors and insertion of protein water channels (aquaporins) in the luminal membranes of collecting-duct cells. Aquaporins are stored in endosomes inside cells and ADH causes their translocation to the cell membrane via a cyclic AMP pathway. In this way, the urine becomes concentrated and its volume decreases in response to an increase in plasma osmolality and a rise in ADH; this osmoregulatory action of ADH is a good example of a homeostatic mechanism. Vasoconstriction is mediated via V1 receptors (and the phosphoinositol pathway). The latter effect has an important role in maintaining arterial blood pressure in haemorrhagic shock.

Hypersecretion of ADH occurs in the syndrome of inappropriate ADH release (SIADH). Diabetes insipidus is the syndrome that results when there is ADH deficiency (cranial form), or when the kidney fails to respond to the hormone (nephrogenic form). It should not be confused with diabetes mellitus; the term 'diabetes' is derived from the Greek meaning 'siphon', and simply reflects the excessive passing of urine in both conditions.

309C: Have a peak incidence in those less than 50 years of age

Carcinomas are much more common than sarcomas. The former are malignant neoplasms derived from epithelium, whereas sarcomas are malignant neoplasms derived from connective tissue. Sarcomas have a peak incidence in those under 50 years of age. The preferred route of metastasis for sarcomas is via the bloodstream; this contrasts with carcinomas, which usually metastasize by the lymphatics. Understandably the liver and lungs are most frequently involved secondarily in such haematogenous dissemination since all portal drainage flows to the liver and all caval blood flows to the lungs.

No in-situ phase has been identified for sarcomas, unlike in carcinomas where there is often an in-situ phase. As a result sarcomas generally carry a poor prognosis.

310D: Elevated serum gamma-glutamyl transpeptidase

Elevated serum gamma-glutamyl transpeptidase (GGT) may be the only laboratory abnormality in patients who are dependent on alcohol. Heavy drinkers may also have an increased MCV.

311A: Valvulae conniventes

The following distinguish large bowel from small bowel in the cadaver, at laparotomy and on imaging. Large bowel has the following three characteristic features:

- haustra (synonymous with sacculations)
- appendices epiploicae
- taeniae coli.

Valvulae conniventes (synonymous with plica circulares) are a feature of small bowel rather than large bowel.

312D: The kidney is able to generate new bicarbonate from glutamine

The precision with which hydrogen ion concentration is regulated emphasizes its importance to the various cell functions. The normal pH of the blood is held remarkably constant in the range 7.35–7.45. It is essential that the pH be kept within these stringent limits to prevent the denaturing of body proteins and enzymes. This is yet another example of homeostasis, whereby the constancy of the 'internal milieu' is essential to life.

There are three primary systems that regulate the pH in the body:

- the chemical buffer systems of the body fluids
- the respiratory system (which regulates the removal of CO_2 and therefore carbonic acid from the blood)
- the kidneys.

The bone and liver also play a small role in the regulation of pH. When there is a change in pH, the buffer systems work fastest (within a fraction of a second) to minimize the change in pH. Of these, the bicarbonate buffer system is the most important extracellular buffer. The second line of defence is the respiratory system which acts within a few minutes. These first two lines of defence keep the pH constant until the more slowly responding third line of defence, the kidneys, can eliminate the excess acid or base from the body. Although the kidneys are relatively slow to respond compared with the other defences (taking hours to days), they are the most powerful of the acid–base regulatory systems.

The renal tubule actively secretes hydrogen ions and reabsorbs bicarbonate ions. Acute renal failure therefore results in an inability to excrete acid and metabolic acidosis. There are three main methods by which the kidney absorbs bicarbonate:

- replacement of filtered bicarbonate with bicarbonate that is generated in tubular cells
- generation of new bicarbonate by the phosphate buffer system which carries excess hydrogen ions into the urine
- generation of new bicarbonate from glutamine molecules that are absorbed by the tubular cell (the ammonia buffer system).

313B: Tumour growth obeys Gompertzian kinetics

Consider the growth of a tumour. A cell divides to form two cells, these divide to form four cells, and so on. Assuming no cell losses, the tumour will double in cell numbers every few days (a typical cell cycle in a mammalian cell is about 24 hours). Cells continue to multiply because there is loss of the normal regulatory mechanisms that restrict tissue growth (such as contact inhibition). It is unusual for a tumour to become clinically obvious until there are about 10^9 cells (30 divisions), or one gram of tumour cells (corresponding to a tumour diameter of approximately 1 cm).

However, as the tumour continues to grow it begins to outstrip its own blood supply so that an increasing number of cells are lost by apoptosis. Also, as the tumour expands, more and more cells are shed through exfoliation, hypoxia, non-viability, metastasis and host defences. The result of this is two-fold. First, the rate of tumour growth begins to slow down from the initial exponential pattern. The tumour growth curve therefore tends to assume a sigmoidal shape (Gompertzian kinetics).

Second, it means the growth fraction (the proportion of cells within the tumour population that are in the proliferative pool) of smaller tumours is greater than that of larger tumours. As tumours continue to grow, cells leave the replicative pool in ever-increasing numbers, owing to shedding or lack of nutrients, by differentiating and by reversion to the resting phase of the cell cycle, G_0. Thus, by the time the tumour is clinically detectable, most cells are not in the replicative pool (and so are

relatively resistant to the effects of chemoradiotherapy). The growth fraction is usually 4 per cent to 80 per cent, with an average of less than 20 per cent. Even in some rapidly growing tumours, the growth fraction is only approximately 20 per cent. Indeed, some normal tissues, such as bone marrow and alimentary mucosa, have larger growth fractions and shorter mitotic cycle times than many cancers, even cancers of those tissues. Ultimately the progressive growth of tumours and the rate at which they grow are determined by the excess of cell production over cell loss.

It is very important to recognize that the clinical phase of a tumour – that is, the time from it becoming clinically apparent until it causing the death of the patient (assuming no treatment) – is short in comparison to the preclinical phase. Thus, by the time a solid tumour is detected, it has already completed a major portion of its life cycle. During the long preclinical phase there is time for invasion and metastasis to occur. In addition there is time for cell heterogeneity to develop within the tumour. This means that over and above the initial mutations, further genetic events occur in sub-populations of the tumour, leading to variation and the outgrowth of sub-populations with different patterns of differentiation and properties (a form of Darwinian evolution).

314E: Locus coeruleus

The locus coeruleus is located in the pons and produces most of the noradrenergic output to the brain. It has receptors for opiates and autoreceptors for noradrenaline and GABA. The locus coeruleus is involved in alertness (reticular activating system) and the anxiety response.

315D: It is stimulated to contract by cholecystokinin

The gall bladder has three main functions: it stores bile, concentrates bile (5- to 20-fold), and adds mucus to the bile secreted by the liver. It has a capacity of about 50 mL. Its mucous membrane is a lax areolar tissue lined with simple columnar epithelium. Under the epithelium there is a layer of connective tissue, followed by a muscular wall that contracts in response to cholecystokinin, a peptide hormone secreted by the duodenal mucosa in response to the entry of fatty foods into the duodenum.

The gall bladder is supplied by the cystic artery, usually a branch of the right hepatic artery. It runs across the triangle formed by the liver, common hepatic duct and cystic duct to reach the gall bladder (Calot's triangle). Calot's triangle reliably contains the cystic artery, the cystic lymph node (of Lund), connective tissue and lymphatics. It is important to dissect out this triangle at laparoscopic cholecystectomy in order to successfully identify and ligate the cystic artery prior to removal of the gall bladder.

The gall bladder is not essential for life. Indeed rats and horses manage perfectly well without gall bladders. Patients who have had their gall bladder removed lead a normal life and can expect a normal life expectancy. Removal of the gall bladder (cholecystectomy) is a common operation. Indications usually relate to gallstone disease, but rarely it may be performed for conditions such as carcinoma of the gall bladder. It may be performed open, but is mostly performed nowadays by the laparoscopic (keyhole) route.

316D: The low blood flow in the vasa recta assists in the formation of concentrated urine

In a normal adult human the combined blood flow through both kidneys is about 1200 mL/min, or about 20 per cent of the cardiac output. Considering that the kidneys constitute only about 0.4 per cent of the total body weight, they receive an extremely high blood flow compared with other tissues. The high flow to the kidneys greatly exceeds their metabolic demands (the kidneys account for only 6 per cent of total oxygen consumption). The purpose of this additional flow is to supply enough plasma for the high rates of glomerular filtration that are necessary for precise regulation of body fluid volumes and solute concentrations. Organic para-aminohippuric acid has traditionally been used to measure renal blood flow.

The kidneys have effective mechanisms for maintaining the constancy of renal blood flow and GFR over an arterial pressure range between 70 and 170 mmHg, a process called autoregulation. This helps to maintain a normal excretion of metabolic waste products, such as urea and

creatinine, that depend on GFR for their excretion. Autoregulation is an intrinsic property of the kidney; therefore transplanted kidneys will autoregulate. There are two main theories to explain how renal autoregulation of blood flow occurs: tubuloglomerular feedback and the myogenic mechanism.

Angiotensin II preferentially constricts the efferent more than the afferent arteriole. This has the effect of raising glomerular filtration pressure, while reducing renal blood flow. Under the circumstances of decreased arterial blood pressure (when angiotensin II is released) this helps to prevent decreases in GFR (tubuloglomerular feedback method of autoregulation); at the same time by reducing renal blood flow it causes increased reabsorption of sodium and water. In cases of renal artery stenosis, maintenance of the glomerular filtration pressure is dependent on the angiotensin II-dependent vasoconstriction of the efferent arteriole. Administration of ACE inhibitors abolishes the vasoconstriction of the efferent arteriole, resulting in an abrupt fall in the glomerular filtration rate. This explains why ACE inhibitors are contraindicated in renal artery stenosis.

Flow to the renal medulla is supplied by long capillary loops called the vasa recta. These descend into the medulla in parallel with the Loops of Henle. The blood flow in them is very low compared with flow in the renal cortex. This helps to maintain the hyperosmotic medullary interstitial gradient, thereby assisting in the formation of a concentrated urine.

317B: It is highly dependent on VEGF

As soon as tumours grow to more than about 1–2 mm^3 they require the development of new blood vessels to sustain them, a process called angiogenesis (not to be confused with apoptosis which is programmed cell death). This is because the 1–2 mm zone represents the maximum distance across which oxygen and nutrients can diffuse from blood vessels. Beyond 1–2 mm the tumour fails to enlarge without blood vascularization because hypoxia induces apoptosis by activation of p53. Neovascularization has a dual effect on tumour growth: perfusion supplies nutrients and oxygen to the growing tumour, and newly formed endothelial cells stimulate the growth of adjacent tumour cells through the secretion of cytokines.

Tumour cells elaborate angiogenic factors that induce new blood vessel formation. Of the dozen or so tumour-associated angiogenic factors that have been discovered, the two most important are vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). Much attention has focused on the use of angiogenesis inhibitors to cure cancer since angiogenesis is critical for the growth and metastasis of tumours. Whether this theoretical benefit translates into clinical practice is another matter and clinical trials are currently in progress.

Angiogenesis is also a hallmark of granulation tissue. It plays an important physiological role in wound healing by assisting in the delivery of oxygen and nutrients to healing tissue, where it is required for growth and repair. Granulation tissue produces a rich 'cytokine soup', including secretion of VEGF and bFGF which stimulates angiogenesis.

318B: Delirium

Hypernatraemia and hyperkalaemia indicate dehydration which is the most common cause of delirium.

319B: It may refer pain to the right shoulder tip

The surface marking of the gall bladder is opposite the tip of the right ninth costal cartilage; that is, where the lateral edge of the right rectus sheath crosses the costal margin. This is an important landmark as it is the site of maximal abdominal tenderness in gall bladder disease.

Gallstone disease may refer pain to the right shoulder tip (Kehr's sign). There is an important anatomical explanation underlying this phenomenon. An inflamed or distended gall bladder may irritate the diaphragm which is supplied by the phrenic nerve ('C3, C4, C5, keeps the diaphragm alive!'). These very same nerve roots also provide sensation to the right shoulder tip by way of the

supraclavicular nerves (C3, 4, 5). The body misinterprets the signals that it receives and interprets the pain signals as coming from the right shoulder tip. This is the concept of referred pain (pain felt remote from the site of tissue damage). The very same phenomenon may occur in a ruptured ectopic pregnancy, or splenic rupture, but in this instance the diaphragmatic irritant is free blood within the peritoneal cavity. Indeed, anything that irritates the diaphragm may cause referred pain to the right shoulder tip.

Courvoisier's law states that, in the presence of obstructive jaundice, a palpable gall bladder is unlikely to be due to gallstones. The reason is that gallstones cause chronic inflammation, fibrosis and a shrunken gall bladder. Rather, the law implies that a palpable gall bladder is more likely to be caused by carcinoma of the head of pancreas causing an obstruction to biliary outflow. Note, however, that the law is not true the other way round (i.e. in the presence of obstructive jaundice an impalpable gall bladder is always due to gallstones) as 50 per cent of dilated gall bladders cannot be palpated on clinical examination, due to either the patient's obesity or because of overlap of the liver.

Cholelithiasis (the presence of gallstones) is a common condition. Often they are picked up incidentally on ultrasound scan. The stones are of two types: calcium bilirubinate and cholesterol. In Europe and the United States, 85 per cent are cholesterol stones. Three factors seem to be involved in the formation of cholesterol stones: bile stasis, supersaturation of bile with cholesterol (lithogenic bile) and nucleation factors. Crucially, however, 80 per cent of patients with gallstones remain asymptomatic throughout their life. Therefore in a patient with proven gallstones on ultrasound scan a good history is imperative in order to assess whether, or not, the patient's symptoms are really due to the gallstones. If not, they are unlikely to benefit from having the gall bladder removed.

320D: The glomerular filtration barrier comprises three layers

In the normal adult human the GFR (or normal renal clearance) averages 125 mL/min, or 180 litres a day. The entire plasma volume (about 3 L) can therefore be filtered and processed by the kidney approximately 60 times each day. The rate of urine production in humans is dominated by tubular function and not by GFR. The GFR remains relatively constant through autoregulation.

After 35 years of age, GFR falls at about 1 mL/min each year. By the age of 80, GFR has fallen to about 50 per cent of its youthful level. GFR can decrease by as much as 50 per cent before plasma creatinine rises beyond the normal range. Consequently, a normal creatinine does not necessarily imply normal renal function, although a raised creatinine does usually indicate impaired renal function.

A substance used to measure the GFR must be freely filtered at the glomerulus, not be secreted by the tubules, not be reabsorbed, not be metabolized or synthesized in the body, not alter the renal function/GFR, be non-toxic and be soluble in plasma. Such a substance is the polyfructose molecule, inulin. However, it is too cumbersome to use in routine clinical practice. Instead, GFR is more commonly quantified by measuring the 24-hour urinary creatinine excretion. Para-aminohippuric acid is used to measure renal blood flow and not GFR.

The glomerular filtration barrier comprises three layers:

- the capillary endothelium
- basement membrane
- a layer of epithelial cells (podocytes).

From the anatomy of the glomerulus, it is clear that the 'actual filter' (and the primary restriction point for proteins) is the basement membrane layer.

321D: Hepatocellular carcinoma and polyvinyl chloride exposure

A carcinogen is a substance, form of energy or organism capable of inducing a cancer. The following carcinogens have been strongly associated with the workplace:

- scrotal cancer (Pott's cancer) in chimney sweeps
- mesotheliomas in people exposed to asbestos (workers in the building industry, ship construction and demolition)
- transitional cell bladder carcinoma in rubber and dye workers, due to exposure to β-naphthylamine
- angiosarcomas in workers exposed to polyvinyl chloride
- skin carcinoma in workers exposed to ultraviolet radiation (principally outdoor occupations, e.g. farmers).

322B: Exercise

Exercise promotes glucose utilization and increased insulin sensitivity. All other options tend to exacerbate insulin resistance.

323E: The right subhepatic space or hepatorenal pouch (of Rutherford–Morison) is the most dependent part of the peritoneal cavity

The liver capsule is composed of two adherent layers: a thick fibrous inner layer called Glisson's capsule (note Gerota's fascia surrounds the kidney) and an outer serous layer that is derived from the peritoneum. Glisson's capsule covers the entire surface of the liver and the serous layer covers most of the liver surface, excluding the 'bare' area of the liver near the diaphragm, the porta hepatis, and the area where the gall bladder is attached to the liver. So tough is Glisson's capsule that a subcapsular haematoma occurring as a result of liver parenchymal injury may be effectively contained by the capsule. The capsule is richly innervated by autonomic fibres, so capsular stretching as a result of malignancy, for example, may be intensely painful.

The liver receives a dual blood supply, from the hepatic artery and the portal vein. The portal vein provides 75 per cent of the total hepatic blood flow, the hepatic artery 25 per cent. The portal vein contains blood from the gut, rich in products of digestion, but is only approximately 85 per cent saturated with oxygen. The hepatic artery oxygen concentration, however, is approximately 99 per cent. Each vessel therefore supplies approximately equal amounts of oxygen to the liver.

The ligamentum venosum is a remnant of the ductus venosus (a channel that shunts blood from the left umbilical vein directly into the inferior vena cava, during gestation, thereby bypassing the liver and preserving oxygenated blood for the head and neck region). The ligamentum teres (or round ligament), in the free edge of the falciform ligament, is a remnant of the left umbilical vein.

Within the peritoneal cavity proper there are various spaces that are potential sites in which pus may collect (forming an abscess). The most important spaces to recognize are the right and left subphrenic (subdiaphragmatic) spaces, the pelvis, the right and left paracolic gutters and the right subhepatic space (also known as the hepatorenal pouch of Rutherford–Morison). When lying supine, the latter space is the most dependent part of the peritoneal cavity and hence is an area where intraperitoneal fluid is likely to accumulate in the form of an abscess (or 'collection'). The left subhepatic space is the lesser sac.

324E: The maximum concentrating ability of the human kidney is 1200 mOsm/L

The filtered load of glucose normally undergoes complete reabsorption in the proximal convoluted tubule (remember the most important substances for survival are generally absorbed first). Therefore, no glucose is usually found in the urine. However, when the filtered load exceeds the capacity of the tubules to reabsorb glucose (as in uncontrolled diabetes mellitus), urinary excretion of glucose occurs (glycosuria).

Seventy per cent of sodium reabsorption takes place in the proximal convoluted tubule, 20 per cent takes place in the ascending limb of the Loop of Henle, and only 10 per cent takes place in the distal convoluted tubule and collecting ducts. It is only the latter which is aldosterone-dependent.

The maximum concentration of urine that can be excreted by the human kidney is 1200 mOsm/L, four times the osmolality of plasma. This is primarily a function of the length of

the Loop of Henle, the hyperosmotic medullary interstitial gradient and the concentration of ADH. A counter-current multiplication system sets up an osmotic gradient in the renal medulla which allows an efficient way for urine to be concentrated over a relatively short distance along the nephron with minimal energy expenditure. The descending limb of the Loop of Henle is permeable to water (but only slightly permeable to salt and urea). Therefore water is progressively absorbed down the limb, becoming more concentrated (up to 1200 mOsm/L). The ascending limb is impermeable to water but permeable to sodium chloride. The tubular fluid is therefore hypotonic by the time it reaches the distal convoluted tubule and collecting ducts. In the presence of a high concentration of ADH, by the time the urine is excreted it has a high osmolality (up to 1200 mOsm/L).

The limited ability of the human kidney to concentrate urine to a maximal concentration of 1200 mOsm/L helps to explain why severe dehydration occurs on drinking seawater. The osmolality of seawater averages 2400 mOsm/L, so drinking one litre of seawater would give a total solute concentration of 2400 mOsm. If the maximal urine concentrating ability of the human kidney is 1200 mOsm/L, two litres is required to rid the body of these solutes. This would result in a net loss of one litre for every litre of seawater drunk, explaining the rapid dehydration that occurs in shipwreck victims who drink seawater. In short, if lost at sea, you are better off drinking nothing than drinking seawater.

325C: Burkitt's lymphoma

Oncogenic microorganisms are capable of producing tumours. Most are viral. However, *Helicobacter pylori* is a good example of a bacterium that has been associated with gastric carcinoma and gastric lymphoma, while *Schistosoma haematobium* is a good example of a parasitic infection that is capable of producing squamous cell carcinoma of the bladder.

Viruses are obligate intracellular parasites that rely on the host cell's replicative machinery to reproduce themselves. Oncogenic viruses have therefore evolved to induce host-cell replication by activating genes for cell growth. This confers a survival advantage on the virus. However, it is when proliferation becomes uncoordinated and excessive that carcinoma results.
The Epstein–Barr (DNA) virus has been implicated in the pathogenesis of three human cancers:

- Burkitt's lymphoma
- nasopharyngeal carcinoma
- Hodgkin's disease.

Other well-described oncogenic viruses, besides EBV, include two RNA viruses

- human T-cell leukaemia virus (HTLV-1)
- hepatitis C virus, leading to hepatocellular carcinoma

and three DNA viruses

- hepatitis B virus, leading to hepatocellular carcinoma
- human herpes virus type 8 (HHV-8), leading to Kaposi's sarcoma in HIV individuals
- human papilloma virus, leading to cervical carcinoma or anal carcinoma.

There are several *mechanisms* by which viruses can induce malignancy:

- directly, by becoming integrated into a cell's genome and by activation of cellular oncogenes
- indirectly, through processes (e.g. chronic inflammation) which predispose to malignancy – the mitotically active tissue presumably provides a fertile soil for mutations
- by the production of proteins that inactivate tumour suppressor proteins, such as p53.

326C: Papillary thyroid cancer

In the UK the most common primary thyroid cancer seen is the papillary variant which typically affects young women. Risk factors include previous radiation exposure (e.g. Chernobyl) and

previous radiotherapy. Secondary thyroid cancers (metastases) are rare but can arise secondary to renal cell carcinomas. In the developing world, the follicular variant is most common and is associated with iodine deficiency and longstanding goitres. Medullary thyroid tumours (associated with multiple endocrine neoplasia type 2) and lymphomas are less common.

327B: They feature at the lower end of the oesophagus

Portosystemic anastomoses are important sites in the body at which the portal venous circulation meets the systemic venous circulation. There are five principal sites where this takes place:

- lower end of the oesophagus
- upper end of the anal canal
- periumbilical region of the anterior abdominal wall
- bare area of the liver
- retroperitoneum.

In liver failure (cirrhosis), fibrosis of the liver takes place with obliteration of the blood vessels within it. Blood from the portal vein is then unable to drain through the liver into the inferior vena cava. As a result, 80 per cent of the portal blood flow is shunted into collateral channels, so that only 20 per cent reaches the liver. The portosystemic anastomoses open up in liver failure (but not in renal failure) and act as collateral channels, allowing an alternative path for blood to flow. Nevertheless, the opening up of the collaterals does not decrease the level of pressure within the portal system and portal hypertension ensues. The consequence of this is splenomegaly as a result of portal hypertension. However, the spleen *per se* is not a site of portosystemic anastomosis.

The most important area to remember as a site of portosystemic anastomosis is the lower end of the oesophagus, because of its clinical significance. The veins from the lower third of the oesophagus drain downwards to the left gastric vein (portal system) and above this level oesophageal veins drain into the azygous and hemiazygous systems (systemic system). Subsequently in portal hypertension, dilatations of the veins within the lower end of the oesophagus may take place. These are known as oesophageal varices. The same effect also takes place at the other sites of portosystemic anastomosis. However, there is one key difference between the lower oesophagus and these other sites – that is, oesophageal varices have thin walls and are prone to rupture, as predicted by LaPlace's law. Rupture of oesophageal varices may result in a catastrophic upper gastrointestinal bleed that is often fatal.

Dilatations of veins within the anterior abdominal wall (also a site of portosystemic anastomosis) are known as caput medusae, because of their resemblance to the hair of the Greek mythological character, Medusa. Venous dilatations within the upper end of the anal canal in portal hypertension may lead to the formation of haemorrhoids. However, in practice, they rarely lead to problems and the presence of oesophageal varices is far more significant.

328D: It is richer in potassium than any other gastrointestinal secretion

The salivary glands can be divided into the major (parotid, submandibular and sublingual) glands and minor glands.

- Parotid secretion is mainly serous.
- Submandibular secretion is mainly mixed (mucinous and serous).
- Sublingual secretion is mainly mucinous.

In humans, about 1–1.5 litres of saliva are secreted each day. In the unstimulated state, most of the saliva originates from the submandibular gland, but when active most of the saliva arises from the parotid gland. Secretion is an active process. The two-stage hypothesis of salivation states that a primary secretion is first formed by secretory end-pieces (that resembles an ultrafiltrate of plasma), which is then modified as it flows along the duct system. Na^+ and Cl^- are absorbed, and

K^+ and HCO_3^- are secreted, as saliva flows along the ductal system. In addition, the ducts have a low water permeability. The final saliva is hypotonic with respect to plasma and contains a higher potassium concentration than any other gastrointestinal secretion of the body.

Saliva contains principally water, mucus, enzymes (principally salivary amylase, lingual lipase and the antibacterial enzyme, lysozyme), antibodies and inorganic ions. It does not contain trypsin which is secreted by the exocrine pancreas.

Sialolithiasis (stone formation) may occur in any major salivary gland but is most common in the submandibular gland. There are two reasons for this phenomenon. The submandibular saliva is rich in mucus and is, thus, more viscous than parotid saliva. In addition the submandibular duct ascends against gravity when the body is upright, bends at the posterior edge of the mouth, and takes a long and tortuous course. This means there is a particular tendency in this gland to secretory congestion and calculus formation.

329A: They behave in a dominant fashion

Cancer is a genetic disease. Oncogenes are growth-promoting genes that are expressed in normal cells (the correct name for its normal precursor is proto-oncogene). They encode for oncoproteins (growth factors, growth receptor molecules, signal transducing molecules, nuclear transcription factors, regulators of the cell cycle) that positively regulate growth and are involved in the growth and differentiation of normal cells. Transcription of oncogenes is tightly regulated in normal cells.

Over-expression of oncoproteins, or mutations of oncogenes resulting in the inappropriate activation of oncoproteins, leads to abnormal cell growth and survival (i.e. tumourigenesis). Mutations in oncogenes that result in tumours are generally gain-of-function mutations, so oncogenes behave in a dominant manner to promote cell transformation; that is, only one copy of the defective gene is sufficient to cause cancer.

Proto-oncogenes are converted into oncogenes through a variety of mechanisms that include:

- point mutations
- chromosomal rearrangements
- gene amplification
- incorporation of a new promoter (by viruses)
- incorporation of enhancer sequences (by viruses).

The last two mechanisms are also referred to as insertional mutagenesis.

BRCA-1 is a tumour suppressor gene that accounts for a small proportion of breast cancers.

330B: GABA

Axons of the Purkinje neurones have GABA as the neurotransmitter, which is inhibitory in nature.

331E: Splenectomized patients are at high risk of post-splenectomy sepsis

The spleen, the largest of the lymphoid organs, lies under the diaphragm on the left side of the abdomen. It may be summarized by 1, 3, 5, 7, 9, 11. That is, it measures $1 \times 3 \times 5$ inches, weighs 7 ounces (200 g) and lies beneath the 9th to 11th ribs. The spleen lies at the far left margin of the lesser sac below the diaphragm. Thus, if one's hand is placed in the lesser sac (via the epiploic Foramen of Winslow) the spleen is the most laterally placed structure palpable.

Accessory spleen (splenunculi) represent congenital ectopic splenic tissue and are found in up to 20 per cent of individuals. One or several may be found, usually along the splenic vessels or in the peritoneal attachments. They are rarely larger than 2 cm in diameter.

Two 'pedicles', the gastrosplenic and lienorenal ligaments, connect the hilum of the spleen to the greater curvature of the stomach and the anterior surface of the left kidney, respectively. The splenic vessels and pancreatic tail lie in the lienorenal ligament. The short gastric and left gastro-epiploic vessels run in the gastrosplenic ligament.

The functions of the spleen may be summarized by FISH:

- **F**iltration and removal of old blood cells and encapsulated microorganisms
- **I**mmunological functions (production of IgM and opsonins)
- **S**torage function (30 per cent of the total platelets within the spleen)
- **H**aematopoiesis (in the developing fetus).

It has recently been evoked that the spleen has an endocrine function through the production of an immuno-potentiating peptide called tuftsin. The kidney, rather than the spleen, is the major site of erythropoietin secretion. Note that the spleen only acts as a site of haematopoiesis in the adult in diseased states where extramedullary haematopoiesis is a feature, such as thalassaemia.

Splenectomy (i.e. removal of the spleen) may be performed as an emergency procedure when the spleen has ruptured through trauma, or as an elective (i.e. scheduled) procedure, usually for haematological disorders where hypersplenism has caused an abnormality in one or more blood parameters. It is essential to understand the anatomical relations of the spleen (e.g. the pancreatic tail, stomach, splenic flexure of the colon, left kidney, diaphragm) in order to prevent inadvertent injury to these at splenectomy. Splenectomized patients are at high risk of post-splenectomy sepsis, especially from encapsulated organisms such as *Haemophilus*, *Meningococcus* and *Streptococcus*. Prophylaxis consists of the relevant vaccinations and lifelong penicillin.

332E: Parietal cells

Goblet cells are mucus-secreting cells widely distributed in epithelial surfaces, but especially dense in the gastrointestinal and respiratory tracts.

Kupffer cells have phagocytic properties and are found in the liver. They participate in the removal of ageing erythrocytes and other particulate debris.

The gastric mucosa contains many cell subtypes including acid-secreting cells (also known as parietal or oxyntic cells), pepsin-secreting cells (also known as peptic, chief or zymogenic cells) and G-cells (gastrin-secreting cells). Peptic cells synthesize and secrete the proteolytic enzyme, pepsin. Parietal cells actively secrete hydrochloric acid into the gastric lumen accounting for the acidic environment encountered in the stomach. However, parietal cells are also involved in the secretion of the glycoprotein, intrinsic factor.

Intrinsic factor plays a pivotal role in the absorption of vitamin B_{12} from the terminal ileum. Autoimmune attack against parietal cells leads to a lack of intrinsic factor and hydrochloric acid, leading to vitamin B_{12} deficiency and achlorhydria. This is known as pernicious anaemia.

333D: p53 and Rb-1 are tumour suppressor genes

Tumour suppressor genes encode proteins that negatively regulate cell proliferation and thus suppress tumour growth. p53 and Rb-1 are good examples located on chromosomes 17 and 13 respectively. Normal p53 is the so-called 'guardian of the genome' and triggers apoptosis and cell-cycle arrest in genetically damaged cells (i.e. it is pro-apoptotic). Mutations in p53 therefore result in the propagation of genetically damaged cells and tumourigenesis. Indeed, approximately 50 per cent of human tumours contain mutations in the p53 gene. p53-related cancers are more aggressive and have a poorer prognosis.

In contrast to oncogenes, tumours caused by tumour suppressor genes are generally caused by mutations that result in a loss of function of the gene product; neoplastic growth resulting from the loss of the protective role of tumour suppressor genes. Loss of tumour suppressor function usually requires the inactivation of both alleles of the gene, so that all of the protective effect of tumour suppressor genes is lost. That is, tumour suppressor genes are generally deemed to behave in a recessive manner.

Cellular proliferation is therefore tightly regulated by two sets of opposing functioning genes: the growth-promoting genes (proto-oncogenes) and the negative cell-cycle regulators (tumour suppressor genes). Abnormal activation of proto-oncogenes and/or loss of function of tumour suppressor genes leads to the transformation of a normal cell into a cancer cell.

334C: Buccinator

Buccinator is a muscle of facial expression and is therefore innervated by the facial nerve. The lateral pterygoid, masseter, anterior belly of digastric and temporalis are all muscles of mastication and therefore innervated by the mandibular division of the trigeminal nerve (Vc).

335D: It lies level with the hilum of the kidneys

The transpyloric plane (of Addison) is an important landmark. It lies halfway between the suprasternal notch and the symphysis pubis at the level of L1. It coincides with the following:

- L1 vertebra
- fundus of gall bladder
- hilum of kidneys
- hilum of spleen
- pylorus of the stomach (hence the name transpyloric)
- termination of the spinal cord in adults
- neck of pancreas
- origin of the portal vein
- origin of the superior (not inferior) mesenteric artery
- duodenojejunal flexure
- attachment of transverse mesocolon
- tip of ninth costal cartilage.

The aorta bifurcates at the level of L4, not L1.

336B: It is potentiated by histamine

There are three classic phases of gastric acid secretion:

- *Cephalic* (preparatory) phase [significant]. This results in the production of gastric acid before food actually enters the stomach. It is triggered by the sight, smell, thought and taste of food acting via the vagus nerve.
- *Gastric* phase [most significant]. This is initiated by the presence of food in the stomach, particularly protein-rich food.
- *Intestinal* phase [least significant]. The presence of amino acids and food in the duodenum stimulate acid production.

Gastric acid is *stimulated* by three factors:

- acetylcholine – from parasympathetic neurones of the vagus nerve that innervate parietal cells directly
- gastrin – produced by pyloric G-cells
- histamine – produced by mast cells.

Histamine stimulates the parietal cells directly and also potentiates parietal cell stimulation by gastrin and neuronal stimulation. H_2 blockers such as ranitidine are therefore an effective way of reducing acid secretion.

Gastric acid is *inhibited* by three factors:

- somatostatin
- secretin
- cholecystokinin.

337E: Results from loss of heterozygosity of the normal Rb gene

Retinoblastoma is a fascinating condition and important to know about. Much is known about retinoblastoma because the gene responsible for the condition was the first tumour suppressor gene to be discovered. In addition, studying the tumour has provided us with valuable information

into how tumour suppressor genes function. Retinoblastoma is caused by a mutation in Rb-1 (a tumour suppressor gene) on the long arm of chromosome 13. Approximately 60 per cent of cases are sporadic and 40 per cent are inherited, being transmitted as an autosomal dominant trait. Although inherited as an autosomal dominant trait, cancer results only when both copies of the normal gene are lost. This apparent paradox is explained by Knudson's two-hit hypothesis.

Knudson suggested that, in inherited cases, one genetic change (first hit) is inherited from an affected parent (i.e. the condition is inherited in an autosomal dominant manner) and is therefore present in all somatic cells of the body, whereas the second mutation (second hit) occurs after birth through some form of somatic mutation in one of the many retinal cells (which already carry the first mutation). In other words, loss of heterozygosity of the normal Rb gene results in cancer.

The mutation rate for the gene is thought to be 1 per 10 million, about the same as the number of divisions that are needed to form the adult retina; thus the chance of a somatic mutation occurring in a subject with only one functioning gene is very high. In sporadic cases, however, both mutations (hits) occur somatically within a single retinal cell. Patients with familial forms of retinoblastomas are at increased risk of developing extraretinal cancers (such as osteosarcomas) because the newborn child carries an inherited mutant Rb allele in all somatic cells of the body.

338C: Third branchial pouch

The following structures arise from each branchial pouch:

- first pouch – Eustachian tube, middle ear, mastoid, and inner layer of the tympanic membrane
- second pouch – middle ear, palatine tonsils
- third pouch – inferior parathyroid glands, thymus
- fourth pouch – superior parathyroid glands, ultimobranchial body which forms the parafollicular C-cells of the thyroid gland, musculature and cartilage of larynx (along with the sixth pharyngeal pouch)
- fifth pouch – rudimentary structure
- sixth pouch – along with the fourth pouch, contributes to the formation of the musculature and cartilage of the larynx.

339D: The anterior surface of the right adrenal gland is overlapped by the inferior vena cava

The adrenal glands lie anterosuperior to the upper part of each kidney. They weigh approximately 5 g each and measure 50 mm vertically, 30 mm across and 10 mm thick. They are somewhat asymmetrical, with the right adrenal being pyramidal in shape and left adrenal being crescentic, and lie within their own compartment of (Gerota's) renal fascia. A fascial septum separates the adrenal gland from the kidney, which explains why in nephrectomy (removal of the kidney) the latter gland is not usually displaced (or even seen).

Each gland, although only weighing a few grams, has three arteries supplying it: a direct branch from the aorta, a branch from the renal artery and a branch from the inferior phrenic artery. This reflects the high metabolic demands of the tissue. The single main suprarenal vein drains into the nearest available vessel: on the right it drains into the inferior vena cava and on the left directly into the renal vein. The right adrenal gland is tucked medially behind the inferior vena cava. In addition, the right suprarenal vein is particularly short and stubby. Both these features make the inferior vena cava vulnerable to damage in a right adrenalectomy.

The adrenal gland comprises an outer cortex and an inner medulla, which represent two developmentally and functionally independent endocrine glands within the same anatomical structure. The medulla is derived from the neural crest (ectoderm). It receives preganglionic sympathetic fibres from the greater splanchnic nerve and secretes adrenaline (70 per cent) and noradrenaline (30 per cent). The cortex is derived from mesoderm and consists of three layers, or zones. The layers from the surface inwards may be remembered by the mnemonic GFR (which also stands for glomerular filtration rate):

- G = zona **g**lomerulosa (secretes aldosterone)
- F = zona **f**asciculata (secretes cortisol and sex steroids)
- R = zona **r**eticularis (secretes cortisol and sex steroids).

340C: It stimulates gastric acid production

Gastrin is secreted by gastrin-secreting cells (G-cells) found in two locations: the pyloric region of the stomach and the upper half of the small intestine. Gastrin is released by:

- vagal stimulation
- distension of the pyloric antrum
- proteins (especially partially digested proteins) in the food.

Gastrin is inhibited by:

- a low pH in the lumen of the pyloric antrum (negative feedback loop)
- somatostatin.

Gastrin has three main actions:

- it stimulates gastric acid secretion
- it stimulates gastric motility
- it stimulates exocrine pancreatic secretions.

Overproduction of gastrin leads to excessive gastric acid secretion and the formation of multiple peptic ulcers. This is known as the Zollinger–Ellison syndrome and is often due to a gastrin-secreting tumour (gastrinoma).

341C: May produce paraneoplastic syndromes

Currently lung cancer is the most common cause of death from cancer in both men and women. It is estimated that some 50 per cent of bronchial carcinomas have metastasized by the time of clinical presentation. Lung carcinoma is most commonly due to squamous cell carcinoma as a result of squamous cell metaplasia from smoking. Tobacco smoking is believed to account for 80–90 per cent cases of lung carcinoma; the remainder are associated with radon gas and asbestos exposure.

The pathological effects of any tumour may be local or distant; distant effects may be metastatic or non-metastatic (paraneoplastic). Applying this to lung carcinoma we have:

Local effects

- *Pulmonary involvement* – cough (infection distal to airway blocked by tumour caused by disruption of the mucociliary escalator), haemoptysis (ulceration/necrosis of tumour), breathlessness (local extension of tumour), chest pain (involvement of pleura and/or chest wall), wheeze (narrowing of airways).
- *Local invasion* – hoarseness (recurrent laryngeal nerve infiltration), Horner's syndrome (infiltration of the ipsilateral sympathetic chain), wasting of the intrinsic hand muscles (brachial plexus infiltration), diaphragmatic paralysis (phrenic nerve invasion), pleural effusions (tumour spread into pleura), pericarditis (pericardial involvement), superior vena cava obstruction (direct compression by tumour).

Distant effects

- *Metastatic* – pathological fractures (bone metastases), neurological symptoms (brain metastases), hepatomegaly or jaundice (liver metastases).
- *Non-metastatic* (paraneoplastic) effects – ectopic hormone production (ADH, ACTH, PTHrP, serotonin etc.), common generalized symptoms (weight loss, anorexia, lassitude) from the acute-phase response (IL-1, IL-6, TNFα).

Paraneoplastic syndromes are symptoms and signs associated with a malignant tumour that are not due to direct local effects of the tumour or the development of metastases.

342A: Peptidoglycan

Prokaryotes have peptidoglycan in their cell walls which makes them susceptible to penicillin. Sterol and endoplasmic reticulum are features of eukaryotic cells. Bacteria generally contain single, circular chromosomes (plasmids). Prokaryotes contain 70S, rather than 80S ribosomes which are characteristic of eukaryotes.

343D: It is unimportant in humans

The vermiform (worm-shaped) appendix is a blind-ending tube varying in length (commonly 6–9 cm) which opens into the posteromedial wall of the caecum, where the taeniae coli converge. The appendix is an intraperitoneal structure and therefore has its own short mesentery, the mesoappendix. Within the mesentery lies the appendicular artery, a branch of the ileocolic artery which arises from the superior mesenteric artery.

The surface marking of the base of the appendix is situated one-third of the way up the line joining the anterior superior iliac spine to the umbilicus (McBurney's point). This is an important landmark when making an appendicectomy (McBurney's or Gridiron) incision. The position of the free end of the appendix, however, is very variable. The most common, as found at operation, is the retrocaecal or retrocolic position (75 per cent of cases), with the subcaecal or pelvic position next in order of frequency (20 per cent of cases). Less commonly, in 5 per cent of cases it lies in the pre-ileal or retro-ileal positions, or lies in front of the caecum, or in the right paracolic gutter.

The appendix has no known physiological function in man and can therefore be removed without any consequences. It probably represents a degenerated portion of the caecum that, in ancestral forms, aided in cellulose digestion. In the other animals, the appendix is much larger and provides a pouch off the main intestinal tract, in which cellulose can be trapped and be subjected to prolonged digestion. The abundance of lymphoid tissue within the submucosa of the appendix has prompted the concept that the appendix is the human equivalent of the avian bursa of Fabricius as a site of maturation of thymus-independent lymphocytes. While no discernible change in immune function results from appendicectomy, the prominence of lymphatic tissue in the appendix of young adults seems important in the aetiology of appendicitis.

344D: The main stimulation for secretion occurs during the intestinal phase

The pancreas is a mixed endocrine (ductless) and exocrine gland that forms embryologically from the fusion of separate dorsal and ventral pancreatic buds (endodermal outgrowths from the primitive foregut). The embryology helps to explain how aberrations of development lead to the formation of an annular pancreas, or pancreas divisum, either of which may lead to problems in later life.

The exocrine component of the pancreas consists of closely packed secretory acini which drain into a highly branched duct system. Approximately 1500 mL of pancreatic juice is secreted each day into the duodenum via the pancreatic duct. The alkaline pH of the pancreatic secretion (approximately 8.0) is due to a high content of bicarbonate ions and serves to neutralize the acidic chyme as it enters the duodenum from the stomach.

With regard to the secretion of gastric acid, it is possible to distinguish cephalic, gastric and intestinal phases in the pattern of secretion. The weak cephalic phase contributes only 15 per cent of the total response, an enzyme-rich secretion caused by vagal efferents. The weak gastric phase also contributes only 15 per cent of the total response and is again enzyme-rich, caused by vaso-vagal reflexes originating in the stomach and gastrin secretion. The main stimulation (70 per cent of the total response) is the intestinal phase caused by food entering the duodenum from the stomach. Secretin, a hormone released by endocrine cells scattered in the duodenal mucosa, promotes the secretion of copious watery fluid rich in bicarbonate. The major stimulus for the release of secretin

is acid. Cholecystokinin, also derived from duodenal endocrine cells, stimulates the secretion of enzyme-rich pancreatic fluid. Secretin and cholecystokinin act synergistically.

345E: Secondary carcinoma

Tumours or neoplasms may be benign or malignant. Malignant tumours may be primary or secondary. The commonest intracerebral neoplasms are secondaries, accounting for approximately 50 per cent of all intracerebral tumours. The five most common primary sites are the lung, breast, skin (melanoma), kidney and gastrointestinal tract.

Ninety per cent of normal brain tissue is composed of glial (supporting) cells, while the remaining 10 per cent is composed of neurones. That is, there are about 10 times as many glia as there are neurones in normal brain parenchyma. Primary intracerebral neoplasms therefore predominantly arise from the glial cells, rather than the neurones. Astrocytoma is the commonest type of glioma. Meningiomas originate from the arachnoid granulations and press into the brain tissue from outside.

346D: Liver

After metastasing to the pericolonal lymph nodes, colonic tumour cells are then usually drained by the mesenteric lymphatics into blood vessels, the portal vein and finally into the liver. The other choices are less likely sites of initial distant tumour spread.

347B: It may result in thrombosis of the appendicular artery (endarteritis obliterans)

Acute appendicitis is the most common acute surgical condition of the abdomen. Approximately 7 per cent of the population will have appendicitis in their lifetime, with the peak incidence occurring between the ages of 10 and 30 years. Appendicitis is relatively uncommon at the two extremes of life since obstruction of the lumen is the usual cause of appendicitis and the lumen of the appendix is relatively wide in the infant and is frequently completely obliterated in the elderly.

Afferent nerve fibres concerned with the conduction of visceral pain from the appendix accompany the sympathetic nerves and enter the spinal cord at the level of T10. Consequently, the appendix refers visceral pain to the T10 dermatome which lies at the level of the umbilicus. Only later, when the parietal peritoneum overlying the appendix becomes inflamed, does the pain become more intense and localize to the right iliac fossa in the region of McBurney's point.

The following three factors contribute to why the appendix is prone to infection:

- It is a long, narrow blind-ended tube which encourages stasis of large bowel contents.
- It has a large amount of lymphoid tissue in its wall (submucosa).
- The lumen has a tendency to become obstructed by hardened intestinal contents (enteroliths or faecoliths) which leads to further stagnation of its contents.

The sequence of events underlying acute appendicitis is worth understanding. The initial event is probably related to obstruction of the mouth of the appendix. The most common cause of obstruction is a faecolith. This leads to formation of a closed system and the build-up of mucinous secretions (appendiceal mucocele). The distended appendix can become secondarily infected and inflamed (appendicitis). This may subsequently lead to formation of an appendix mass, or abscess. Alternatively, the pressure within this closed system may begin to rise until the point is reached that it begins to compress the superficial veins in the wall of the appendix. Obstruction to venous outflow leads to oedema and a further increase in pressure. The pressure continues to rise until eventually the appendiceal artery is compressed and thromboses (endarteritis obliterans). Since the appendiceal artery is an end-artery and does not anastomose with any other artery, it therefore represents the entire vascular supply of the appendix. The appendix subsequently undergoes ischaemic necrosis and gangrene, that may eventually result in a perforated appendix.

Acute appendicitis almost always requires surgical intervention. This may be performed by open or laparoscopic techniques. It rarely resolves with conservative management and 'watchful waiting'

risks progression to perforation and generalized peritonitis, which carries with it a high mortality. There is only one situation in which conservative management is a feasible alternative to surgery, and that is when an appendix mass (or abscess) is present and the patient is not compromised. Even then, however, it is advisable to remove the appendix later after an interval of 6–8 weeks.

348A: Trypsin is a powerful activator of other pancreatic proteolytic enzymes

The pancreatic enzymes degrade proteins, carbohydrates, lipids and nucleic acids. The pancreatic proteolytic enzymes, trypsin and chymotrypsin, are secreted as inactive proenzymes that require activation in the small intestine. Enterokinase (enteropeptidase), an enzyme secreted by the duodenal mucosa, activates trypsinogen to form trypsin; trypsin then activates chymotrypsinogen to form chymotrypsin and other proenzymes into active enzymes. Trypsin can also activate trypsinogen; therefore once some trypsin is formed, there is an autocatalytic chain reaction. By releasing the enzymes as inactive zymogens that become activated far from their site of origin, this mechanism prevents autodigestion of the pancreas.

However, the powerful nature of these proteolytic enzymes necessitates another mechanism to prevent digestion of the pancreas. The same cells that secrete the proteolytic enzymes also secrete another substance called trypsin inhibitor (not a trypsin activator which would be disastrous!). Trypsin inhibitor surrounds the enzyme granules and prevents activation of trypsin both inside the secretory cells and in the acini and ducts of the pancreas. It therefore acts as an additional safeguard should some of the trypsinogen be activated to trypsin. Following exocytosis this inhibitor is diluted out and becomes ineffective. Since trypsin activates the other pancreatic proteolytic enzymes too, trypsin inhibitor therefore also prevents the subsequent activation of the others.

When the pancreas becomes severely damaged or when the duct becomes blocked, large quantities of pancreatic secretion become pooled in the damaged areas of the pancreas. Under these circumstances, the effect of trypsin inhibitor is overwhelmed, in which case the pancreatic secretions rapidly become activated and literally digest the entire pancreas, giving rise to a condition known as acute pancreatitis. This can be lethal; even if not fatal, it may lead to a lifetime of pancreatic insufficiency.

349E: Secondary carcinoma

Tumours or neoplasms may be benign or malignant. Malignant tumours may be primary or secondary. Secondary bone tumours (i.e. metastases) are the commonest malignant tumour of bone, occurring in 70 per cent of patients with disseminated malignant disease. They are more common than all the primary malignant tumours put together. After the liver and lung, the bone is the third most common site for metastatic spread. The commonest primary malignant tumour of bone is the osteosarcoma.

The six most common tumours that spread to bone are:

- multiple myeloma
- breast
- bronchus (lung)
- prostate
- kidney
- thyroid (follicular subtype).

Secondary bone tumours may be associated with an osteolytic (bone-dissolving) or osteoblastic (bone-forming) reaction within the bone. Interestingly both prostate and breast carcinoma have a propensity to form osteoblastic lesions within the bone. The direct effect of metastatic tumours on the bone is one explanation for the hypercalcaemia that is commonly seen in malignancy. Other factors seem to play a role, however, such as the release of parathyroid hormone-related protein (PTHrP) by tumour cells.

350D: Autoclaving

Bacillus anthracis is a Gram-positive, spore-forming microbe. Autoclaving is the best option for killing vegetative cells and spores.

351D: It provides a route of access to the lesser sac

The greater omentum (or gastrocolic omentum) is a double sheet of peritoneum, fused and folded on itself to form an integral structure comprising four layers. It contains adipose tissue of variable amount, depending on the nutritional status of the patient, and hangs down like an apron overlying loops of intestine. The anterior two layers descend from the greater curvature of the stomach (the lesser omentum, not the greater omentum, arises from the lesser curvature of the stomach) where they are continuous with the peritoneum on the anterior and posterior surfaces of the stomach. Posteriorly, they ascend to the transverse colon where they loosely blend with the peritoneum on the anterior and posterior surfaces of the transverse colon and the transverse mesocolon above it.

The right and left gastroepiploic arteries run between the layers of the greater omentum and supply it, close to the greater curvature of the stomach. The greater omentum may undergo torsion, and if this is extensive the blood supply to part of it may be cut off causing necrosis. The lesser sac may be accessed through the greater omentum (by incising between the greater curvature of the stomach and the transverse colon and lifting the stomach up).

The greater omentum is of paramount surgical importance. Surgeons sometimes use the omentum to buttress an intestinal anastomosis, or in the closure of a perforated gastric or duodenal ulcer ('omental patch repair'). One important function of the greater omentum is to attempt to limit the spread of intraperitoneal infections. Indeed, the greater omentum is often referred to by surgeons as the 'great policeman of the abdomen'. The lower, right and left margins are free and it moves about the peritoneal cavity in response to peristaltic movements of the neighbouring gut. In an acutely inflamed appendix, for example, the inflammatory exudate causes the omentum to adhere to the appendix and wrap itself around the infected organ. By this means, the infection is often localized to a small area of the peritoneal cavity, thus saving the patient from a serious generalized peritonitis. The greater omentum is also commonly found plugging the neck of a hernial sac, thereby preventing the entry of coils of small intestine and strangulation of bowel. In the first two years of life, the greater omentum is poorly developed and thus is less protective in a young child.

352C: Islets of Langerhans make up only 2 per cent of the volume of the gland

The endocrine tissue of the pancreas forms Islets of Langerhans. They make up about 2 per cent of the volume of the pancreas, whereas the exocrine portion makes up 80 per cent and ducts and blood vessels make up the rest. Pancreatic endocrine tissue, like all endocrine tissue, is ductless.

There are several different types of islet cell, each producing a different hormone:

- α-islet cells secrete glucagon
- β-islet cells secrete insulin
- δ-islet cells secrete somatostatin
- F-islet cells secrete pancreatic polypeptide.

Each of these hormones passes directly into the bloodstream.

Glucagon has a reciprocal action to that of insulin. It is glycogenolytic, gluconeogenic, lipolytic and ketogenic.

353D: May be seen in histological section

Apoptosis (from the Greek meaning 'to fall off', as the leaves from a tree) is programmed cell death. It acts to eliminate unwanted cells or damaged cells with abnormal DNA. It involves the death of individual cells, rather than large groups of adjacent cells (which is usually the case in

necrosis). Apoptosis is usually unaccompanied by inflammation (as is the case in necrosis). A key feature of apoptosis is that cells can be eliminated with minimal disruption to adjacent cells.

Apoptosis may be physiological (as a normal part of growth and development), as well as pathological, where balancing the production of new cells enables a stable cell population. A good example of physiological apoptosis is the shaping of the hands in embryogenesis. Under normal conditions, apoptosis is precisely regulated by pro-apoptotic (p53, c-myc, Bax, Bad) and anti-apoptotic (Bcl-2, Bcl-XL) factors. Alteration in the fine balance of pro-apoptotic and anti-apoptotic factors may result in neoplasia (e.g. loss of p53 is found in many tumours).

Apoptosis is clearly visible in histological sections; apoptotic cells are seen as rounded membrane-bound bodies ('apoptotic bodies'). These bodies are eventually phagocytosed and digested by adjacent cells so that no clump of cellular debris is left permanently behind. The key differences between necrosis and apoptosis are summarized in Table 5.

Table 5 Apoptosis and necrosis compared

Apoptosis	Necrosis
Energy dependent (active process)	Energy independent
Internally programmed or 'suicide'	Response to external injury
Affects single cells	Affects groups of cells
No accompanying inflammation	Accompanied by inflammation
Physiological or pathological	Always pathological
Plasma membrane remains intact	Loss of plasma membrane integrity
Cell shrinkage, fragmentation and formation of apoptotic bodies	Cell swelling and lysis

354E: Destroys CD4 T-lymphocytes

HIV is the virus responsible for causing AIDS. It multiplies in CD4 lymphocytes and this multiplication leads to severe lymphopenia due to the lysis of the CD4 cells. HIV is a member of the retrivirus group and contains single-stranded RNA and an enzyme that synthesizes DNA from RNA (reverse transcriptase). It also has an envelope.

355B: They enter the bladder obliquely forming a flap valve

The ureters are segmental muscular tubes, 25 cm long, composed of smooth (involuntary) muscle throughout their entire length. They are lined by transitional epithelium (urothelium) throughout their length. Indeed the whole urinary tract, including the renal pelvis and bladder, with the exception of the terminal urethra, is lined by transitional epithelium. The clinical significance of this is that the whole urinary tract epithelium is susceptible to widespread malignant change in response to carcinogens and, as a result, tumours of the urothelium are more often multifocal compared to other sites (the so-called 'field effect'). Only the terminal (glandular part of the urethra) is lined by stratified squamous epithelium.

It is important to recognize and distinguish the ureter from surrounding vessels and nerves in the living body during surgery in order to prevent inadvertent damage. The ureter is characteristically a whitish, non-pulsatile cord, which shows peristaltic activity when gently pinched with forceps (i.e. it vermiculates). There is no situation where it is more important to recognize and preserve the ureters than at hysterectomy where the ureters lie in close proximity to the uterine vessels and ligaments. Incorrect ligation of the ureters instead of the uterine vessels may be prevented by correctly identifying the ureters (by assessing for vermiculation) and by remembering the mnemonic 'water under the bridge' (i.e. the ureters are crossed above by the uterine arteries).

Blood supply to the ureters, like the oesophagus, is segmental. The upper third is supplied by the renal arteries, the middle third from branches given off from the descending abdominal aorta, and the lower third by the superior and inferior vesical arteries. Blood supply to the middle third is

the most tenuous. Consequently, the middle third of the ureter is most vulnerable to postoperative ischaemia and stricture formation if blood supply to it is endangered by stripping the ureter clean of its surrounding tissue at surgery.

Along the course of the ureter are three constrictions worth remembering as they are often the site of hold-up for ureteric calculi (stones):

- the pelviureteric junction
- where the ureter crosses the pelvic brim in the region of the bifurcation of the common iliac artery
- the vesicoureteric junction.

The last is the point of narrowest calibre.

In both sexes the ureters run obliquely through the bladder wall for 1–2 cm before reaching their orifices at the upper lateral angles of the trigone. This forms a flap valve preventing reflux of urine retrogradely back up the ureters. If this flap valve is congenitally deficient, vesicoureteric reflux results.

356B: It is actively concentrated in the gall bladder

The liver secretes approximately 500 mL of alkaline bile daily. It is composed of 97 per cent water, 0.7 per cent bile salts (sodium and potassium salts of bile acids), 0.2 per cent bile pigments (bilirubin and biliverdin) and 2 per cent of other substances (bicarbonate, fatty acids, cholesterol, lecithin). Bile salts are derived from cholesterol – do not confuse them with bile pigments which are the breakdown products of the haem component of haemoglobin. In addition it is the accumulation of bile pigments (bilirubin) that leads to jaundice.

Bile salts are responsible for the emulsification of fat in the chyme, by the formation of micelles. This aids in their absorption. Bile contains no digestive enzymes.

Between 90 and 95 per cent of the bile salts are absorbed from the small intestine and then excreted again from the liver; most are absorbed from the terminal ileum. This is known as the enterohepatic circulation. The entire pool recycles twice per meal and approximately 6–8 times a day. Disruption of the enterohepatic circulation, either by terminal ileal resection or through a diseased terminal ileum (e.g. Crohn's disease), results in decreased fat absorption and cholesterol gallstone formation. The latter is believed to result because bile salts normally make cholesterol more water-soluble through the formation of cholesterol micelles.

Between meals the Sphincter of Oddi which guards the opening of the bile duct into the duodenum is constricted and bile passes into the gall bladder. The gall bladder serves three main functions. It concentrates bile (5- to 20-fold) by the active reabsorption of salt and water through the gall bladder epithelium. It also stores bile and secretes mucus into the bile. The periodic discharge of bile from the gall bladder aids digestion but is not essential for it.

357D: Inflammation is intimately connected with the clotting system

Acute inflammation is a stereotyped, non-specific response to tissue injury. It occurs in response to a variety of different tissue insults (both exogenous or endogenous) and not just from infection. For example, it also occurs after ischaemia (hypoxic injury), physical trauma, or in response to noxious chemicals, such as insect bites. Inflammation is fundamentally a protective response, the ultimate goal of which is to rid the organism of both the initial cause of cell injury (e.g. microbes, toxins) and the consequences of such injury (e.g. necrotic tissues). In some situations, however, inflammation may be harmful to the host (a good example is meningitis).

The four cardinal features of acute inflammation are redness (rubor), swelling (tumour), heat (calor) and pain (dolor). Some also add a fifth, such as loss of function (functio laesa), or increased secretion (fluor). Acute inflammation is part of the innate immune response occurring prior to the development of any adaptive immune response that may later occur. In this way acute inflammation acts as a 'danger signal' augmenting the adaptive immune response. The

inflammatory response is immediate, but non-specific, whereas the adaptive immune response is slower to develop but is highly specific and acquires memory.

Acute inflammation is initiated by a variety of chemical mediators, all of which interact in a synergistic manner to produce inflammation. These include bacterial-derived products, histamine, serotonin, arachidonic acid metabolites, cytokines and members of the complement, kinin, clotting and fibrinolytic systems. The clotting system and inflammation are intimately connected. Therefore bleeding at the site of injury can initiate acute inflammation.

There are three main phases of acute inflammation:

- widespread vasodilatation (hyperaemia)
- increased vascular permeability
- leucocyte extravasation and phagocytosis.

The predominant cell type in acute inflammation is the neutrophil (the macrophage predominates in chronic inflammation). Acute inflammation is of relatively short duration, lasting for minutes, several hours or a few days. If it persists for longer then it is generally regarded as chronic inflammation.

358E: Sixth cervical vertebra

C6 is the critical boundary of the root of the neck. To enter the neck from the chest, the vascular structures pass through a ring-like opening bounded by the scalene muscles laterally, the sternum and 1st rib anteriorly and the vertebra (C6).

359D: It contains the pampiniform plexus

The contents of the spermatic cord are easily remembered using the 'rule of 3's':

- '3 constituents' – vas deferens (the round ligament is the female equivalent), lymphatics, obliterated processus vaginalis
- '3 nerves' – genital branch of the genitofemoral nerve (motor to cremaster, sensory to cord), ilioinguinal nerve (within the inguinal canal but outside the spermatic cord), autonomics
- '3 arteries' – testicular artery, artery to the vas (from the superior or inferior vesical artery), cremasteric artery (from the inferior epigastric artery)
- '3 veins' – pampiniform plexus, vein from the vas, cremasteric vein
- '3 fascial coverings' – internal spermatic fascia, external spermatic fascia, cremasteric muscle & fascia (not dartos muscle which is contained within the wall of the scrotum).

360B: Gastric acid assists in the absorption of iron

Every day 7–10 litres of water enter the alimentary canal. Most of this is absorbed by the end of the small intestine so that only 500–600 mL enters the colon. Further reabsorption occurs in the colon so that only about 100 mL are lost from the body in the faeces.

Glucose absorption is dependent on sodium absorption, via a sodium (secondary active) cotransport mechanism. Conversely, the presence of glucose in the intestinal lumen facilitates the absorption of sodium. Water follows by osmosis. This is the physiological basis for the treatment of sodium and water loss in diarrhoea by oral administration of solutions containing sodium chloride and glucose (oral rehydration therapy). Most of the ingested sodium is reabsorbed (normally less than 0.5 per cent of intestinal sodium is lost in the faeces) because of its rapid absorption through the intestinal mucosa. If absorption is greater than the body requirements, the excess is excreted by the kidneys.

A good way to think about the order of absorption of substances throughout the gastrointestinal tract is to remember that the most important substances for survival are generally absorbed first, followed by the less important ones. Thus, glucose takes place mainly in the upper small intestine (duodenum and jejunum), but vitamin B_{12} is absorbed further down, in the terminal ileum (since bodily stores of vitamin B_{12} can last up to 2 years in the complete absence of vitamin B_{12} intake).

Iron is absorbed more readily in the ferrous state (Fe^{2+}), but most of the dietary iron is in the ferric (Fe^{3+}) form. Gastric acidity releases iron from the food and favours the ferrous form which is absorbed more easily. The importance of this function in humans is indicated by the fact that iron deficiency anaemia is a troublesome and relatively frequent complication of partial gastrectomy.

361D: Amyloidosis

The four possible outcomes of acute inflammation are:

- resolution (with the complete restoration of normal tissue architecture and function)
- abscess formation (a localized collection of pus surrounded by granulation tissue; pus is a collection of neutrophils in association with dead and dying organisms)
- progression to chronic inflammation
- death (a good example being meningitis).

Amyloidosis follows chronic inflammation, rather than acute inflammation.

362B: Lunate

The lunate is the most commonly dislocated carpal bone; it usually displaces anteriorly by rotation on its proximal, convex surface which articulates with the radius. The displaced bone may compress the median nerve in the carpal tunnel. The scaphoid bone is the most commonly fractured carpal bone and has an increased risk of avascular necrosis.

363D: It is supplied by T10 sympathetic nerves

The testis is supplied by the testicular artery which arises directly from the descending abdominal aorta at the level of approximately L2. Although at first glance this may seem illogical, when the testis is in closer proximity to other blood vessels such as the internal iliac, the explanation lies in the fact that the testis develops high up on the posterior abdominal wall early in embryonic life. As it descends into the scrotum during development, the testis carries with it the same blood supply that it received whence it was positioned on the posterior abdominal wall (i.e. from the aorta).

The testis drains by way of the pampiniform plexus into the inferior vena cava on the right side, but into the left renal vein on the left side. This may account for the fact that varicoceles (varicosities of the pampiniform plexus secondary to incompetent venous valves) are more common of the left compared with the right. The accumulation of serous fluid around the testis is known as a hydrocele.

As a general rule regarding lymphatic drainage, superficial lymphatics (i.e. in subcutaneous tissues) tend to run with superficial veins, whereas deep lymphatics run with arteries. The testis thus drains lymph to the para-aortic set of lymph nodes, since the testicular artery arises from the aorta. The testis never drains to the inguinal group of lymph nodes, although the scrotum may. The clinical consequence of this is that a testicular carcinoma never results in inguinal lymphadenopathy, unless the scrotum is also involved. A scrotal carcinoma, on the other hand, would be expected to produce inguinal lymphadenopathy and this holds true in clinical practice.

The testis is supplied by T10 sympathetic nerves. The consequences of this are two-fold. First, it results in testicular pain (trauma, testicular torsion etc.) being referred to the umbilicus (T10 dermatome). Second, the ureters are also supplied by T10 sympathetics. Thus a renal calculus may refer pain down to the testis, as is seen in classical renal colic.

364D: Protein is spared until relatively late

Starvation is a chronic state resulting from inadequate intake of energy. Four main metabolic processes occur during starvation: glycogenolysis, gluconeogenesis, lipolysis and ketogenesis. No significant hypoglycaemic episodes occur until the end stage of starvation is entered.

During the immediate phase of starvation (0–24 hours), reserves of glycogen from liver and skeletal muscle are utilized. Glucose produced from glycogen lasts only 24 hours. The blood

glucose is maintained after glycogen is depleted by gluconeogenesis for which the main substrates are amino acids, lactic acid and glycerol.

In general, fats spare nitrogen so that protein is preserved until relatively late in starvation. During prolonged starvation, ketone bodies (acetone, acetoacetate, β-hydroxybutyrate) derived from fats are used by the brain and other tissues (such as heart muscle). Although the brain is usually heavily dependent on glucose as its energy source, during starvation it adapts to using ketones.

When fat stores are finally used up, protein catabolism increases and death follows from proteolysis of vital muscles (cardiac muscle, diaphragm). The average time to death is about 60 days.

365B: It usually heals by organization and repair

Chronic inflammation is inflammation of prolonged duration (weeks or months) in which active inflammation, tissue destruction and attempts at repair are occurring simultaneously. It may follow acute inflammation (secondary chronic), or it may occur *de novo* in the absence of a preceding acute inflammatory phase (primary chronic).

Chronic inflammation arises in situations where the injurious stimulus persists, as when:

- the injurious agent is endogenous (e.g. acid in stomach and peptic ulceration)
- the injurious agent is non-degradable (e.g. dust particles in pneumoconiosis)
- the injurious agent evades host defence mechanisms (e.g. many intracellular organisms such as tuberculosis)
- the host attacks components of self (e.g. autoimmunity)
- host resistance (immunity) is suppressed (e.g. malnutrition, HIV).

Neutrophils are a feature of acute, rather than chronic, inflammation. Chronic inflammation is characterized by more extensive tissue destruction than acute inflammation owing to the lengthy nature of the process and the greater lysosomal rupture with the release of numerous lytic enzymes. The destroyed tissue is replaced by granulation tissue. Healing occurs by organization and repair (with fibrosis leaving a scar), rather than through resolution (which is typical of acute inflammation).

The pathological consequences of chronic inflammation include:

- tissue destruction and scarring
- development of cancer – the mitotically active tissue provides a fertile ground for the accumulation of mutations
- amyloidosis –the extracellular deposition of abnormal and insoluble, β-pleated proteinaceous deposits.

Amyloid causes its pathological effects by accumulating in body tissues.

366A: Proximal convoluted tubule

The concentration of glucose is highest in the proximal convoluted tubule and therefore most reabsorption takes place here. The concentration of glucose in the other portion of the nephron is close to zero.

367B: It lies medial to the obturator nerve and anterior to the ureter

The ovary is ovoid in shape, measuring about 3 cm long, 2 cm wide and 1 cm thick (smaller than the testis), being smaller before menarche and postmenopausally. The anterior border of the ovary is attached to the posterior leaf of the broad ligament by a double fold of peritoneum, the mesovarium. The ovary is thus an intraperitoneal structure and the surface of the ovary, covered with cuboidal epithelium faces the peritoneal cavity. Therefore ova extruded from the ovary actually pass into the peritoneal cavity. One consequence of this is that an ectopic pregnancy may occur within the peritoneal cavity, in addition to occurring within the fallopian tube.

The ovary flops laterally to lie in the ovarian fossa on the lateral pelvic wall. Immediately behind the fossa is the ureter which may be damaged while operating on the ovary and lateral to the

ovary is the obturator neurovascular bundle. A diseased ovary may therefore cause referred pain along the cutaneous distribution of the obturator nerve on the inner side of the thigh. Nerve supply to the ovary is sympathetic originating at T10 and therefore ovarian pain may also be referred to the peri-umbilical region.

The suspensory ligament of the ovary transmits the ovarian artery, vein and lymphatics. As a general rule regarding lymphatic drainage, superficial lymphatics (i.e. in subcutaneous tissues) tend to run with superficial veins, whereas deep lymphatics run with arteries. As the artery starts from the aorta, lymph drainage therefore passes to the para-aortic lymph nodes. The same applies with the testis in the male.

368C: TSH

The pituitary gland (hypophysis) is the conductor of the endocrine orchestra. It is divided into an anterior part and a posterior part. The anterior pituitary (adenohypophysis or pars distalis) secretes six hormones:

- FSH and LH – reproduction
- ACTH – stress response
- TSH – basal metabolic rate
- GH – growth
- prolactin – lactation.

The posterior pituitary (neurohypophysis or pars nervosa) secretes only two hormones:

- ADH (vasopressin) – osmotic regulation
- oxytocin – milk ejection and labour.

Testosterone is produced from Leydig cells in the testis and from the adrenal glands. CRH is produced by the median eminence of the hypothalamus.

369C: Tuberculosis

Granulomatous inflammation is a distinctive pattern of chronic inflammation characterized by granuloma formation. It usually occurs in response to the presence of indigestible matter within macrophages. Histologically, a granuloma consists of a microscopic aggregation of activated macrophages that are transformed into epithelium-like cells (epithelioid macrophages), surrounded by a collar of mononuclear leucocytes, principally lymphocytes and occasionally plasma cells. Epithelioid cells may coalesce to form multinucleate giant cells. Their nuclei are often arranged around the periphery of the cell – Langhans' giant cells. Do not confuse the term granuloma with granulation tissue; the latter is a wound-healing phenomenon and does not contain granulomas.

Tuberculosis is the archetypal granulomatous disease, but it can also occur in other disease states such as other infections (e.g. leprosy, schistosomiasis), foreign bodies, which may be endogenous (bone, adipose tissue, uric acid crystals) or exogenous (e.g. silica, suture materials). Some causes are idiopathic, such as Crohn's disease and sarcoidosis. Note that Crohn's disease, but not ulcerative colitis, is associated with the presence of granulomas. Lobar pneumonia and bronchopneumonia do not characteristically form granulomas.

If the granuloma is large it may outstrip its own blood supply, resulting in central necrosis. Tuberculosis is characteristically associated with caseating granulomas, with central caseous necrosis. Other conditions such as Crohn's disease and sarcoidosis are associated with non-caseating granulomas.

370D: Tricuspid

Clinically this patient has bacterial endocarditis. In drug abusers, it usually affects the tricuspid valve because contamination from dirty needles drains into the right side of the heart. It is usually caused by *Staphylococcus aureus*.

371A: It is drained by tributaries of both the inferior mesenteric and internal iliac veins

The rectum is 12 cm long, starting at the level of S3 and ending at the puborectalis (levator ani-pelvic floor). It is lined by typical columnar intestinal epithelium with many mucous secreting cells (transitional epithelium is almost exclusively confined to the urinary tract of mammals where it is highly specialized to accommodate a great deal of stretch and to withstand the toxicity of the urine).

The rectum has no mesentery and is therefore regarded as retroperitoneal. It is covered by peritoneum on its front and sides in its upper third, only on its front in its middle third and the rectum lies below the peritoneal reflection in its lower third. Do not be confused; although the rectum has no mesentery, the visceral pelvic fascia around the rectum is often referred to by surgeons as the mesorectum. The pararectal lymph nodes are found within the mesorectum, which is removed together with the rectum as a package during rectal excision for carcinoma.

Blood supply is by way of the superior rectal (inferior mesenteric), middle rectal (internal iliac) and inferior rectal (internal pudendal) arteries. The importance of understanding the blood supply of the rectum lies in its vulnerability during the resection of a rectal carcinoma and the formation of a join (anastomosis) from the two remaining ends of the bowel. If blood supply to the anastomosis is tenuous, then the anastomosis may break down in the postoperative period with disastrous consequences. The venous drainage is as for the arteries. Note, however, that there is a portosystemic anastomosis in the lower rectal and upper anal canal walls, as branches of the superior rectal (portal) and inferior/middle rectal veins (systemic) meet in the external and internal venous plexuses. This poses a site where haemorrhoids may form in portal hypertension.

The rectum receives parasympathetic fibres from the pelvic splanchnic nerves, or nervi erigentes, originating from S2 to S4. It functions to relax the internal sphincter, contract the bowel and transmit a sense of fullness. Note that the vagus nerve only supplies the bowel up to two-thirds along the transverse colon. The whole of the rest of the bowel inferior to this level (the so-called hindgut) receives parasympathetic fibres by way of the pelvic splanchnic nerves. Remember parasympathetic outflow from the spinal cord is craniosacral, whereas sympathetic outflow is thoracolumbar. Sympathetic supply to the rectum is through the lumbar splanchnics and superior hypogastric plexus. Sympathetics contract the internal sphincter, relax the bowel and transmit pain.

372D: Identical twins show 90 per cent concordance

In type 1 diabetes mellitus identical twins have 50 per cent concordance, whereas in type 2 there is 90 per cent concordance. Type 1 is associated with HLA DR 3/4, whereas type 2 has no HLA association. Type 1 is a disorder of insulin deficiency and therefore presentation is with weight loss and ketone production, usually early in life in the teenage years. Type 2, which commonly presents after the age of 40, is associated with obesity and insulin resistance rather than insulin deficiency *per se*.

373A: Granulation tissue actively contracts

The stages of wound healing are as follows:

- coagulation/haemostasis (immediate)
- inflammation (0–4 days) – initially neutrophils and then macrophages which remove tissue debris
- fibroplasia and epithelialization (4 days to 3 weeks) – neovascularized tissue is known as granulation tissue
- contraction, maturation and remodelling (3 weeks to 18 months) – fibroblasts differentiate into myofibroblasts which are responsible for active wound contraction.

Maximal wound tensile strength is achieved at about day 60, when it is 80 per cent of normal.

Resolution is the most favourable outcome of the healing process because it refers to the complete restitution of normal tissue architecture and function. It can occur only if tissue damage is slight, followed by rapid removal of debris. No scar tissue forms in pure resolution.

Repair, on the other hand, is the replacement of damaged tissue by fibrosis or gliosis, which fills or bridges the defect, but has no intrinsic specialized function relevant to the organ in which repair occurs. It occurs when there is substantial damage to the specialized connective tissue framework and/or the tissue lacks the ability to regenerate specialized cells. The result of repair is a scar.

Tissue repair occurs through the formation of granulation tissue. It derives its name from the granular appearance seen by early military surgeons in the bases of wounds that were about to heal, hence the association with a favourable outcome. The granules are caused by the sprouting of endothelial buds as a result of angiogenesis. Granulation tissue replaces a disorganized mess with orderly new fibrous tissue, a process called organization. Granulation tissue should not be confused with granulomas (aggregates of activated macrophages), which are not an integral part of granulation tissue.

Granulation tissue is defined by the presence of three cell types:

- macrophages – responsible for removing tissue debris
- fibroblasts – responsible for laying down the collagen in fibrous tissue that aids wound contraction
- endothelial cells – responsible for the formation of new blood vessels (angiogenesis).

Lymphocytes and plasma cells may also be present.

Healing by primary intention refers to incised wounds where the edges can be apposed. *Healing by secondary intention* is where there has been tissue loss and the edges cannot be suitably apposed. Healing by secondary intention is slower since granulation tissue has to form from the base of the wound and re-epithelialization has to occur from the edges to cover this. The granulation tissue eventually contracts, resulting in scar formation.

374E: Transitional cell carcinoma

Ninety per cent of bladder cancers are transitional cell carcinomas derived from the bladder urothelium. Risk factors include industrial chemicals, smoking and infection. Schistosomiasis and bladder stones predispose to the squamous cell variety.

375E: The ureter is closely related to the lateral fornix of the cervix

The supports of the uterus are extremely important. The lateral (or transverse) cervical ligaments condense around the uterine artery and run to the lateral pelvic wall. The uterosacral ligaments are primarily condensations of fascia running backwards from the cervix of the uterus past the rectum and attaching to the sacrum. The round ligament of the uterus is the female remnant of the embryonic gubernaculum which guides the testis to the scrotum in the male. It is a continuation of the ovarian ligament which is in the broad ligament attaching the ovary to the uterus. The round ligament then continues from the wall of the uterus in the anterior leaf of the broad ligament to the pelvic wall and then through the deep inguinal ring and inguinal canal to fade out into the labium majorum. It is important only in helping to hold the uterus in its usual anteverted, anteflexed position (i.e. the uterus tends to lie tipped forwards over the female bladder).

Some support is also offered by the anterior pubocervical ligaments. Similarly the broad ligament holds the uterus in that position but it does not contribute a great deal to preventing uterine prolapse (procidentia). The latter is a condition where the pelvic floor is so weakened, usually following multiple childbirth, that the uterus tends to prolapse through the vagina. This can adversely affect the base of the bladder or even obstruct the ureters and therefore may lead to urinary infections, incontinence or renal failure.

The blood supply comes mainly from the uterine artery, which takes a very tortuous course up the uterus (to allow for expansion in uterine hypertrophy, e.g. pregnancy). It is a branch of the internal iliac. In so reaching the uterus, the uterine artery must pass across and above the ureter which is heading past the uterus to the bladder. During hysterectomy this relationship is enormously important as the uterine arteries must be ligated and cut. Clearly one must recognize the difference and realize the close proximity of the ureter and uterine artery.

The ureters lie adjacent to the lateral fornix of the cervix. Consequently a ureteric calculus may be felt in the lateral fornix on vaginal examination. The posterior fornix actually has overlying it the peritoneum of the recto-uterine Pouch of Douglas, which is normally occupied by coils of small intestine or sigmoid colon and lies between the uterus anteriorly and the rectum posteriorly. The Pouch of Douglas is the most dependent part of the pelvis. Consequently, blood may collect here in a ruptured ectopic pregnancy. A needle may be passed into this space (in an attempt to aspirate blood) in order to diagnose the condition (culdocentesis). Furthermore, the instrument used in illegal abortions, if missing the cavity of the uterus, could actually penetrate the posterior fornix and subsequently the peritoneal cavity, often leading to fatal peritonitis and sepsis.

376C: A fasting glucose of 7.5 mM on two occasions is consistent with a diagnosis

It is vital to be aware of the diagnostic criteria for diabetes. A fasting glucose of >7 mM, or a glucose of >11.1 mM two hours after a 75 g glucose load, is diagnostic. A random glucose of >11.1 mM is also consistent with a diagnosis. One abnormal laboratory value is diagnostic in symptomatic individuals; two abnormal values are needed in asymptomatic individuals. Impaired glucose tolerance is defined as a glucose level of 7.8–11.1 mM two hours after 75 g glucose, and impaired fasting glucose is defined as a fasting glucose level above 6 but less than 7 mM.

377B: Peripheral neurones

The cells of the body are divided into three groups on the basis of their proliferative capacity:

- Continuously dividing cells (self-renewing or labile cells) continue to proliferate throughout life. This includes surface epithelia and cells of the bone marrow. Bone has excellent properties of regeneration, and remodelling of a fractured callus can produce complete restoration of a fractured bone.
- Quiescent (or stable) cells normally demonstrate a low level of replication. However, they can undergo rapid division in response to stimuli and are thus capable of reconstituting the tissue of origin. They are considered to be in G0 of the cell cycle but can be stimulated into G1. In this category are the parenchymal cells of virtually all the glandular organs of the body. This is best exemplified by the ability of the liver to regenerate after hepatectomy and after toxic, viral or chemical injury. However, regeneration does not necessarily mean restoration of normal structure. Thus if damage to the liver continues while replication occurs, there may not be a complete return to original architecture, and if the damage is severe then cirrhosis may result.
- Non-dividing (or permanent) cells have left the cell cycle and cannot replicate so that regeneration is not possible. Neurones of the central nervous system (brain and spinal cord) and skeletal and cardiac myocytes belong to this group. That these cells cannot regenerate probably reflects the fact the spatial organization of these tissues is so specific that regeneration would result in functional chaos. The result is that damaged areas of cardiac muscle are replaced by fibrous scar tissue following a myocardial infarction.

The absence of regeneration within the central nervous system reflects not only the intrinsic properties of the neurones themselves, which are incapable of dividing, but also the inhibitory environment present within the central nervous system. Under normal circumstances, the physiological purpose of the inhibitory environment present within the CNS is to prevent the formation of unwanted connections and to help to maintain the structural integrity of white

matter tracts. However, this is detrimental in the setting of injury. Thus, gliosis is the only reaction that the brain and spinal cord can make following injury, and the inability of central neurones to regenerate may result in permanent loss of function (e.g. permanent paralysis in the case of spinal cord trauma).

Peripheral nerves, on the other hand, unlike their central nervous system counterparts, are able to regenerate following injury, with axonal growth occurring at a rate of around 1 mm per day. A better understanding of why regenerative capacity is so much greater in the peripheral than in the CNS may open up new therapeutic windows for repairing the damaged CNS in patients for whom there is currently little hope.

378E: Factor XII

Deficiency of factor XII (Hageman factor) results in thrombosis rather than bleeding. The mechanism appears to be deficient activation of fibrinolysis and both thrombophlebitis and myocardial infarction have occurred in severe cases. It is inherited in an autosomal recessive manner. Deficiencies of the other factors listed are associated with bleeding.

379D: The gastroduodenal artery is a branch of the common hepatic artery

The blood supply of the stomach is initially quite confusing, easily forgotten and commonly asked about, but a few key rules make this a simple area of anatomy that will never be forgotten.

Rule 1

The coeliac trunk divides into three main branches, which can be easily remembered by the mnemonic left-hand side (LHS):

- left gastric artery (L)
- common hepatic artery (H)
- splenic artery (S).

Rule 2

For the purposes of remembering the blood supply to the stomach, the stomach can be divided into three main areas:

- lesser curvature
- greater curvature
- fundus.

Rule 3

The lesser curvature is supplied by the left and right gastric arteries. The left gastric, as already mentioned, comes directly off the coeliac trunk. The right gastric is a branch of the common hepatic artery.

Rule 4

The greater curvature is supplied by the right and left gastroepiploic arteries. The right gastroepiploic artery comes off the gastroduodenal artery. The left gastroepiploic artery comes off the splenic artery.

Rule 5

The fundus is supplied by the six, or so, short gastric arteries which arise from the splenic artery.

Rule 6

The gastroduodenal artery is an important artery to remember for clinical purposes. It arises from the common hepatic artery and lies posterior to the first part of the duodenum. A posteriorly situated duodenal ulcer may erode through the duodenal wall into the blood vessel causing catastrophic, life-threatening haemorrhage. Urgent endoscopy or laparotomy may be required to stop the bleeding.

380D: It is an anabolic hormone

Insulin acts via cell membrane spanning receptors which have intrinsic receptor tyrosine kinase activity. When insulin binds to the receptor, the tyrosine kinase is phosphorylated, resulting in a cascade of intracellular signalling mechanisms which results in glucose uptake into the cell. It is secreted by beta cells of the pancreas. Somatostatin is secreted by delta cells. Secretion is inhibited by somatostatin, which is always considered an inhibitory hormone. Insulin is considered an anabolic hormone; i.e. it takes up glucose into the cell and converts it to larger 'building blocks' such as proteins and fats. Release of insulin is stimulated not only by the ingestion of glucose but also amino acids which it will convert into larger proteins.

381C: Liquefactive necrosis classically occurs in the brain

Necrosis is abnormal tissue death during life. Necrosis is always pathological and is accompanied by inflammation. Groups of cells are involved and undergo swelling and lysis. Necrotic cells are phagocytosed by inflammatory cells. There are several different types of necrosis:

- *Coagulative* (structured) necrosis is the most common form. It results from interruption of blood supply. Tissue architecture is preserved. It is seen in organs supplied by end-arteries, such as the kidneys, heart, liver and spleen.
- *Liquefactive* (colliquative) necrosis occurs in tissues rich in lipid where lysosomal enzymes denature the fat and cause liquefaction of the tissue. It characteristically occurs in the brain.
- *Caseous* (unstructured) necrosis has a gross appearance of soft, cheesy, friable material. Tissue architecture is destroyed. It is commonly seen in tuberculosis.
- *Fat* necrosis can occur following direct trauma (e.g. breast) or enzymatic lipolysis (e.g. pancreatitis).
- *Fibrinoid* necrosis is seen in the walls of arteries that are subjected to high pressures, as in malignant hypertension. The muscular wall undergoes necrosis and is associated with deposition of fibrin.
- *Gangrenous* necrosis is irreversible tissue death characterized by putrefaction. It may be wet, dry or gaseous. The tissues appear green or black because of breakdown of haemoglobin.

382B: Left atrium

Pressure in the left atrium can be approximated by wedging an arterial catheter in the small branch of the pulmonary artery. The pulmonary vascular tree abuts the left atrium anatomically. The pulmonary artery carries deoxygenated blood from the right ventricle into the pulmonary circulation where it is oxygenated and then returned into the left atrium via the pulmonary veins.

383E: Cloquet's node lies most medially within the femoral canal

The boundaries of the femoral triangle are the inguinal ligament superiorly, the medial border of adductor longus medially and the medial border of sartorius laterally.

The contents of the femoral triangle from lateral to medial may be easily remembered by the mnemonic NAVY:

- **N** = nerve (femoral) outside the femoral sheath
- **A** = artery (femoral) within the femoral sheath
- **V** = vein (femoral) within the femoral sheath
- **Y** = Y-fronts (most medially).

Within the femoral sheath lies the femoral artery, vein and a space most medially known as the femoral canal. The purpose of the femoral canal is to allow the laterally placed femoral vein to expand into it thereby encouraging venous return. However, a piece of bowel or omentum may extend down into the femoral space, causing a femoral hernia. Within the space of the femoral canal normally lies extraperitoneal fat and a lymph node which is often given its eponymous name, Cloquet's lymph node. Cloquet's lymph node drains the lower limb, perineum and anterior

abdominal wall inferior to the umbilicus. It may be enlarged (as inguinal lymphadenopathy) in cases of carcinoma and infection at these sites.

The femoral artery lies at the mid-inguinal point (half-way between the anterior superior iliac spine and symphysis pubis), as opposed to mid-point of the inguinal ligament (half-way between the anterior superior iliac spine and the pubic tubercle) which is the surface marking of the deep inguinal ring. The surface marking of the femoral artery is imperative to understand as, not only does it provide a site for the clinician to assess the femoral pulse, but it also provides the clinician with a surface landmark for gaining access to the femoral artery for procedures such as coronary angioplasty and lower limb angiography and embolectomy.

384B: Prolactin is under dominant inhibitory regulation

Oxytocin and ADH are synthesized in the paraventricular and supraoptic nuclei of the hypothalamus. They are transported from the hypothalamus down into the posterior pituitary gland (or neurohypophysis) via magnocellular neurones and are stored in the posterior pituitary as vesicles prior to release into the bloodstream.

GH, ACTH, TSH, prolactin and LH/FSH are released from the anterior pituitary gland. Prolactin is under inhibitory control by dopamine but can also be stimulated by TRH/TSH. Catecholamines, serotonin and thyroxine are amine hormones, whereas cortisol, aldosterone, androgens, oestrogens, progesterone and vitamin D are steroid hormones. All other hormones are peptide hormones.

Insulin, growth hormone and prolactin act via tyrosine kinase receptors. Adrenaline, ACTH, TSH, LH/FSH, glucagon and somatostatin act via G-protein receptors coupled to cAMP. The G-protein coupled receptor activates adenylate cyclase which in turn generates cAMP in an amplification process. GnRH and TRH act via G-protein receptors coupled to intracellular calcium as a second messenger. This is undertaken through activation of phospholipase C. It is the steroid hormones which bind to intracellular receptors.

385B: Digestion of dead tissue by saprophytic bacteria

In gangrene, tissue that is dead is digested by bacteria which are incapable of invading and multiplying in living tissue (saprophytes), a process known as putrefaction. Gas production may be present in some forms of gangrene (e.g. gas gangrene from clostridial anaerobic infection), but not others.

Necrosis of tissue is an essential prerequisite for gangrene. Necrosis, however, may be caused by ischaemia (secondary gangrene, or dry gangrene), or by bacterial toxins (primary gangrene, or moist gangrene).

386D: Cholecystokinin

Cholecystokinin (CCK) is responsible for stimulation of gall bladder contraction. The release of CCK is stimulated by dietary fat. It is produced in the I-cells of the duodenum and jejunum. Moreover, CCK also stimulates the release of pancreatic enzyme secretion and decreases the rate of gastric emptying.

387B: It has high mobility at the expense of stability

The shoulder joint, like the hip joint, is a synovial joint of the ball and socket variety. The joint cavity, as is the case with all synovial joints, is lined by articular hyaline cartilage and not fibrocartilage. As with all joints, stability is brought about by the way the various bones articulate with one another (through their incongruous surfaces) and through the various ligaments, tendons and muscles that surround the joint. Clearly, it is impossible to have a joint that is both highly mobile and perfectly stable, as a highly mobile joint requires a wide range of movement, in all possible degrees of freedom, which is in itself intrinsically unstable. In contrast to the hip joint where stability is of paramount importance, in the shoulder joint, mobility comes at the expense of stability.

The rotator cuff muscles are the most important factor in maintaining the stability of the shoulder joint and preventing dislocation. The ligaments and bones are less important in the case of the shoulder joint. There are only four muscles of the rotator cuff, and these may be remembered by the mnemonic SITS:

- **s**upraspinatus
- **i**nfraspinatus
- **t**eres minor
- **s**ubscapularis.

Note that teres major is not a rotator cuff muscle. Note also that the first three muscles are placed posteriorly, behind the shoulder joint, while only one of the rotator cuff muscles (subscapularis) is positioned anteriorly. This may in part explain why the shoulder more commonly dislocates anteriorly, rather than posteriorly. An alternative explanation may relate to the deficiency of the joint capsule inferiorly, which makes the shoulder susceptible to antero-inferior dislocation when in the abducted, externally rotated position. The above two explanations are not mutually exclusive.

It should never be forgotten that the axillary nerve lies in close proximity to the shoulder joint and the surgical neck of the humerus. Consequently, it is vulnerable to injury at the time of a shoulder dislocation, or while attempting to reduce the shoulder back into its normal position following a dislocation. It is therefore imperative (from both clinical and medicolegal points of view) that the integrity of the axillary nerve be documented, both after seeing the patient who has a dislocated shoulder, but also following successful reduction.

388E: It has a peak hormonal concentration in the morning

Cortisol is a steroid hormone that is released in stress to cause an increase in blood glucose. It is a catabolic hormone. It is stimulated by ACTH released from the anterior pituitary. ACTH is stimulated by CRH released from the median eminence of the hypothalamus. It has a diurnal variation and peaks on waking up in the morning. Its lowest level is around midnight and this is why a 'midnight cortisol' is used to detect excess cortisol production in Cushing's syndrome.

389A: Immobility

A thrombus is solid material formed from the constituents of blood in flowing blood. Three primary influences predispose to thrombus formation, the so-called Virchow's triad:

- damaged vessel wall – denuded endothelium
- changes in blood flow – turbulence, stasis
- alterations in blood constituents – platelets, clotting factors, blood, hyperlipidaemia, hyperviscosity etc.

The normal, intact endothelium is anti-thrombotic. This prevents the clotting of blood within the normal circulation. When the endothelium is injured, thrombosis occurs. Under physiological circumstances this prevents haemorrhage, as part of the normal haemostatic response to injury. Only when the formation of thrombus becomes excessive does it become pathological, resulting in vascular obstruction or migration of the thrombus to a distant site (embolization).

Heparin and warfarin both reduce the risk of thrombosis by their action on the clotting cascade. Thrombocytopenia means a low platelet count which also reduces the risk of thrombosis. Increased blood viscosity increases the risk of thrombosis ('thicker blood clots more easily'). Immobility increases the risk of thrombosis by stasis.

390D: Second rib

The palpable space immediately inferior to the clavicle is the first intercostal space, and below is the 2nd rib.

391B: It may refer pain to knee

The hip joint, like the shoulder joint, is a synovial joint of the ball and socket variety. In general it can be said that in all joints stability and range of movement are inversely proportional to one another. The shoulder joint is the most commonly dislocated joint in the body because it has adapted for a high degree of mobility at the expense of stability. The hip joint is an exception to the rule and provides a remarkable example of a joint that has a high degree of both mobility and stability. Its stability is largely a result of the adaptation of the acetabulum and femoral head to one another, with a snug fit of the femoral head into the acetabulum, deepened by the labrum and further reinforced by three ligaments on the outside of the capsule (the iliofemoral, ischiofemoral and pubofemoral ligaments). The iliofemoral ligament (of Bigelow) is the strongest of the three ligaments. The short muscles of the gluteal region are important muscular stabilizers. Since the hip is such a stable joint, it requires considerable force to become dislocated. When it does occur, it usually dislocates in the setting of a road traffic accident, where typically the hip joint dislocates posteriorly. The hip's great range of mobility results from the femur having a long neck that is much narrower than its head.

The hip joint lies deep to the pulsation of the femoral artery at the mid-inguinal point (half-way between the anterior superior iliac spine and the symphysis pubis, in contrast to the middle of the inguinal ligament which is half-way between the anterior superior iliac spine and the pubic tubercle, which marks the site of the deep inguinal ring). The mid-inguinal point is the surface marking of the hip joint and pain at this point may indicate pathology originating in the hip joint. Posterior to the hip lies the important sciatic nerve. Consequently, the sciatic nerve is at risk in a posterior surgical approach to the hip, or in a posterior dislocation.

The hip joint is innervated by the sciatic, femoral and obturator nerves (Hilton's law). The knee joint is also innervated by the same nerves. This may explain why hip pathology commonly refers pain to the knee. In a child who presents with a painful knee, examination should always consist of examination of the ipsilateral hip joint, in addition to examination of the knee, so as not to miss a diseased hip.

The blood supply to the femoral head originates from three important sources.

- The most important is via retinacular vessels that run up from the trochanteric anastomosis and then along the neck of the femur to supply the major part of the head. The trochanteric anastomosis is formed by an anastomosis of the medial and lateral circumflex femoral arteries and the superior and inferior gluteal arteries.
- The second supply is from the obturator artery in the ligamentum teres (round ligament). This is usually more important in the young child.
- A third supply is via the nutrient, or diaphyseal, artery of the femur, originating from the profunda femoris artery.

A fractured neck of femur may disrupt these vessels and consequently disrupt the blood flow to the femoral head, resulting in avascular necrosis. This condition frequently occurs in osteoporotic elderly women following a fall. The femoral head must be taken out and replaced with a prosthesis quickly so that mobility may be regained.

392D: PTH acts directly on osteoblasts in bone

Four hormones are primarily concerned with the regulation of calcium metabolism:

- parathyroid hormone (PTH)
- activated vitamin D (1,25-dihydroxycholecalciferol)
- calcitonin (secreted from the parafollicular cells – also known as the clear or C-cells – of the thyroid gland, and relatively unimportant in humans)
- parathyroid hormone-related protein (PTHrP), important in the hypercalcaemia of malignancy.

The main regulatory tissues are bone, kidney and intestine.

Activated vitamin D

The 25-hydroxylation step of vitamin D activation occurs in the liver, whereas the 1-hydroxylation step occurs in the kidneys. Activation of vitamin D requires both activation steps and PTH.

- *Intestine*. 1,25-dihydroxycholecalciferol promotes the intestinal absorption of calcium and phosphate. Absence leads to rickets in children and osteomalacia in adults.
- *Kidneys*. Increased tubular reabsorption of calcium and phosphate.
- *Bone*. Mobilization of calcium and phosphate.

Effects of PTH

PTH is secreted from the chief cells (also known as principal cells) of the parathyroid glands. The major regulator of PTH secretion is extracellular calcium. Circulating ionized calcium acts directly on the parathyroid glands in a negative-feedback fashion to regulate the secretion of PTH. The pituitary gland does not play a role in the secretion of PTH.

- *Bone*. Resorption with calcium and phosphate release into the bloodstream. PTH acts directly on osteoblasts and osteocytes that contain membrane receptors for PTH. Osteoclasts do not themselves have membrane receptors for PTH. Instead, it is believed that the activated osteoblasts and osteocytes send a secondary but "unknown" paracrine signal to the osteoclasts causing them to resorb bone.
- *Kidney*. PTH acts on the kidneys to increase calcium reabsorption and increase phosphate excretion (phosphaturic effect). There is one caveat to this; although PTH enhances renal calcium reabsorption, in hyperparathyroidism urinary calcium excretion is paradoxically increased because the reabsorbing mechanism is saturated. This increases the tendency to renal stone formation in hyperparathyroidism.
- *Intestine*. PTH increases the formation of activated vitamin D and this increases calcium absorption from the gut.

393E: It generally has a worse outcome than thrombus

- A thrombus is an organized mass of blood constituents that forms in flowing blood (i.e. in the living body).
- A clot is a solid mass of blood constituents formed in stationary blood when blood is allowed to coagulate outside the body or post-mortem.
- An embolus is an abnormal mass of undissolved material (of solid, liquid or gaseous origin) that is carried in the bloodstream from one place to another.

Thrombus and clot can be readily distinguished from one another at post-mortem (Table 6).

Table 6 Distinguishing thrombus and post-mortem clot

Thrombus	Post-mortem clot
Grey	Dark purple-red
Organized structure forming lines of Zahn (the pale lines are platelet aggregates enmeshed in fibrin, whilst the intervening dark lines are composed of red blood cells)	Separation of red blood cells and plasma producing a 'chicken fat' appearance since red cells often gravitate to the bottom of post-mortem clot
Dull surface and firm consistency	Shiny surface and gelatinous consistency ('redcurrant jelly')
Adherent to vessel wall	Peels away easily from the vessel wall
Dry, granular and friable	Moist and rubbery
Conforms to shape of vessel	Does not conform to shape of vessel
May show features of recanalization	

Veins, rather than arteries, are the most common source of emboli. Emboli most commonly arise from thrombosis formed within the deep veins of the lower limb and pelvis; thrombus formed here is known as a deep vein thrombosis. Anatomy ensures that emboli of venous origin lodge in pulmonary arteries. The size of the pulmonary artery blocked depends on the size of the thrombo-embolus. Usually they are small and lodge in small pulmonary arteries, but sometimes an extensive thrombus from the deep veins ends up as a saddle embolus blocking the main pulmonary artery. This massive pulmonary embolus is the commonest preventable cause of death in hospitalized, bed-bound patients.

An embolus is not always due to thrombus, although about 95 per cent of all emboli are thrombotic. Other emboli include:

- solid material – fat, tumour cells, atheromatous material, foreign matter
- liquid material – amniotic fluid
- gaseous material – air, nitrogen bubbles.

The ischaemia resulting from an embolus tends to be worse than that due to thrombosis because the blockage is so sudden. Thrombi tend to slowly occlude the vessel lumen. Thrombi are therefore less likely to cause infarction since they provide time for the development of alternative perfusion pathways by way of collaterals.

394B: Left suprarenal vein

The left suprarenal vein empties into the left renal vein which crosses the vertebral column to reach the inferior vena cava. The left renal vein also receives the left gonadal vein.

395E: The pulsation of the radial artery may be felt at its base

The contents and boundaries of the anatomical snuffbox are shown in Table 7.

Table 7

Base	From proximal to distal – radial styloid, scaphoid, trapezium, base of 1st metacarpal
Roof	Skin Fascia
Medially (ulnar side)	Extensor pollicis longus tendon
Laterally (radial side)	Extensor pollicis brevis tendon Abductor pollicis longus tendon
Contents	Cephalic vein (beginning in its roof) Terminal branches of radial nerve (supplying the overlying skin) Radial artery (on its floor)

The anatomical snuffbox is an important region clinically for three reasons. First, tenderness within the anatomical snuffbox may indicate a fractured scaphoid bone. This is important to recognize since X-rays are often unremarkable in the early stages and, if left untreated, there is a risk of avascular necrosis of the scaphoid (in fact, the proximal scaphoid segment necroses since it receives its blood supply from distal to proximal). Second, tendonitis of the abductor pollicis longus and extensor pollicis brevis tendons may occur; this is known as DeQuervain's tenovaginitis stenosans. Third, the cephalic vein is almost invariably found in the region of the anatomical snuffbox. The anatomical snuffbox therefore forms a useful landmark for the purpose of gaining intravenous access.

396C: Thyroxine promotes the growth and development of the brain

The thyroid gland primarily produces T4 which is converted to T3 (the more active form) in the periphery. Thyroxine is released when TSH, produced from the anterior pituitary, binds

to cell surface receptors on the thyroid gland. TRH is a hypothalamic hormone which causes TSH secretion. TSH release is under inhibitory control by dopamine. Thyroxine increases basal metabolic rate. Protein, carbohydrate and fat metabolism is increased. Thyroxine, although not a steroid, does not act on cell surface receptors, but acts on intracellular receptors bound to promoters of genes. It directly affects gene transcription in this way. Thyroxine plays an extremely important role in the myelination of axons during brain development. Neonatal deficiency leads to reduced axonal conduction velocities at the critical time in development when the brain is growing and maturing, resulting in developmental delay and mental retardation. This is known as cretinism or congenital hypothyroidism. Thyroid replacement therapy must be initiated soon after birth if mental retardation is to be prevented. Affected infants should be identified on neonatal biochemical screening (Guthrie test).

397C: It is an abnormal reduction of the blood supply to, or drainage from, an organ or tissue

- *Ischaemia* is an abnormal reduction of the blood supply to, or drainage from, an organ or tissue.
- *Infarction* is the death of tissues specifically caused by ischaemia or loss of blood supply.
- *Necrosis* refers to generalized tissue death due to toxins, trauma or vascular occlusion.

Ischaemia is most commonly due to vascular narrowing or occlusion from atherosclerosis. However, blood supply to tissues may be inadequate for a variety of reasons, besides vascular occlusion. Thus ischaemia may also result from states of shock (i.e. circulatory collapse with low arterial blood pressure). The commonest causes of shock are insufficient blood volume (hypovolaemia), sepsis and heart failure. In all cases there is a low blood pressure. All tissues may therefore become ischaemic and any organ may fail as a result.

The outcome of ischaemia is determined by a variety of factors:

- The nature of the vascular supply (the most important factor). The presence of collaterals is protective against the effects of ischaemia. Conversely, blockage of an end-artery will almost always cause infarction.
- The tissue involved. The brain and heart are more susceptible to the effects of hypoxia.
- The speed of onset. Slowly developing occlusions are less likely to cause infarction since they provide time for the development of alternative perfusion pathways.
- The degree of obstruction and the calibre of the vessel occluded.
- The oxygen content of the blood supplying the ischaemic tissue.
- The presence of concomitant heart failure.
- The state of the microcirculation, as in diabetes mellitus.

398E: The submucosa of the duodenum

The Brunner glands are located in the submucosa of the duodenum. These glands are connected to the interstitial lumen by ducts that open into certain crypts. They secrete an alkaline product that protects the duodenal mucosa from the acidic chyme and helps achieve an optimal pH for the enzymes.

399C: The suprapatellar bursa (pouch) communicates with the knee joint

The knee joint is a synovial joint (the largest in the body), of the modified hinge variety. The bony contours contribute little to the stability of the joint. Nevertheless, the ligaments and muscles make it a very stable joint which rarely dislocates.

The cruciate ligaments are two very strong ligaments that cross each other within the joint cavity, but are excluded from the synovial cavity by a covering of synovial membrane (they are therefore described as being intracapsular, but extrasynovial). They are crucial in the sense that they are essential for stability of the knee. They are named anterior and posterior according to their tibial attachments. Thus the anterior cruciate ligament is attached to the anterior intercondylar

area of the tibia and runs upwards, backwards and laterally to attach itself to the medial surface of the lateral femoral condyle. The anterior cruciate prevents anterior displacement of the tibia on the femur. Backward displacement of the tibia on the femur is prevented by the stronger posterior cruciate ligament. The integrity of the latter is therefore important when walking down stairs or downhill. Tears of the anterior cruciate ligament are common in sports injuries, whereas tears of the posterior cruciate ligament are rare since it is much stronger than the anterior cruciate.

Bursae are lubricating devices found wherever skin, muscle or tendon rubs against bone. There are approximately a dozen bursae related to the knee joint. The details are not important, only the salient points. For instance, it would be important to remember that the suprapatellar bursa communicates with the knee joint. An effusion of the knee may therefore extend some 3–4 finger-breadths above the patella into the suprapatellar pouch. The prepatellar and infrapatellar bursae do not communicate with the knee joint, but may become inflamed causing a painful bursitis. Inflammation of the prepatellar bursa is known as housemaid's knee, whereas that of the infrapatellar bursa is called clergyman's knee.

The menisci, or semilunar cartilages, are cresent-shaped laminae of fibrocartilage, the medial being larger and less curved than the lateral. They have an important role in:

- distributing the load by increasing the congruity of the articulation
- contributing to stability of the knee by their physical presence and by acting as providers of proprioceptive feedback
- acting as shock absorbers through a 'cushioning' effect
- probably assisting in lubrication.

However, the menisci do not play a role in the locking/unlocking mechanism of the knee joint. This is primarily the responsibility of the popliteus muscle.

The menisci are liable to injury from twisting strains applied to a flexed weight-bearing knee. The medial meniscus is much less mobile than the lateral meniscus (because of its strong attachment to the medial collateral ligament of the knee joint) and it cannot as easily accommodate abnormal stresses placed on it. This, in part, explains why meniscal lesions are more much common on the medial side than on the lateral.

The menisci are so effective that if they are removed, the force taken by the articular hyaline cartilage during peak loading increases by about 5-fold. Meniscectomy (removal of the menisci), or damage to the menisci, therefore exposes the articular hyaline cartilage to much greater forces than normal and evidence of degenerative osteoarthritis is seen in 75 per cent of patients 10 years after meniscectomy.

400C: Hyperkalaemia occurs

Diabetic ketoacidosis results from insulin deficiency. Insulin is normally responsible for the uptake of glucose by cells in the body. Most of the pathological features can be attributed to one of the following effects of insulin lack:

- hyperglycaemia in the blood, or
- intracellular glucose deficiency.

A good way of thinking about diabetic ketoacidosis is therefore 'starvation in the midst of plenty'.

Insulin deficiency results in lipolysis, glycogenolysis, gluconeogenesis and ketogenesis, in an analogous way to starvation. The production of ketone bodies results in an acetone breath and a metabolic acidosis with a fall in blood pH. The resulting acidosis stimulates the respiratory centre. This leads to a characteristic breathing pattern seen in diabetic ketoacidosis known as Kussmaul's breathing. Glucose spills over into the urine (glyosuria) when glucose levels exceed the capacity of the kidneys to reabsorb glucose. This produces an osmotic diuresis (with consequent polyuria and polydipsia). The overall effect is a massive loss of fluid in the urine causing dehydration and circulatory collapse. Dehydration is worsened by the vomiting and hyperventilation that may also

occur. Circulatory failure in itself worsens the metabolic acidosis (through lactic acidosis, acute renal failure etc.) and leads to uraemia. A vicious circle is set up leading to coma and death.

Insulin is normally responsible for driving potassium into cells. Insulin deficiency therefore results in hyperkalaemia. This is worsened by any dehydration, metabolic acidosis, or renal impairment from circulatory failure, that may also be present. Despite the hyperkalaemia, total body potassium content is actually low (secondary to vomiting, renal losses etc.).

The aims of treatment in diabetic ketoacidosis are three-fold: insulin replacement, rehydration with intravenous fluids and potassium replacement. The latter requires special attention; although potassium is initially high, when insulin is given potassium is rapidly driven into cells resulting in hypokalaemia. Potassium therefore needs to be cautiously and judiciously replaced during the treatment of ketoacidosis.

401C: It induces acute inflammatory changes, maximal at 1–3 days post-infarct

Myocardial infarction is infarction of the myocardium as a result of severe ischaemia leading to necrosis of the myocardium. It is usually due to coronary artery occlusion secondary to atherosclerosis, with or without superimposed thrombosis or plaque haemorrhage. Only rarely is a myocardial infarct due to an embolic event. In at least 10 per cent of patients myocardial infarction is painless or 'silent'; this is particularly true in diabetics and elderly patients because of the accompanying autonomic neuropathy.

If a patient survives an acute infarction, the infarct heals through the formation of scar tissue. The infarcted tissue is not replaced by new cardiac muscle because cardiac myocytes are permanent (non-dividing) cells and cardiac muscle is therefore unable to regenerate. Scar tissue does not possess the usual contractile properties of normal cardiac muscle; the result is contractile dysfunction or congestive cardiac failure.

The macroscopic and microscopic changes of myocardial infarcts follow a predictable sequence of events. The chief features are coagulative necrosis, inflammatory cell infiltration, followed by organization and repair where granulation tissue replaces dead muscle and is gradually converted into scar tissue. The entire process from coagulative necrosis to the formation of well-formed scar tissue takes 6–8 weeks (Table 8).

Table 8 Macroscopic and microscopic changes

Time	Macroscopic changes	Microscopic changes
0–12 hours	None	None
12–24 hours	Infarcted area appears pale with blotchy discolouration	Infarcted muscle brightly eosinophilic with intercellular oedema; beginning of neutrophilic infiltrate
24–72 hours	Infarcted area appears soft and pale; mottling with a yellow-tan infarct centre	Coagulation necrosis and acute inflammatory response most prominent; loss of nuclei and striations; marked infiltration by neutrophils
3–10 days	Hyperaemic border develops around yellow dead muscle	Organization of infarcted area and replacement with granulation tissue; dying neutrophils with macrophages predominating; disintegration and phagocytosis of dead myofibres
Weeks to months	Tough grey-white scar	Progressive collagen deposition; infarct replaced by dense acellular scar

402D: Calcaneo-fibular ligament

The most common ankle sprain is lateral which occurs as a result of excessive inversion of the foot and dorsiflexion of the ankle. The deltoid ligament, also known as the medial ligament of the ankle, is very strong and located at the medial malleolus. Excessive eversion would be the most likely mechanism of injury.

403E: Roots lie in the neck between the scalenus anterior and medius muscles

There are two principal enlargements of the spinal cord, the cervical and lumbar enlargements, that give rise to the brachial and lumbrosacral plexuses respectively, that innervate the upper and lower limbs. Both enlargements are due to the greatly increased mass of motor cells in the anterior horns of grey matter in these situations.

The brachial plexus has root values C5–8 and T1. In 10 per cent of cases the brachial plexus may be either pre-fixed (C4–8) or post-fixed (C6–T2) as an anatomical variant. The anatomical relations of the different parts of the brachial plexus are important:

- *roots* – exit their respective intervertebral foraminae between the scalenus anterior and medius muscles (interscalene space)
- *trunks* – at the base of the posterior triangle of the neck, lying on the 1st rib posterior to the third part of the subclavian artery
- *divisions* – behind the middle third of the clavicle
- *cords* – in the axilla, in intimate relation to the second part of the axillary artery
- *terminal branches* – in relation to the third part of the axillary artery.

The relationships of the roots, trunks and divisions of the brachial plexus to the scalene muscles, 1st rib and clavicle are important. Compression within a fixed space (the thoracic outlet) may lead to symptoms resulting from compression of the brachial plexus and/or nearby vascular structures (subclavian artery and vein). This is known as the thoracic outlet syndrome.

The serratus anterior muscle is innervated by the long thoracic nerve of Bell (C5, 6, 7). This may be remembered by the old aphorism 'C5, 6, 7 – Bell's of heaven'. Denervation of the serratus muscle may result in winging of the scapula.

There are two recognized types of brachial plexus palsy; both usually occur as a result of trauma or obstetric injury. The first type follows injury to the upper roots of the brachial plexus (typically C5–7) and is known as the Erb–Duchenne palsy. The arm typically lies in a waiter's tip position. The second type follows injury to the lower roots of the brachial plexus (typically C8, T1) and is known as Klumpke's palsy. The hand in this case typically takes on the position of a 'claw'.

404E: Congenital adrenal hyperplasia (adrenogenital syndrome) results in virilization and salt wasting

Disorders of the adrenal gland may relate to the adrenal cortex, medulla, or both. There is only one disorder worth mentioning that selectively affects the adrenal medulla. That is a phaeochromocytoma – a tumour of the adrenal medulla that results in the overproduction of catecholamines (such as adrenaline and noradrenaline). This leads to hypertension, headaches, palpitations and sweating (all known effects of adrenaline).

Conditions of the adrenal cortex may result from an overproduction or an underproduction of hormones. An overproduction of cortisol is known as Cushing's syndrome. There are several causes of Cushing's syndrome, the most common being iatrogenic (the use of exogenous steroids). However, the term Cushing's disease is strictly used to describe Cushing's syndrome as a result of an ACTH-producing pituitary tumour, or adenoma.

An overproduction of aldosterone from the zona glomerulosa of the adrenal cortex, as a result of a functioning adenoma, is known as Conn's syndrome. The overproduction of aldosterone leads to increased excretion of potassium and hydrogen ions from the distal convoluted tubule and collecting ducts of the kidney resulting in a hypokalaemic metabolic alkalosis.

Adrenal insufficiency (also known as Addison's disease) results in decreased production of glucocorticoids and mineralocorticoids from the adrenal cortex. It is most commonly a result of destruction of the adrenal cortex by autoimmune adrenalitis. Decreased mineralocorticoid activity results in sodium loss and decreased potassium excretion, with consequent hyperkalaemia, hyponatraemia, volume depletion and hypotension. Hypoglycaemia may occasionally occur as

a result of glucocorticoid deficiency and impaired gluconeogenesis. Stresses such as infections, trauma or surgery may precipitate a life-threatening adrenal crisis, which may prove fatal unless corticosteroid therapy is begun immediately.

Congenital adrenal hyperplasia (or adrenogenital syndrome) represents a group of autosomal recessive, inherited metabolic disorders characterized by a deficiency in a particular enzyme involved in the biosynthesis of cortical steroids, particularly cortisol and aldosterone. 21-hydroxylase deficiency accounts for 90 per cent of cases. Steroidogenesis is then channelled into other pathways leading to increased production of androgens, leading to virilization in females and genital enlargement and/or precocious puberty in males. Simultaneously, the deficiency of cortisol results in increased secretion of ACTH, resulting in adrenal hyperplasia. Impaired aldosterone secretion leads to salt wasting. Patients are treated with exogenous steroids which, in addition to providing adequate levels of glucocorticoids, suppress ACTH levels and thus decrease the synthesis of the steroid hormones responsible for many of the clinical abnormalities.

405B: Most commonly occurs at branching points within the circulation

Atherosclerosis is a focal disease of the tunica intima of large and medium-sized arteries and consists of the gradual accumulation of focal raised patches (plaques) on the arterial lining in response to arterial wall injury. Its complications are the main cause of death in urbanized societies.

The anatomical sites of atherosclerosis are somewhat predictable. Plaques generally occur at branching points and bends in arteries exposed to high pressure, pulmonary arteries being relatively spared, veins completely so. The turbulence and eddy currents set up at branching points exposes the intimal surface to haemodynamic injury and encourages the uptake of circulating lipoproteins and macrophages into the vessel wall. Thus atherosclerotic plaques are common at sites of bifurcation such as:

- the entrance to the coronary ostia (causing a myocardial infarction)
- close to where the descending abdominal aorta bifurcates into the common iliac arteries (resulting in an abdominal aortic aneurysm)
- in the internal carotid artery close to where the common carotid bifurcates into internal and external branches (resulting in a cerebrovascular accident)
- close to where the renal arteries break off the aorta (resulting in renal artery stenosis)
- in the ileo-femoral arteries of the lower limb (causing lower limb ischaemia).

The lesions are essentially foci of chronic inflammation in which the macrophages seem to be doing harm. The basic lesion consists of a raised focal plaque within the intima with a core of lipid (mainly cholesterol) and a covering fibrous cap.

The four most important risk factors for atherosclerosis to remember are those that are potentially controllable, namely high cholesterol, diabetes mellitus, smoking and hypertension. All are associated with intimal injury and accelerate atherosclerosis. Atherosclerosis is a reversible disease process so that risk-factor modification ameliorates the size of atherosclerotic plaques. Risk-factor modification forms an essential part of the management of patients with known atherosclerotic disease.

406E: Tibial nerve

Tarsal tunnel syndrome results from entrapment of the tibial nerve as it passes deep to the flexor retinaculum between the medial malleolus and calcaneus.

407C: The musculocutaneous nerve arises from the lateral cord

This is a common question! The three cords of the brachial plexus lie in close relation to the second part of the axillary artery. Thus the posterior, lateral and medial cords lie posteriorly, laterally and medially to the second part of the axillary artery, respectively, in the axilla. There is no anterior cord:

- lateral cord – musculocutaneous nerve
- medial cord – ulnar nerve
- posterior cord – radial nerve, axillary nerve
- medial and lateral cords – median nerve.

408D: It is essential for spermatogenesis

Testosterone is a steroid hormone, secreted by the interstitial cells (of Leydig) within the mature testis. It is essential for the growth and division of the germinal cells in forming sperm and in the development of the secondary sexual characteristics. Sertoli cells, on the other hand, are postulated to act as 'nurse' cells, providing structural and metabolic support for the developing spermatogenic cells.

Whereas follicle stimulating hormone (FSH) is trophic to Sertoli cells, luteinizing hormone (LH) is trophic to the Leydig cells. LH, secreted by the anterior pituitary, stimulates the Leydig cells to secrete testosterone through the formation of cyclic AMP via the G-protein coupled serpentine LH receptor. The secretion of LH in turn depends on the pulsatile release of gonadotrophin-releasing hormone (GnRH) from the hypothalamus. Androgen production from the adrenal cortex (and to a lesser extent from the ovaries) of females is normal and is responsible for the growth of pubic and axillary hair.

409C: One of the first signs of toxicity is perioral paraesthesia

Two separate classes of local anaesthetics exist: amides and esters. Amides account for the majority of local anaesthetics in clinical use, although cocaine is an ester. Local anaesthetics work by blocking sodium channels. This prevents depolarization and thereby propagation of pain impulses along the nerve.

Local anaesthetics tend to block the smaller fibres before the larger ones; that is the smaller pain fibres are blocked first (Aδ and C fibres) with sparing of the larger neurones such as the motor fibres.

The addition of adrenaline to local anaesthetic has three effects. First, it prevents bleeding by a direct effect of adrenaline on the local vasculature causing vasoconstriction. Second, by way of vasoconstriction it prevents systemic absorption of the local anaesthetic thereby preventing toxicity/side effects and increasing the local duration of action. Third, by preventing systemic absorption it allows larger doses to be used than would otherwise be allowed in the absence of adrenaline. However, because of this 'vasoconstrictive effect', adrenaline must never be used on pedicles that contain an end-artery (e.g. digits, nose tips, ear lobe, penis) where ischaemic necrosis may result.

It is important that the maximum dose of local anaesthetic not be exceeded, otherwise the consequences may be lethal. This is because local anaesthetics are cardiotoxic by way of blocking sodium channels and interfering with cardiac conduction. One of the earliest and reliable signs of systemic toxicity is perioral tingling. This may be followed by cardiovascular collapse and death.

410E: Caudate lobe of the liver

The greater sac communicates with the lesser sac through the epiploic Foramen of Winslow. The superior boundary is the caudate lobe of the liver. The common bile duct lies in the free edge of the lesser omentum, that forms the anterior boundary. The first part of the duodenum is the inferior boundary. The posterior boundary is the inferior vena cava.

411D: It contains ten tendons within it

The carpal tunnel is a fibro-osseous tunnel situated on the flexor aspect of the proximal part of the hand and lying between the flexor retinaculum and the carpal bones. It contains the median nerve and ten flexor tendons that include:

- four tendons of flexor digitorum superficialis
- four tendons of flexor digitorum profundus

- flexor carpi radialis tendon
- flexor pollicis longus tendon.

The flexor retinaculum is attached to the tubercle of the scaphoid and pisiform proximally and the hook of the hamate and trapezium distally. Its function is to prevent bow-stringing of the flexor tendons at the wrist.

Since the carpal tunnel exists as a confined space, entrapment of the median nerve may occur within it. This is commonly due to a build-up of fluid within the carpal tunnel, or because of hypertrophy of the bones/ligaments/tendons that surround, or are contained within, the carpal tunnel. Compression of the median nerve within the carpal tunnel is known as carpal tunnel syndrome. Note this is different to cubital tunnel syndrome which refers to compression of the ulnar nerve behind the medial epicondyle at the elbow. The ulnar artery and nerve do not pass through the carpal tunnel, but instead pass superficial to the carpal tunnel in their own fibro-osseous tunnel commonly given the name Guyon's canal. The ulnar nerve and artery are therefore unaffected in carpal tunnel syndrome.

The clinical features of carpal tunnel syndrome relate to loss of function of the median nerve. There are both motor and sensory components. The median nerve supplies four muscles in the hand, given by the mnemonic LOAF:

- **l**ateral two lumbricals
- **o**pponens pollicis
- **a**bductor pollicis brevis
- **f**lexor pollicis brevis.

All four muscles are weak in someone with carpal tunnel syndrome. In addition, there is loss of sensation over the lateral three and a half digits, which is median nerve territory. However, since the palmar cutaneous branch of the median nerve passes superficial to the carpal tunnel, there is no loss of sensation over the thenar eminence in someone with carpal tunnel syndrome.

412A: The menopause is associated with an increase in follicle stimulating hormone

Oestrogen production during the menstrual cycle is principally 17β-oestradiol. It increases steadily during the follicular phase to reach a peak prior to ovulation (when it has a positive feedback effect on the anterior pituitary initiating the FSH and LH surges). Both FSH and LH are needed in order for ovulation to take place.

Fertilization of the human ovum normally takes place in the outer third of the fallopian tubes. Over the next 5–7 days the fertilized ovum travels along the uterine tube and spends several days free in the uterus prior to implantation. This involves a complex series of events. A defect in any of the processes leading up to implantation may result in an abnormal extrauterine (ectopic) pregnancy.

At the menopause, follicles disappear and are replaced by fibrous tissue. The decreased production of oestrogens from the ovaries results in loss of the negative-feedback effect of oestrogens on the anterior pituitary and a rise in FSH. This rise in FSH can be measured and used to verify commencement of the menopause.

Oestrogen production is mainly confined to ovarian tissue, but both the adrenal cortex and adipose tissue contribute to oestrogen production. Adipose tissue contains an aromatase enzyme that converts androgens to oestrogens. Oestrogen continues to be produced therefore after the menopause and provides an ongoing stimulus for the formation of breast cancer. Tamoxifen blocks the action of oestrogen on breast tissue and is used in the treatment of breast cancer. Newer aromatase inhibitors block the peripheral conversion of androgens to progesterone. They are used to treat breast cancer in postmenopausal patients when oestrogen production from the ovaries ceases and where the peripheral conversion of androgens to oestrogens becomes more important.

413C: Inhibits platelet aggregation

Aspirin irreversibly blocks the action of the cyclo-oxygenase enzyme that is involved in arachidonic acid metabolism, leading to prostaglandin and thromboxane A2 production. It does this by acetylating a serine residue at the active site, thereby excluding arachidonic acid. Aspirin has anti-inflammatory, analgesic, antipyretic and antiplatelet actions. All four actions result from the decreased production of prostaglandins and thromboxane A2. Aspirin has no effect on the coagulation cascade. The antiplatelet effect of aspirin deserves special mention and is widely used therapeutically in the primary and secondary prevention of cardiovascular and cerebrovascular disease. Aspirin has also recently been shown to have a protective effect against colorectal carcinoma.

The antiplatelet effect of aspirin largely arises through the opposing effects of thromboxane A2 (produced by platelets) in promoting platelet aggregation and prostaglandin I2 (produced by endothelial cells) inhibiting platelet aggregation. Aspirin, by inhibiting the cyclo-oxygenase enzyme, results in decreased production of thromboxane A2 from platelets (thus inhibiting platelet aggregation) and prostaglandin I2 from endothelial cells (thus promoting platelet aggregation). However, the thromboxane A2 effect outweighs the prostaglandin I2 effect for two reasons:

- Aspirin is taken orally, high concentrations of aspirin are found within the portal vein which results in platelets being exposed to a high concentration of aspirin. This is contrary to endothelial cells that are in contact with lower concentrations of aspirin once it has been diluted throughout the body and because of presystemic metabolism of aspirin to salicylate by esterases in the liver.
- Platelets have no nuclei. This means once cyclo-oxygenase is inhibited, production is abolished for the rest of the platelet's lifespan. Thromboxane A2 synthesis does not therefore recover until the affected cohort of platelets is replaced in 7–10 days. Endothelial cells, on the other hand, are nucleated so are able to resynthesize new cyclo-oxygenase enzyme (and therefore prostaglandin I2).

414A: Aortic

The lymphatic drainage of an organ is related to its blood supply. The lymphatic drainage of the testis drains along the testicular artery to reach the lymph nodes along the aorta.

415E: The dorsalis pedis pulse is lateral to the extensor hallucis longus tendon

The arterial supply to the lower limb is important since atherosclerosis within the arteries can lead to peripheral vascular disease and symptoms of intermittent claudication. Determining the level of arterial obstruction requires being able to palpate the pulses of the various parts of the arterial tree. This requires a precise knowledge of anatomy.

The aorta bifurcates into the common iliac vessels at the level of L4. The common iliac bifurcates into the external and internal iliac vessels. As the external iliac artery passes under the inguinal ligament it changes its name to the common femoral artery. Thus the femoral artery is a direct continuation of the external iliac artery. The pulsation of the femoral artery may be palpated at the mid-inguinal point (at a point half-way between the anterior superior iliac spine and the symphysis pubis). This is different from the mid-point of the inguinal ligament which corresponds to a point half-way along the inguinal ligament (between the anterior superior iliac spine and the pubic tubercle) which marks the site of the deep inguinal ring.

Between 3 and 4 cm below the inguinal ligament the common femoral artery divides into superficial femoral and deep femoral (profunda femoris) branches. The superficial femoral artery is the commonest site for peripheral vascular disease in the lower limb. The superficial femoral artery continues through the adductor canal (also known as the subsartorial or Hunter's canal) and after passing through the adductor hiatus becomes known as the popliteal artery. Within the

popliteal fossa, the popliteal artery lies deep to the tibial nerve and the popliteal vein. This explains why a normal popliteal artery is so difficult to feel. A palpable popliteal artery normally implies it is aneurysmal (abnormally dilated).

The popliteal artery bifurcates into anterior and posterior tibial arteries. The posterior tibial artery is easily palpated posterior to the medial malleolus at the level of the ankle. A useful mnemonic for remembering the order of structures behind the medial malleolus (from anterior to posterior) is 'Tom, Dick and Harry':

- Tom = **t**ibialis posterior tendon (most anteriorly)
- Dick = flexor **d**igitorum longus tendon
- and = **a**rtery (posterior tibial), **n**erve (tibial nerve)
- Harry = flexor **h**allucis longus tendon (most posteriorly).

The anterior tibial artery continues down into the foot as the dorsalis pedis artery. However, in 10 per cent of subjects this is absent. The pulsation of dorsalis pedis may be felt lateral to the extensor hallucis longus tendon, between the first and second metatarsals. A useful mnemonic for remembering the order of structures in the anterior compartment of the leg (from medial to lateral) is 'Tim hath a very nasty disease, parathyroid':

- Tim = **t**ibialis anterior tendon (most medially)
- hath = extensor **h**allucis longus tendon
- a very nasty = neurovascular bundle consisting of **a**rtery (dorsalis pedis), **v**eins (venae comitantes of anterior tibial) and **n**erve (deep peroneal nerve)
- disease = extensor **d**igitorum longus tendon
- parathyroid = **p**eroneus tertius tendon (most laterally).

416A: Acclimatization of the sweating mechanism occurs in response to heat

Thermoregulation is one of the principal functions of the hypothalamus (not thalamus). The central thermodetectors are located primarily within the preoptic area of the hypothalamus and to a lesser extent the adjacent areas of the anterior hypothalamus.

The apocrine sweat glands of the axilla, perineum and breast areolae play little role in thermoregulation. They are analogous to the odiferous glands of many mammals, but their biological significance in humans is unknown. It is the eccrine sweat glands that play an important role in heat loss by evaporation.

Non-shivering thermogenesis in brown fat is particularly important in keeping human infants and hibernating mammals warm. This process involves the uncoupling of oxidative phosphorylation within mitochondria via a specialized protein in the inner mitochondrial membrane called thermogenin. In adults, however, the importance of brown adipose tissue in heat generation is relatively small.

Humans are one of only a few animals who acclimatize actively to heat. When exposed to hot weather for a period of 1–6 weeks, a person sweats progressively more profusely. This increased effectiveness of the sweating mechanism is caused by a direct increase in the sweating capability of the sweat glands themselves. Also associated with acclimatization is a decrease in the concentration of sodium chloride in the sweat, which allows the conservation of body salt. Most of this effect is caused by increased secretion of aldosterone.

417A: Reduced surface mucus secretion

Within the normal gastric epithelium there is a fine balance between the normal damaging forces (such as gastric acidity and peptic enzymes) and various protective mechanisms (such as surface mucus production, bicarbonate secretion, mucosal blood flow, elaboration of prostaglandins, tight junctions between cells, epithelial regenerative capacity etc.). Any disruption to this fine balance, either as a result of increased damaging forces, or through impaired defences, may result in epithelial damage and formation of a peptic ulcer. One of the main drawbacks of aspirin is the

risk of gastric erosions and peptic ulcer disease that is associated with its use. This is principally brought about through the following mechanisms:

- a direct irritant effect of aspirin
- a reduction in PGE2 (that normally serves to increase local mucus and bicarbonate secretion thereby protecting the gastric mucosal lining)
- a reduction in PGI2 (thereby resulting in reduced blood flow to the gastric lining, mucosal ischaemia and preventing the elimination of acid that has diffused into the submucosa)
- increased acid production from gastric parietal cells (prostaglandins normally inhibit acid secretion)
- the anti-platelet effect of aspirin which propagates any bleeding that may result from an already injured gastric mucosal surface.

Aspirin has no effect on gastric motility. Patients over 65 years old, or those with a history of a previous peptic ulcer, should have a proton pump inhibitor (such as omeprazole) co-administered with aspirin. This has been shown to reduce the risk of gastrointestinal bleeding and peptic ulceration.

418A: Superior rectal vein

Internal haemorrhoids are formed by varicosities of the branches of the superior rectal vein. External haemorrhoids are formed by varicosities of the branches of the inferior rectal vein.

419A: The cephalic vein lies within the deltopectoral groove

The superficial venous drainage of the upper and lower extremities forms an important piece of applied anatomy. There are four veins that the student should know well: the cephalic and basilic veins in the upper limb and the long and short saphenous veins of the lower limb. All run from superficial to deep and contain valves within their lumen. Both these factors prevent the reflux of blood and encourage venous return to the heart.

The cephalic vein of the upper limb commences in the roof of the anatomical snuffbox and runs up the lateral border of the arm. It lies within the groove between the deltoid and pectoralis major muscle (the deltopectoral groove) and ends by piercing the clavipectoral fascia to enter the axillary vein.

The basilic vein runs up the medial border of the upper limb. It perforates the deep fascia in the middle of the arm, half-way between the elbow and axilla, and becomes the axillary vein at the lower border of teres major.

The long (great) saphenous vein, the longest vein in the body, begins as the upward continuation of the medial marginal vein of the foot. It courses upwards in front of the medial malleolus, in close proximity to the saphenous nerve, and runs up to lie a hand's breadth behind the medial border of the patella. It ends by passing through the cribriform fascia that covers the saphenous opening of the fascia lata. Here it joins the femoral vein at the saphenofemoral junction.

The long saphenous vein is important clinically for three reasons. First, incompetence of the valves within it may lead to the formation of superficial venous dilatations in the distribution of the long saphenous vein. These are known as varicose veins. Second, because the anatomy of the long saphenous vein is so reliable (more so than any other vein in the body), it makes the long saphenous vein a good choice for a venous cut-down, if emergency venous access is required. Third, because of its remarkably constant anatomy and because the long saphenous vein is the longest vein in the body, the long saphenous vein is often harvested in vascular surgery and used to bypass arterial obstructions, a good example being in the case of coronary artery bypass grafting procedures where the long saphenous vein is one of many grafts that may be used to bypass blocked coronary arteries.

The short (small) saphenous vein drains the lateral margin of the foot and lies with the sural nerve behind the lateral malleolus. It passes upwards in the subcutaneous fat to the midline of the

calf and pierces the deep fascia to enter the popliteal vein at the saphenopopliteal junction. Like the long saphenous vein, the short saphenous vein is vulnerable to the formation of varicosities.

A number of tributaries join the great saphenous vein in the region of the saphenous opening. This is important for two reasons. First, they may form a site for recurrence following varicose vein surgery. Second, the fact that the upper end of the long saphenous vein has these tributaries converging upon it easily distinguishes it from the femoral vein, which at this level only receives the long saphenous vein itself. It is imperative that the long saphenous vein is distinguished from the femoral vein at the saphenofemoral junction, during varicose vein surgery, in order to prevent inadvertent ligation of the femoral vein, which one hears about from time to time in medicolegal reports.

If surgery is performed for varicose veins (a high ligation tie and stripping of the vein), the saphenous nerve (a branch of the femoral nerve) is vulnerable to injury when stripping the long saphenous vein because of its close proximity to the long saphenous vein. Likewise, the sural nerve is at risk of being injured in stripping of the short saphenous vein.

420A: Cyclizine acts on the histaminergic system

Antiemetics are drugs that are used clinically to suppress the vomiting reflex. This is mediated primarily through their suppressive effect at specialized sites within the central nervous system wherein the vomiting reflex is mediated, namely the vomiting centre, chemoreceptor trigger zone in the area postrema (an area of the brain which is devoid of blood–brain barrier and thereby in direct contact with emetogenic chemicals within the bloodstream) and the vestibular system (the latter site explains motion sickness).

A vast array of drugs are used within the clinical setting, all of which act at different sites within the nervous system and upon different neurochemical systems, yet all result in a similar desired effect (i.e. suppression of vomiting). The clinical importance of this is pharmacological synergy, namely the additive effect of two different antiemetics used in combination being greater than the sum of the two separate effects because of the different mechanisms of action. It also allows the astute clinician to pick and choose an antiemetic (and thereby a mode of action) that conforms well to a specified clinical scenario (Table 9).

Table 9

Chemical neurotransmitter	Examples of drugs
Acetylcholine	Anticholinergics (e.g. hyoscine)
Histamine	Antihistamines (e.g. cyclizine)
5-hydroxytryptamine (serotonin)	5-HT3 receptor antagonists (e.g. ondansetron, granisetron)
Dopamine	Dopamine antagonists (e.g. metoclopramide, domperidone, prochlorperazine)

A good example is motion sickness which seems to depend on the influential effect of the environment on the vestibular system, the effects of which in turn are mediated through the cholinergic system. It is thus easy to see why hyoscine is the most efficacious drug in the setting of motion sickness, but is less efficacious in other situations. Dopamine antagonists, such as metoclopramide, and 5-HT3 antagonists are ineffective in the treatment or prevention of motion sickness. Similarly, domperidone is the drug of choice in Parkinson's disease since it is a dopamine antagonist that does not cross the blood–brain barrier; if metoclopramide were to be used instead (similarly a dopamine antagonist but does cross the blood–brain barrier) symptoms of Parkinson's disease would be exacerbated.

421E: Ulnar nerve

A 'claw hand' is associated with injury to the ulnar nerve at the wrist affecting the interossei, lumbricals and hypothenar muscles of the hand. It is characterized by hypothenar eminence wasting, hyperextended metacarpophalangeal joints and flexed interphalangeal joints.

422B: All the interossei are supplied by the ulnar nerve

The basic action of the interossei and lumbrical muscles is to cause extension at the interphalangeal joints and flexion at the metacarpophalangeal joints. In addition, the palmar interossei adduct the fingers (PAD), while the dorsal interossei abduct the fingers (DAB). The lateral two lumbricals are supplied by the median nerve and the medial two lumbricals by the ulnar nerve. However, all the interossei are supplied by the ulnar nerve. As a general rule all the intrinsic muscles of the hand are supplied by the ulnar nerve (T1), except for the LOAF muscles (lateral two lumbricals, opponens pollicis, abductor pollicis brevis and flexor pollicis brevis muscles).

The hand receives a rich arterial supply from both the radial and ulnar arteries. In the palm they anastomose to form two palmar arterial arcades, the superficial and deep palmar arches. The superficial palmar arch is formed by a direct continuation of the ulnar artery meeting the superficial palmar branch of the radial artery. The deep palmar arch is an arterial arcade formed by the terminal branch of the radial artery anastomosing with the deep branch of the ulnar artery. For a visual assessment of the contribution of the radial and ulnar arteries to the blood supply of the hand, Allen's test may be performed. Make a clenched fist and occlude the radial and ulnar arteries. When the fist is released the skin of the palm is seen to be pale, but colour should return rapidly on the release of either one of the arteries. If there is an obvious delay after releasing the ulnar artery compared with the radial, it suggests that the radial supply is dominant and that procedures that might damage the radial artery (such as cannulation) should be avoided.

The deep fascia of the palm is known as the palmar aponeurosis. It is continuous proximally with the flexor retinaculum and widens distally in the hand by dividing into four slips, one for each finger. The palmar aponeurosis is firmly attached to the skin of the palm and assists the latter in gripping an object. Also by virtue of its toughness, it protects the underlying tendons and synovial sheaths. Contracture of the palmar aponeurosis and its digital slips may occur, resulting in fixed flexion deformities of the fingers concerned (usually the ring and little fingers). This is known as Dupuytren's contracture. Dupuytren's contracture is a phenomenon of the palmar aponeurosis and has nothing to do with the underlying muscles or tendons. Ischaemic contracture of muscle is known instead as Volkmann's ischaemic contracture. The latter usually results from an arterial injury, as a complication of a fracture, or following compartment syndrome. It results from the replacement of muscle by fibrous tissue, which contracts to produce a deformity.

423D: Streptokinase

Thrombolytics are substances that break down fibrin (fibrinolytics). Streptokinase is used as a therapeutic fibrinolytic agent in the management of acute myocardial infarction. Warfarin prevents the formation of thrombus by decreasing the amount of vitamin K-dependent clotting factors, but it does not possess fibrinolytic activity. Heparin potentiates the action of antithrombin and also prevents the formation of thrombus, but has no fibrinolytic activity. Aspirin is an antiplatelet agent that acts by reducing the aggregation of platelets. Fibrinogen is a precursor of fibrin, which is involved in the formation of thrombus.

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Section 2
Principles of Surgery-in-General

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Extended matching questions

1. Blood transfusions

A Group A RhD-negative
B Group B RhD-positive
C Group O RhD-positive
D Group O RhD-negative
E Anti-D immunoglobulin
F Iron sulphate tablets

For each of the patients described below, select the single best treatment from the options listed above. Each option may be used once, more than once or not at all.

1 A 35-year-old woman with blood group B RhD-negative following a left-sided nephrectomy is found to have a haemoglobin level of 6.5.
2 A 66-year-old man with prostate carcinoma and blood group A RhD-positive is found to have a haemoglobin level of 7.1.
3 A patient with blood group B RhD-positive following a right-sided hemicolectomy is found to have a haemoglobin level of 9.4.
4 A 75-year-old man with metastatic colorectal carcinoma and blood group O RhD-negative is found to have a haemoglobin level of 7.3.
5 A woman with blood group B RhD-negative and thyroid disease is found to have a haemoglobin level of 11.0 having just given birth to a baby with blood group B RhD-positive.

2. Lumps in the groin

A Testicular cancer
B Testicular torsion
C Direct inguinal hernia
D Indirect inguinal hernia
E Varicocele
F Hydrocele
G Sebaceous cyst
H Epididymal cyst
I Epididymo-orchitis

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

6 A 27-year-old man presents with a soft lump in the right scrotum. On examination there is a positive cough impulse and the doctor is unable to get above the lump. The patient is able to push the lump back, and when the doctor places his fingers over the right groin the lump does not reappear even when the patient coughs.
7 A 26-year-old man presents with a 3-day history of pain in the left scrotum. On examination the scrotum is hot, swollen and tender.

8 A 22-year-old man presents with a painless swelling in the right scrotum. On examination the swelling is non-tender but contains a firm mass which does not seem separate from the testicle. The scrotal swelling brightly transilluminates.
9 A 32-year-old man presents complaining of a 'dragging' sensation in the left scrotum. On examination, the doctor can palpate a soft mass which feels like a 'bag of worms' but only when the patient is standing.
10 A 21-year-old man presents with sudden onset of left testicular pain which came on 2 hours ago. When the doctor tries to examine him, he almost jumps off the bed.

3. Lumps in the neck

A Lymph node
B Branchial cyst
C Thyroglossal cyst
D Cystic hygroma
E Epidermal cyst
F Salivary gland calculus
G Warthin's tumour
H Pleomorphic adenoma
I Multinodular goitre

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

11 A 34-year-old man presents with a firm lump in the right side of his neck just below the mandible. The lump measures 3 cm. The skin appears attached to the lump and there is a small punctum visible.
12 A 25-year-old man has a small lump in the midline of his neck. The lump is non-tender and rises on protruding the tongue.
13 A 33-year-old woman is referred by her GP with a 3 cm firm lump on the right side of her neck. The lump moves on swallowing but does not move on protruding the tongue. Her mother had thyroid cancer.
14 A 14-year-old girl presents with a 2 cm soft, fluctuant lump on the right side of her neck adjacent to the angle of the mandible. The lump transilluminates and is cystic on ultrasound.
15 A 45-year-old man complains of an intermittent swelling that is sometimes painful on the left side of his face and upper jaw. He has linked it to meal times and tried different foods but there has been no improvement.

4. Diseases of the hepatobiliary system

A Plain abdominal X-ray
B Pelvic X-ray
C Ultrasound scan
D Non-contrast-enhanced CT
E Contrast-enhanced CT
F Endoscopic retrograde cholangiopancreatogram (ERCP)
G Magnetic resonance cholangiopancreatogram (MRCP)
H Percutaneous transhepatic cholangiopancreatogram (PTC)

For each of the patients described below, select the single best investigation from the options listed above. Each option may be used once, more than once or not at all.

16 A 65-year-old woman is referred with a 4-month history of weight loss and progressive jaundice. Her CA19-9 is raised and her ultrasound reveals dilated hepatic ducts. ERCP was attempted but was abandoned due to failure of passage of the scope beyond the distal common bile duct stricture.
17 A 43-year-old woman who is rather overweight presents with a 3-day history of right upper quadrant pain, fevers and vomiting. Her liver biochemistry is within normal limits but she does demonstrate a neutrophilia.
18 A 60-year-old woman with a previous history of gallstones presents with colicky abdominal pain and vomiting. Her abdomen is distended and bowel sounds are increased. She is often constipated but feels that this is different.
19 A 35-year-old man with a history of alcohol abuse presents to A&E with a 2-day history of epigastric pain. His amylase on admission is 1200 and he is pyrexial. His liver biochemistry demonstrates an obstructive picture.
20 A 45-year-old woman presents with right upper quadrant pain and vomiting. Her bilirubin and alkaline phosphatase are raised. A stone is seen in the common bile duct on ultrasound and measures 1.2 cm. The common bile duct itself measures 1.3 cm.

5. Fractures of the hip

A Traction
B Dynamic hip screw
C Cannulated screws
D Intramedullary hip screw
E Uncemented hemiarthroplasty
F Cemented hemiarthroplasty
G Total hip replacement

For each of the patients described below, select the single best treatment from the options listed above. Each option may be used once, more than once or not at all.

21 A 67-year-old woman suffers from rheumatoid arthritis which affects both hips. She falls when walking back from town. Her plain X-ray reveals an intracapsular fracture of the femoral neck.
22 A 62-year-old man is knocked off his bike and has an intertrochanteric fracture of the left femur which extends down the shaft.
23 A 35-year-old woman is hit by a car. The plain X-ray shows an intracapsular fracture of the right femoral neck.
24 An 80-year-old woman trips on the pavement and falls. Her plain X-ray reveals an intracapsular femoral neck fracture.
25 An 80-year-old man slips in the bathroom and presents to A&E with a shortened left leg. The plain X-ray demonstrates an extracapsular fracture of the femoral neck.

6. Arterial blood gases

A Metabolic acidosis
B Metabolic acidosis with compensation
C Metabolic alkalosis
D Metabolic alkalosis with compensation
E Respiratory acidosis
F Respiratory acidosis with compensation
G Respiratory alkalosis
H Respiratory alkalosis with compensation

For each of the combination of test results below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

26 pH = 6.95, Po_2 = 10 kPa, Pco_2 = 4.1 kPa, BE = –8.5
27 pH = 7.26, Po_2 = 10 kPa, Pco_2 = 4.0 kPa, BE = –5.2
28 pH = 7.69, Po_2 = 10 kPa, Pco_2 = 6.1 kPa, BE = +1.3
29 pH = 7.59, Po_2 = 10 kPa, Pco_2 = 2.3 kPa, BE = –5.5

7. ATLS classification of haemorrhagic shock

A Class I
B Class II
C Class III
D Class IV

For each of the patients described below, select the single most likely classification from the options listed above. Each option may be used once, more than once or not at all.

30 A 35-year-old woman suffers from endometriosis and bleeds heavily every month. Her heart rate is 105/min and all other parameters are normal.
31 A 13-year-old boy has a nasal angiofibroma and loses 2 per cent of his circulating volume following a nosebleed. His pulse is 120/min.
32 A 25-year-old man is hit by a car and has multiple fractures. His pulse is 133/min, BP is 110/85 mmHg, respiratory rate is 24/min, and urine output is 35 mL/min.
33 An 85 kg man has had a handlebar injury and lacerated his liver. It is estimated that he has bled approximately 2 L into his abdomen.
34 A 45-year-old man is brought in from a road traffic accident. His pulse is 160/min, BP is 75/50 mmHg, and he is unresponsive.

8. Burns

A 1 per cent
B 9 per cent
C 18 per cent
D 27 per cent
E 36 per cent
F 45 per cent
G 54 per cent

For each of the patients described below, select the single best assessment of burns extent from the options listed above. Each option may be used once, more than once or not at all.

35 A man suffers full-thickness burns to his perineum.
36 A man suffers full-thickness burns to the whole of his left arm.
37 A woman suffers full-thickness burns to her face and head.
38 A woman suffers full-thickness burns to the whole of her left leg.
39 A man suffers full-thickness burns to his back.

9. Jaundice

A Biliary colic
B Prehepatic jaundice
C Hepatocellular jaundice

D Gallstone in common bile duct
E Sclerosing cholangitis
F Carcinoma of head of pancreas
G Cholangiocarcinoma
H Pancreatitis
I Gallstone ileus
J Mirizzi syndrome

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

40 A 45-year-old woman presents to A&E with epigastric pain, jaundice, vomiting and fever. Her bilirubin is 125 μmol/L, ALT 135 iu/L, alkaline phosphatase 700 iu/L, WBC 21×10^9/L and amylase 115 U/mL. On ultrasound the gall bladder wall measures 5 mm and gallstones are seen. The common bile duct measures 9 mm in diameter and the intrahepatic ducts are prominent.
41 A 65-year-old woman presents to her GP with general malaise and grumbling abdominal pain. Her daughter thinks she is looking a little yellow. Her GP refers her for a specialist opinion and on examination there is a mass in the right upper quadrant.
42 An obese 40-year-old woman presents to A&E complaining of a 5-day history of epigastric pain, jaundice and vomiting. She has upper abdominal tenderness and deranged liver biochemistry. An ultrasound reveals a common bile duct diameter of 8 mm, no intrahepatic duct dilatation, and a thin-walled gall bladder containing sludge but no gallstones are seen.
43 A 23-year-old man returns from a holiday in the Far East. He presents to A&E with fever and jaundice. His bilirubin and ALT are raised but the rest of his liver biochemistry is within normal limits.
44 A 45-year-old woman presents with epigastric tenderness and jaundice. She has deranged liver biochemistry and a long history of inflammatory bowel disease.
45 A 15-year-old boy of African origin presents with splenomegaly and jaundice. He is complaining of abdominal pain and his bilirubin is 100 μmol/L.

10. Paediatric abdomen

A Gastro-oesophageal reflux disease
B Pyloric stenosis
C Duodenal atresia
D Malrotation
E Volvulus
F Intussusception
G Meconium ileus
H Hirschsprung's disease
I Meckel's diverticulum

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

46 An 8-month-old boy presents with vomiting and rectal bleeding. There is a sausage-shaped mass palpable in the left side of the abdomen.
47 A 3-day-old boy with Down's syndrome presents with vomiting and dehydration. A plain abdominal X-ray demonstrates two bubbles of gas in the upper abdomen.
48 A 7-week-old boy is brought into A&E. He presents with non-bilious vomiting and dehydration, and on examination there is an olive-sized mass in the right upper quadrant.
49 A 4-year-old girl presents with dark-red rectal bleeding. She is anaemic but haemodynamically stable. On examination there are no significant findings.

50 A 3-day-old girl with cystic fibrosis has a palpable mass in the right lower quadrant. A plain abdominal X-ray reveals dilated small bowel loops.

11. Swollen painful joints

A Osteoarthritis
B Gout
C Rheumatoid arthritis
D Tuberculosis arthritis
E Neuropathic joint disease

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

51 A 35-year-old woman develops pain, swelling and stiffness of her hands. On examination, 2 years after the onset of her joint complaints, she is found to have swelling and tenderness in relation to the metacarpo-phalangeal joints. X-rays of the affected joints show diminution of joint space, osteoporosis and marginal erosions of the articulating bones.

52 A 60-year-old woman complains of pain and swelling in both her knees of gradual onset over a duration of 2 years. On examination, there is evidence of excess synovial fluid and synovial thickening in both knee joints and local tenderness. Standing X-rays of her knees show diminution of joint space, sclerosis and cysts in the adjacent bones. Osteophytes are also seen at the articular margins.

12. Pathological fractures

A Osteosarcoma
B Osteomalacia
C Metastatic carcinoma
D Osteoblastoma
E Ewing's sarcoma

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

53 A 14-year-old boy has suffered with left knee pain, which has been gradually increasing in severity over the last month. It is constant in nature and keeps him awake at night. On examination, the overlying skin is warm and shiny. A radiograph of the knee joint demonstrates bone destruction in the metaphysis of the left femur with areas of new bone formation and periosteal elevation.

54 A 16-year-old boy presents with pain in his right upper arm. There is no history of trauma. On examination, he is well with a hot, hard swelling in the middle of his right arm. X-rays demonstrate an onion skin-shaped bone lesion in the medulla of the humerus.

13. Nerve root/nerve injuries

A Forth lumbar nerve root
B Fifth lumbar nerve root
C First sacral nerve root
D Sciatic nerve
E Tibial nerve
F Common peroneal nerve
G Deep peroneal nerve
H Superficial peroneal nerve

For each of the patients described below, select the nerve root or nerve that is the most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

55 A wholesale market producer has been experiencing pain in the lower back for 3 months. During the last 3 weeks he has noticed that the pain radiates down the back of his left leg and now he has difficulty walking. On examination, elevating his left lower limb aggravates the pain. There is diminished sensation on his left heel and along the lateral border of his left foot. The ankle jerk is absent on this side.

56 A construction worker presents with loss of sensation over the front and lateral side of his leg and foot. There is no foot drop, but he is unable to evert his foot.

14. Skin conditions

A Basal cell carcinoma
B Malignant melanoma
C Squamous cell carcinoma
D Solar keratosis
E Keratocanthoma

For each of the patients described below, select the single most likely pathological condition from the options listed above. Each option may be used once, more than once or not at all.

57 An 80-year-old retired builder presents with a chronic and slowly enlarging skin lesion over his left cheek. On examination, this lesion is pearly white with an associated telangiectasia.

58 An 82-year-old retired woman presents with a 2-month history of a facial skin lesion. The lesion has now disappeared.

59 A 34-year-old lawyer presents with an itchy brown pigmented lesion on her right lower limb. She states it occasionally bleeds.

15. Trauma patient

A Tension pneumothorax
B Cardiac tamponade
C Flail segment
D Ruptured spleen
E Haemothorax

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

60 A 39-year-old woman was a pedestrian hit by a car while crossing the road. She complains of chest and abdominal pains. On examination, her GCS score is 14/15 (E4, V4, M6). Her vital observations are as follows: BP 86/32 mmHg; pulse 145/min. She has bruising and tenderness over her lower left 9th and 10th ribs. She has rebound tenderness and guarding over the left upper quadrant of her abdomen. Her chest X-ray demonstrates left rib fractures affecting ribs 8–10.

61 A 44-year-old man is involved in a road traffic accident. He was a driver of a delivery truck, travelling at 50 miles/h and was hit from the side. On arrival at A&E he is unstable. His vital observations are as follows: BP 90/32 mmHg; pulse 160/min; respirator rate 45 breaths/min. On examination, his neck veins are engorged and distended. His trachea is central with quiet heart sounds.

16. Lower leg ulceration

A Chronic obliterative arterial disease
B Venous ulcer
C Traumatic ulcer
D Rheumatoid arthritis
E Squamous cell carcinoma

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

62 A 72-year-old woman presents with an ulcer over the anteromedial aspect of the lower limb. It is flat, with edges sloping towards the centre, and has seropurulent discharge. She does not recall any trauma. She has suffered 'for years' with an aching pain over the leg due to her varicose veins. Over the last 2 months she has noted that this area is now brown in colour.
63 An 80-year-old retired cook has noticed that the edge of an ulcer situated above the medial malleolus for 17 years has recently become 'heaped up' and bleeds easily on contact.

17. Aneurysms

A Immediate ultrasound
B Insert intravenous lines, cross-match blood and transfer to theatre
C Immediate CT head scan
D Immediate CT chest scan
E Immediate endovascular stenting

For each of the patients described below, select the single most appropriate initial line of management from the options listed above. Each option may be used once, more than once or not at all.

64 A 67-year-old man is admitted as an emergency with back pain. He is found to be shocked with a blood pressure of 90/40 mmHg. An epigastric mass is palpable and tender.
65 A 67-year-old man is admitted with a palpable expansive epigastric mass and thoracic back pain. His blood pressure is normal and there is gross widening of the mediastinum on chest X-ray.
66 A 26-year-old man is admitted following a sudden onset of severe headache coupled with photophobia and neck stiffness.

18. Metabolic disorders of adrenal dysfunction

A Cushing's disease
B Cushing's syndrome
C Conn's syndrome
D Addison's disease
E Multiple endocrine neoplasia type 1 (Werner's syndrome)
F Multiple endocrine neoplasia type 2a

For each of the patients described below, select the single most appropriate diagnosis from the options listed above. Each option may be used once, more than once or not at all.

67 A 30-year-old woman with known pernicious anaemia suffers with dizzy spells, fatigue and lethargy. Her investigations reveal a low blood pressure and high serum potassium concentration.
68 A 42-year-old woman presents with epigastric pain. Her past medical history includes: peptic ulcers and hirsutism. She is under investigations for bilateral lower limb oedema. Her recent blood tests demonstrate hypercalcaemia and hypoglycemia.

19. Paediatric urogenital conditions

A Inguinal hernia
B Epispadias
C Hypospadias
D Non-communicating hydrocele
E Communicating hydrocele
F Posterior urethral valves

For each child described below, select the single most appropriate diagnosis from the options listed above. Each option may be used once, more than once or not at all.

69 A newborn is referred, as his mother is concerned that he does not appear to urinate from the end of his penis. His urinary stream points downwards. On examination, his external urethral meatus is located on the ventral aspect of the penile shaft.

70 A 2-year-old boy is referred with a scrotal swelling during the day. At night, it resolves. On examination, there is a fluctuant transilluminable swelling in the right scrotum. It is not possible to get above the swelling. No bowel sounds are auscultated in the swelling.

20. Vomiting

A Gastric volvulus
B Oesophageal varices
C Caecal carcinoma
D Strangulated hernia
E Achalasia

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

71 A 30-year-old woman presents with acute abdominal pain localized to her umbilicus. She also presents with vomiting. She underwent a diagnostic laparoscopy 5 days earlier, which was negative.

72 A 55-year-old writer presents to A&E with abdominal pain and haematemesis. On examination, he is ethanolic with hepatomegaly. He is also noted to have spider naevi and palmar erythema.

21. Paediatric gastrointestinal disorders

A Hypertrophic pyloric stenosis
B Intussusception
C Gastro-oesophageal reflux
D Mesenteric adenitis
E Meckel's diverticulum
F Appendicitis

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

73 A 6-month-old boy presents with colicky abdominal pain, two episodes of bilious vomiting and rectal bleeding. On examination, the abdomen is tender in the right hypochondrium and there is a sausage-shaped palpable mass.

74 A 6-year-old boy presents with two episodes of vomiting, coupled with central abdominal pain. He has a 2-day history of a sore throat and enlarged tonsils. On examination, he is apyrexial (but his mother reports a temperature of 38°C yesterday) with a pulse rate of

100/min. His mucosa membranes are dry with increased skin turgor. His tonsils are enlarged with obvious pus. His abdomen is soft, but tender to palpation.

75 A 2-year-old boy presents with dark-red rectal bleeding and general pallor. There has been no vomiting and abdominal examination is unremarkable.

76 A 4-week-old boy presents with non-bilious vomiting after feeding for 1 week. He has lost weight and is clinically dehydrated.

22. Rectal pain

A Rectal prolapse
B Solitary rectal ulcer syndrome
C Carcinoma of the rectum
D Fissure-in-ano
E Proctalgia fugax
F First-degree haemorrhoids

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

77 An 18-year-old girl presents with a 3-week history of severe pain at defecation, with bleeding. Digit examination is not possible because of the pain.

78 A 23-year-old male university student presents with a 3-month history of severe fleeting rectal pain, which occurs about three times a week. There are no aggravating or relieving factors. He denies any other gastrointestinal symptoms. Digital rectal examination and sigmoidoscopy are normal.

23. Diarrhoea

A Non-bacterial food poisoning
B Carcinoma of the anus
C Typhoid fever
D Acute appendicitis
E Amoebic dysentery
F Ulcerative colitis

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

79 A 25-year-old woman is admitted to hospital with anorexia, abdominal pain and diarrhoea over the previous 24 hours. She has vomited and has a low-grade pyrexia. She is tender in the lower abdomen and on rectal examination.

80 A 70-year-old man recently returned from Bangladesh is admitted with a high temperature and persistent bloody diarrhoea with a grossly abnormal rectal mucosa on sigmoidoscopy.

81 A 64-year-old man is admitted with a 3-month history of intermittent diarrhoea, anorexia and weight loss. He has a recent 1 week history of passing painless motions with dark-red blood mixed within the stool.

24. Dysphagia

A Achalasia
B Oesophageal carcinoma
C Pharyngeal pouch
D Inflammatory stricture
E Plummer–Vinson syndrome
F Retrosternal palsy

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

82 A 75-year-old women presents with a 4-month history of difficulty swallowing. She is now having difficulty swallowing fluids. Of note, she is a regular smoker.

83 A previously fit 32-year-old woman presents with a productive cough and pyrexia. At night, her coughing is worse. Moreover, she has difficulty swallowing fluids and complains of retrosternal pain.

84 A 73-year-old homeless man has a history of recurrent sore throats for which he has completed a course of antibiotics, but there has been no improvement. He presents to A&E with a lump on the left side of his neck.

25. Testicular conditions

A Seminoma
B Teratoma
C Torsion of testis
D Torsion of hydatid of Morgagni
E Inguinal hernia

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

85 A 25-year-old man discovers a hard lump on his left testicle. His GP has arranged a blood test (β-hCG) which is positive.

86 An 18-year-old man, an avid football player, develops a sudden onset of acute pain in his right testicle. There is no history of trauma. On examination, he is apyrexial and there is a small and very tender lump on the superior pole of the right testicle. The testicle is located in a normal anatomical position.

26. Jaundice

A Gilbert's syndrome
B Common bile duct stone
C Acute alcoholic hepatitis
D Carcinoma of head of pancreas
E Primary biliary cirrhosis
F Ascending cholangitis
G Hepatic metastases
H Cholangiocarcinoma
I Primary sclerosing cholangitis

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

87 A 30-year-old man, with a 7-year history of ulcerative colitis, complains of fluctuating jaundice, right upper quadrant pain and weight loss for the previous 6 months. Plasma alkaline phosphatase is 20 U/L (normal range 30–130 U/L).

88 A 25-year-old man has noticed mild intermittent jaundice for the past 6 years. His blood tests demonstrate a moderate unconjugated hyperbilirubaemia with otherwise normal liver function tests and hepatic histology.

89 A 57-year-old woman presents with a 5-week history of jaundice, anorexia and weight loss. She has a pyrexia of 37.8°C. She has tender enlarged liver (12 cm), mild ascites, widespread spider naevi and palmar erythema. Laboratory studies demonstrate a leucocytosis of

20×10^9/L, plasma alanine transaminase 280 U/L (normal range 2–50 U/L), plasma albumin 24 g/L (normal range 35–50 g/L), and prothrombin time of 20 seconds (control 13 s).

90 A 62-year-old man presents with a 3-month history of weight loss, increasing jaundice and nocturnal epigastric pain. Five years ago he underwent an anterior resection of the rectum. On examination, there is a right upper quadrant mass that moves on respiration. Laboratory studies show plasma alkaline phosphatase of 752 U/L (normal range 30–130 U/L).

27. Haematuria

A Transitional cell carcinoma
B Pelvi-ureteric junction obstruction
C Renal cell carcinoma
D Pyelonephritis
E March haemaglobinuria

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

91 A 45-year-old man presents with loin pain and haematuria. He has a palpable mass in his loin.
92 A 24-year-old runner presents after passing blood in his urine after a training session for a marathon race. His physical examination and radiological images are normal.
93 A 68-year-old man presents with acute painless frank haematuria. He had a similar episode several months ago. Moreover, he has noticed recent clots in his urine. On examination, his abdomen is soft and non-tender.

28. Prostate cancer

A Open prostatectomy and radiotherapy
B Hormonal manipulation
C Cytotoxic chemotherapy
D Palliative radiotherapy
E Watchful waiting

For each of the patients described below, select the single most appropriate primary therapy from the options listed above. Each option may be used once, more than once or not at all.

94 An 85-year-old man presents with established carcinoma of the prostate and is noted to have a non-tender fracture of the fourth lumbar vertebra on routine investigations. He earlier underwent a bilateral orchidectomy.
95 A 52-year-old man presents with nocturia. On rectal examination, a hard lump is noted. Biopsy demonstrates a prostatic adenocarcinoma, which is intracapsular and surrounded by normal prostate.
96 A 75-year-old man presents with back pain. Medical treatment has not improved his symptoms. Formal investigations demonstrate a carcinoma of the prostate with metastatic spread to the lumbar spine.

29. Wound infections

A Clean
B Clean contaminated
C Contaminated
D Dirty

For each of the patients described below, select the single most appropriate category from the options listed above. Each option may be used once, more than once or not at all.

97 A 15-year-old man underwent an emergency appendicectomy for a perforated appendix.
98 A 62-year-old man underwent an elective right-sided hemicolectomy for bowel cancer.
99 A 31-year-old man underwent an elective inguinal hernia repair.
100 A 42-year-old woman underwent an open cholecystectomy.

30. Endocrine

A Addison's disease
B Cushing's syndrome
C Diabetes insipidus
D Diabetes mellitus
E Graves' disease
F Hashimoto's thyroiditis
G Hypercalcaemia of malignancy
H Pituitary failure
I Phaeochromocytoma
J Primary hyperparathyroidism
K Primary hypothyroidism
L Secondary hyperparathyroidism

For each patient described below, choose the single most likely diagnosis from the above list of options. Each option may be used once, more than once or not at all.

Normal ranges are: sodium 135–145 mmol/L; potassium 3.4–5.0 mmol/L; calcium 2.20–2.65 mmol/L; phosphate 0.8–1.4 mmol/L; PTH 1.1–6.8 pmol/L.

101 A 30-year-old man complains of polyuria and polydipsia. His fasting blood glucose is 4.7 mmol/L. Biochemical investigations reveal: Na 140 mmol/L; K 4.2 mmol/L; Ca 2.85 mmol/L; phosphate 0.4 mmol/L; PTH 4.2 pmol/L.
102 A 50-year-old Asian woman complains of tingling in her hands and feet. On checking her blood pressure, her hands reveal carpal spasm. Her fasting blood glucose is 4.9 mmol/L. Biochemical investigations reveal: Na 141 mmol/L; K 4.1 mmol/L; Ca 1.85 mmol/L; phosphate 1.4 mmol/L; PTH 80 pmol/L.
103 A 50-year-old Asian woman complains of nocturia and dizziness. Her fasting blood glucose is 3.9 mmol/L. Biochemical investigations reveal: Na 131 mmol/L; K 6.1 mmol/L; Ca 2.75 mmol/L; phosphate 1.0 mmol/L; PTH 1.3 pmol/L.

31. Rheumatology

A Acute gout
B Ankylosing spondylitis
C Enteropathic arthritis
D Haemarthrosis
E Osteoarthritis
F Pseudogout
G Psoriatic arthropathy
H Reactive arthritis
I Reiter's syndrome
J Rheumatoid arthritis
K Septic arthritis
L Systemic lupus erythematosus

For each patient described below, choose the single most likely diagnosis from the above list of options. Each option may be used once, more than once or not at all.

104 A 60-year-old man complains of knee pain and examination reveals a moderate effusion. Withdrawal of fluid and microscopy reveals crystals, which on viewing under polarized light are positively birefringent.

105 A 19-year-old man returns from holiday in Tenerife. Four weeks later he develops a swollen, hot, painful, red knee joint, with an effusion. The knee is tapped and 20 mL of turbid yellow fluid is withdrawn. Microbiology reveals Gram-negative intracellular diplococci.

32. Hepatology

A Autoimmune hepatitis
B Carcinoma of the head of pancreas
C Cholangiocarcinoma
D Crigler–Najjar syndrome
E Dubin–Johnson syndrome
F Gallstones
G Gilbert's syndrome
H Hepatitis A
I Hepatitis B
J Hepatitis C
K Malaria
L Primary biliary cirrhosis
M Primary sclerosing cholangitis

For each patient described below, choose the single most likely diagnosis from the above list of options. Each option may be used once, more than once or not at all.
Normal ranges are: bilirubin 3–17 μmol/L; ALT 3–35 iu/L; ALP 30–300 iu/L.

106 An 18-year-old presents with jaundice. On questioning he admits that the last time he had a cold he went a slightly yellow colour. His brother has had a past episode of jaundice. Liver function tests reveal: bilirubin 80 μmol/L; ALT 25 iu/L; ALP 150 iu/L.

107 A 55-year-old woman presents with painless jaundice and pruritus. On direct questioning she admits to having dark urine and pale stools. On examination, she is noted to have xanthelasma and moderate hepatomegaly. Liver function tests reveal: bilirubin 200 μmol/L; ALT 67 iu/L; ALP 723 iu/L. Antimitochondrial antibodies are positive.

108 A 22-year-old student has just returned from an uneventful holiday in Africa. He is jaundiced and has moderate hepatomegaly. Liver function tests reveal: bilirubin 110 μmol/L; ALT 250 iu/L; ALP 350 iu/L. Also detected are specific IgM antibodies.

33. Abdominal trauma

A Emergency laparotomy
B Diagnostic peritoneal lavage (DPL)
C Wound exploration under local anaesthetic
D Abdominal ultrasound (FAST scan)
E CT abdomen
F Angiography
G Observation

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

109 An 18-year-old man sustains a low-energy gunshot wound from close range to his hypogastric area. His blood pressure is 100/65 mmHg and his pulse is 130 beats/min.

110 A 42-year-old female is involved in a motorcycle accident with a Glasgow Coma Score (GCS) of 7 following a severe head injury. A left-sided pneumothorax was treated with a chest drain insertion and her pulse is now 150 beats/min and blood pressure 120/75 mmHg after two litres of crystalloid. Her abdomen is soft but difficult to assess.

111 A 24-year-old male is brought into hospital with an abdominal stab wound which appears superficial and the abdomen is soft. His pulse is 110 beats per minute and blood pressure is 130/80 mmHg.

34. Lumps

A Neurofibroma
B Lipoma
C Ganglion
D Histiocytoma
E Sebaceous (epidermoid) cyst
F Dermoid cyst
G Ivory osteoma

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

112 A 42-year-old woman has a 1.5 cm swelling above the outer canthus of the eye. On examination, it is soft, deep to the skin, with no deep attachments.

113 A 52-year-old man has a 1 cm cutaneous lump on the anterior aspect of the lower limb which followed an insect bite one year earlier.

114 A 37-year-old man presents with a 3 cm lump on his forehead that has been present for many years. On examination, the lump is hard and deep to the skin.

35. Intestinal polyps

A Anterior resection
B Subtotal colectomy
C Panproctocolectomy
D Regular endoscopic surveillance
E Abdominoperineal excision
F Endoscopic excision
G Restorative proctocolectomy
H No treatment required

For each of the patients described below, select the single most likely treatment option from the list above. Each option may be used once, more than once or not at all.

115 A 45-year-old patient with familial adenomatous polyposis presents with severely dysplastic changes in the sigmoid colon.

116 An elderly patient presents with per-rectal bleeding. She is known to have haemorrhoids but on rigid sigmoidoscopy demonstrates a small polyp 14 cm from the anal verge. Barium enema is normal and histology reveals a metaplastic polyp.

117 A 19-year-old female has longstanding ulcerative colitis affecting the whole colon. She is found to have a malignancy on a biopsy taken 5 cm from the anal verge and severe dysplasia on other biopsies from the colon.

36. Cancer staging

A Dukes' A
B Dukes' B
C Dukes' C
D Dukes' D
E Clarke's level I
F Clarke's level II
G Clarke's level III
H Clarke's level IV
I Clarke's level V

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

118 A melanoma invading the papillary dermis.
119 A melanoma invading the subcutaneous tissue.
120 A sigmoid colon tumour involving the circumferential margins, but no lymph node deposits.
121 A rectal tumour with liver metastases

37. Anaemia

A Iron-deficiency anaemia
B Hereditary spherocytosis
C Vitamin B_{12} deficiency anaemia
D Sickle cell disease
E Beta-thalassaemia
F Pernicious anaemia
G Glucose-6-phosphate dehydrogenase deficiency
H Sideroblastic anaemia

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

122 A 42-year-old African male has recently been diagnosed with malaria and is taking quinine. He presents with fatigue, dark urine and shortness of breath.
123 An 11-year-old Scottish, Caucasian girl presents with mild anaemia and jaundice. Her blood tests reveal a normal MCV, but her red cell osmotic fragility test is increased.
124 A 25-year-old African man presents with severe lumbar back pain and jaundice. His blood tests demonstrate a normocytic, normochromic anaemia, high reticulocyte count. His ESR is low.

38. Complications of blood transfusions

A Immediate haemolytic reaction
B Febrile reaction
C Allergic reaction
D Hypothermia
E Viral hepatitis
F Septicaemia
G Delayed haemolytic reaction

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

125 A 72-year-old male is transfused with blood for an acute gastrointestinal bleed. Thirty minutes later he develops a temperature of 39.5°C, tachycardia and hypotension. There is no evidence of haemolysis on blood film.
126 An 82-year-old woman develops a temperature of 38°C and a moderate headache three hours after her blood transfusion is administered.
127 A 65-year-old woman presents one week post-transfusion with anaemia, jaundice and fever.

39. Fractures

A Transverse
B Spiral
C Stress
D Pathological
E Open
F Comminuted
G Incomplete

For each of the patients described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

128 A marathon runner presents with a fractured metatarsal bone. There is no history of trauma.
129 A 13-year-old boy falls while playing football. He has an abrasion over the site of tenderness and an X-ray shows a fracture through one of the cortices.
130 An 84-year-old woman presents with a painful right tibia. Her X-ray shows abnormal cortical thickening, a visible fracture and thickening in a bowed tibia.

40. Acid–base balance

A Metabolic alkalosis
B Metabolic acidosis
C Uncompensated respiratory alkalosis
D Uncompensated respiratory acidosis
E Compensated respiratory alkalosis
F Compensated respiratory acidosis

For each of the case scenarios described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

131 pH 7.3, Pao_2 8.5 kPa, $Paco_2$ 9.8 kPa, HCO_3 33 mmol/L.
132 pH 7.55, Pao_2 10 kPa, $Paco_2$ 7.3 kPa, HCO_3 43 mmol/L.
133 pH 7.3, Pao_2 8.5 kPa, $Paco_2$ 8.0 kPa, HCO_3 27 mmol/L.

41. Informed consent

A Patient
B Partner
C Parents
D Surgeon
E Psychiatrist
F Judge
G Hospital management

For each of the case scenarios described below, select the single most likely person from the options listed above from whom to take consent. Each option may be used once, more than once or not at all.

134 A 15-year-old girl refuses to have an appendicectomy.
135 An unconscious stabbed patient needs an emergency thoracotomy.
136 A diabetic patient with chronic, stable schizophrenia presents with a gangrenous toe which requires an amputation. He understands the implications but refuses surgery.

42. Neck anatomy

A Phrenic nerve
B Stellate ganglion
C Thoracic duct
D Parathyroid glands
E Recurrent laryngeal nerve
F External laryngeal nerve

For each of the case scenarios described below, select the single most likely structure from the options listed above that is likely to have been injured. Each option may be used once, more than once or not at all.

137 The patient is complaining of tingling in the tips of their fingers.
138 An opera singer complains that her voice is becoming weak after singing for a short period of time.
139 A smoker presents with unilateral ptosis and a small pupil.

43. Innervation of lower limb muscles

A Obturator nerve
B Saphenous nerve
C Femoral nerve
D Tibial nerve
E Superficial peroneal nerve
F Deep peroneal nerve
G Sural nerve

For each of the muscles below, select the single most likely nerve from the options listed above. Each option may be used once, more than once or not at all.

140 Tibilis anterior
141 Quadratus femoris
142 Adductor magnus

44. Brachial plexus injuries

A C5
B C5–6
C C5–7
D C7–8, T1
E C8, T1
F C6–8
G C5–8, T1

For each of the case scenarios described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

143 A healthy full-term baby was born 5 hours ago after a prolonged labour. The child's right arm is medially rotated with the palm of the hand facing backwards.

144 While the patient is holding on to the overhead railing, the bus suddenly stops. The patient presents with weakness of the small muscles of the hand and sensory loss over the medial aspect of the hand and forearm.

145 A motorcyclist is involved in an accident. His right upper limb is paralysed and insensate.

45. Herniae

A Direct inguinal
B Indirect inguinal
C Obturator
D Femoral
E Epigastric
F Para-umbilical
G Umbilical
H Pantaloon

For each of the anatomical locations described below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

146 Arising in the upper, inner thigh.
147 Arising from the umbilicus in the adult.
148 Arising below and lateral to the pubic tubercle.

46. Tumour markers

A CA-125
B Ca19-9
C PSA
D CEA
E LDH
F Alpha-fetoprotein
G Thyroglobulin

For each of the neoplasms below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

149 Ovarian carcinoma
150 Hepatocellular carcinoma
151 Colorectal cancer

47. Adrenal pathology

A Cushing's syndrome
B Phaeochromocytoma
C Conn's syndrome
D Addison's disease
E Multiple endocrine neoplasia 1
F Multiple endocrine neoplasia 2a
G Multiple endocrine neoplasia 2b

For each of the case scenarios below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

152 A 42-year-old woman presents with epigastric pain. Her past medical history includes duodenal ulcers, hirsutism and bilateral pitting leg oedema. Investigations reveal hypercalcaemia.

153 A 72-year-old smoker presents with polydipsia and polyuria. On clinical examination he has a moon face, buffalo hump, abdominal striae and hypertension.
154 A 42-year-old woman (with known pernicious anaemia) faints. She is hypotensive and her blood tests demonstrate hyperkalaemia.

48. Chest pain

A Myocardial infarction
B Pneumonia
C Pulmonary embolus
D Pneumothorax
E Tietze's syndrome (costochondritis)
F Oesophageal spasm
G Dissecting aortic aneurysm

For each of the case scenarios below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

155 A 16-year-old girl presents with a history of asthma and epilepsy with anterior chest pain and shortness of breath. On percussion her anterior chest wall is tender.
156 A 63-year-old man presents with crushing, retrosternal chest pain which radiates to his jaw. A coronary angiogram 3 months previously was normal.
157 A 32-year-old woman presents 3 weeks post-partum with pleuritic chest pain, breathlessness and haemoptysis.

49. Metabolic abnormalities

A Hypokalaemia
B Hyperkalaemia
C Hyponatraemia
D Hypernatraemia
E Hypophosphataemia
F Hyperphosphataemia
G Hyperglycaemia

For each of the case scenarios below, select the single most likely diagnosis from the options listed above. Each option may be used once, more than once or not at all.

158 A 63-year-old woman with congestive cardiac failure is commenced on oral steroids for an acute exacerbation of COPD. She takes regular furosemide and aspirin.
159 A 51-year-old alcoholic man with Boerhaave's syndrome receives a feeding jejunostomy.
160 A 25-year-old man sustains a partial-thickness burn in his left arm. He has proteinuria and his creatine kinase is elevated.

50. Lung volumes

A Inspiratory reserve volume
B Tidal volume
C Functional residual capacity
D Total lung capacity
E Vital capacity
F Residual volume
G Expiratory reserve volume

For each of the equations described below, select the single most likely option from those listed above. Each option may be used once, more than once or not at all.

161 Residual volume + expiratory reserve volume = ?
162 Total lung capacity –vital capacity = ?
163 Vital capacity – (expiratory reserve volume + inspiratory reserve volume) = ?

EMQ answers and explanations

1. Blood transfusions

B&L **For further reading, see *Bailey and Love*, Chapter 2, 'Shock and blood transfusions'.**

1 D
A patient with group B blood has anti-A antibodies and therefore cannot receive group A blood. This patient is also RhD-negative and so cannot receive RhD-positive blood. The patient could take iron sulphate tablets but, with a haemoglobin level of 6.0, a blood transfusion is a better option.

2 A
A patient with group A blood has anti-B antibodies and therefore cannot receive group B blood. This patient is also RhD-positive and so can receive RhD-positive or negative blood. The patient could take iron sulphate tablets but, with a haemoglobin level of 6.0, a blood transfusion is a better option.

3 F
The haemoglobin level is not very low and so a gradual normalization with iron sulphate tablets is a better option compared with the risks associated with blood transfusion. Blood transfusion is usually considered when the haemoglobin level drops below 8 g/dL.

4 D
A patient with group O blood has anti-A and anti-B antibodies and can only therefore receive group O blood. This patient is also RhD-negative and so cannot receive RhD-positive blood.

5 E
A woman who is RhD-negative but exposed to the RhD-antigen via childbirth or transfusion will go on to develop antibodies that would attack a subsequent RhD-positive baby *in utero*. Anti-D immunoglobulin will reduce her immune response and therefore reduce the risk of developing antibodies.

2. Lumps in the groin

B&L **For further reading, see *Bailey and Love*, Chapter 75, 'Testis and scrotum'.**

6 D
There is a positive cough impulse suggestive of bowel herniation. The doctor cannot get above the lump, suggesting that it arises from the inguinal canal. The hernia can be reduced back along the inguinal canal from the scrotum and upon occlusion of the deep inguinal ring the hernia is controlled. This is pathognomonic for an indirect inguinal hernia.

7 I
Epididymo-orchitis is an infection of the epididymis and testis and can be mistaken for torsion. The clue here is the prolonged history.

8 A
Any firm scrotal mass is cancer until proven otherwise. Testicular cancer may often be associated with a hydrocele.

9 E
This is a classic description of a varicocele. These are more common on the left as the left testicular vein drains into the left renal vein whereas the right testicular vein drains directly into the IVC.

10 B
A history of sudden onset of severe testicular pain with such a short duration must be presumed to be testicular torsion until proven otherwise. This is a surgical emergency.

3. Lumps in the neck

B&L **For further reading, see *Bailey and Love*, Chapter 45, 'Pharynx, larynx and neck'.**

11 E
Epidermal cysts originate in the skin and have a characteristic punctum. They commonly occur in the head and neck region.

12 C
This is the classic description of a thyroglossal cyst and forms from a persistent thyroglossal duct.

13 I
Lumps that move on swallowing must be attached to the larynx or trachea and are most commonly thyroid lumps. Multinodular goitres are the most common thyroid lumps.

14 D
A cystic hygroma is a lymphangioma which usually presents in childhood. Cystic hygromas typically occur in the neck and transilluminate.

15 F
Stones can form in the salivary glands, especially in the submandibular glands. Obstruction of the salivary gland duct can cause pain and swelling.

4. Diseases of the hepatobiliary system

B&L **For further reading, see *Bailey and Love*, Chapter 63, 'The gallbladder and bile ducts', and Chapter 64, 'The pancreas'.**

16 H
This woman has a tumour at the head of the pancreas. If retrograde stenting via ERCP is not possible, then anterograde stenting via a percutaneous approach (PTC) is the next step to relieve jaundice.

17 C
This is a classic story of acute cholecystitis which can be diagnosed on ultrasound, which can also detect gallstones.

18 A
This is a story of bowel obstruction which may be due to gallstone ileus. Dilated loops of bowel may be seen and perhaps the gallstone itself.

19 B
This man has acute pancreatitis. The most common causes include alcohol excess and gallstones. There is an obstructive picture, so ultrasound can confirm and may detect the obstructing gallstone. CT is used to detect pancreatic necrosis several days later.

20 F
There is a gallstone obstructing the common bile duct. It can be removed by ERCP.

5. Fractures of the hip

B&L **For further reading, see *Bailey and Love*, Chapter 35, 'Hip and knee'.**

21 G
In elderly patients, hemiarthroplasty is indicated for intracapsular fractures unless there is a diseased acetabulum, when a total hip replacement is preferred.

22 D
An intramedullary screw is indicated in intertrochanteric fractures with extension into the shaft. This is because there is a nail for the shaft and a screw for the head.

23 C
Cannulated screws are preferred in younger patients with intracapsular fractures and thereby preserving the head of the femur. This is because femoral head prostheses have a limited lifespan.

24 E
In elderly patients with an intracapsular fracture, uncemented hemiarthroplasty is preferred to cemented hemiarthroplasty, to decrease the risk of fat embolism.

25 B
Dynamic hip screws are preferred for extracapsular femoral fractures.

6. Arterial blood gases

B&L **For further reading, see *Bailey and Love*, Chapter 13, 'Perioperative care'.**

26 A
The pH is low = acidosis; the PCO_2 is normal = not a respiratory cause; the base excess is negative = metabolic acidosis.

27 A
The pH is low = acidosis; the PCO_2 is normal = not a respiratory cause; the base excess is negative = metabolic acidosis.

28 C
The pH is high = alkalosis; the PCO_2 is high = respiratory compensation; the base excess is normal.

29 H
The pH is high = alkalosis; the PCO_2 is low = respiratory cause; the base excess is negative = metabolic compensation.

7. ATLS classification of haemorrhagic shock

B&L **For further reading, see *Bailey and Love*, Chapter 2, 'Shock and blood transfusions'.**

30 A
Class I shock = 0–15 per cent of circulatory volume blood loss. There is only tachycardia.

31 A
Class I shock = 0–15 per cent of circulatory volume blood loss. There is only tachycardia.

32 B
Class II shock = 15–30 per cent of circulatory volume blood loss. There is tachycardia, tachypnoea, narrowing of pulse pressure, slight drop in urine output (normal is 0.5 mL/kg/h), slight confusion.

33 C
Class III shock = 30–40 per cent of circulatory volume blood loss. There is tachycardia, tachypnoea, drop in systolic blood pressure, oliguria, agitated/drowsy.

34 D
Class IV shock = >40 per cent of circulatory volume blood loss. There is extreme tachycardia, tachypnoea, often undetectable, anuria, unconscious.

8. Burns

B&L **For further reading, see *Bailey and Love*, Chapter 28, 'Burns'.**

Apply Wallace's rule of 9s:

35 A – 1 per cent for perineum
36 B – 9 per cent for each arm
37 B – 9 per cent for face and head
38 C – 18 per cent for each leg
39 C – 18 per cent for the back of trunk

9. Jaundice

B&L **For further reading, see *Bailey and Love*, Chapter 63, 'The gallbladder and bile ducts', and Chapter 65, 'The small and large intestines'.**

40 J
Mirizzi syndrome occurs when a gallstone in the gall bladder causes compression on the common bile duct resulting in obstructive jaundice. There is gallstone cholecystitis here as well.

41 F
This obeys Courvoisier's law which states that a palpable gall bladder in the presence of jaundice is more likely to be malignancy than gallstones.

42 D
This is a classic story of gallstone obstruction of the common bile duct.

43 C
This is most likely to be infective hepatitis.

44 E
This woman has ulcerative colitis which is associated with sclerosing cholangitis.

45 A
This boy is in sickle cell crisis with haemolytic jaundice. Sickle cell anaemia almost exclusively occurs in black Americans and black Africans.

10. Paediatric abdomen

B&L **For further reading, see *Bailey and Love*, Chapter 6, 'Principles of paediatric surgery, Part II: Abdominal'.**

46 F
This is the classic story of intussusception which occurs in young children and is most often idiopathic. There is redcurrant jelly stool due to bleeding.

47 C
This is the double-bubble sign seen on plain X-ray and represents dilated proximal duodenum and stomach due to duodenal atresia. It is associated with Down's syndrome.

48 B
This is the classic story of pyloric stenosis and most commonly affects males in the first few months of life. They usually present with non-bilious projectile vomiting.

49 I
This girl has a Meckel's diverticulum which most likely contains gastric mucosa causing rectal bleeding.

50 G
Most patients with meconium ileus have cystic fibrosis. Meconium is fetal stool and in this case is impacted in the ileum and can be felt as a mass. The obstructing meconium leads to dilatation of small bowel loops more proximally.

11. Swollen painful joints

B&L **For further reading, see *Bailey and Love*, Chapter 37, 'Inflammation and infection and musculoskeletal tumours'.**

51 C
The patient has rheumatoid arthritis. In this chronic inflammatory disorder, patients present with bilateral and symmetrical polyarthropathy affecting the small joints of the hand with sparing of the distal interphalangeal (DIP) joints and involvement of the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints. X-ray findings include narrowing of joint space, periarticular osteopenia, juxta-articular bony erosions (non-cartilage protected bone), subluxation with gross deformity and periarticular soft tissue swelling.

52 A
The patient has osteoarthritis (OA). In degenerative joint disease, patients present with joint pain, tenderness and stiffness due to the process of progressive deterioration of articular cartilage and formation of new bone (osteophytes) at the joint surface. While osteoarthritis can affect any joint in the body, the disorder commonly affects the hands, hips, knees, neck and lumbar spine. In the hands, OA typically targets the PIP, DIP, scaphotrapeziotrapezoid and the first carpometacarpal joints. X-ray shows that the affected joint spaces are narrowed with reactive subchondral sclerosis (eburnation). Bony erosions are centrally located (in contrast to the marginal erosions in rheumatoid arthritis). Other classic radiographic findings include osteophytes and subchondral cysts. Heberden's nodes at the DIP joints and Bouchard's nodes at the PIP joints of the hands are areas of osteophyte formation. Moreover, periarticular soft tissue swelling, intra-articular loose bodies and osseous fusion can also be seen.

12. Pathological fractures

B&L **For further reading, see *Bailey and Love*, Chapter 37, 'Inflammation and infection and musculoskeletal tumours'.**

53 A
The patient has osteosarcoma of the left femur. These highly malignant lesions appear in two age groups: between 10 and 20 years, and those aged over 50 (secondary to Paget's disease). Osteosarcoma usually occurs at the metaphysis of long bones and presents with pain, associated with a history of trauma. X-ray findings include periosteal new bone formation, which produces a speckled triangle (Codman's triangle) with a 'sun-ray speculation'. Resectable tumours are now treated with cytotoxic therapy, followed by surgical resection. The 5-year survival rate is 50 per cent.

54 E
Ewing's sarcoma is a rare malignant bone tumour. The common areas in which it occurs are the pelvis, ribs, humerus and femur (in the long bone medullary cavity). It is more common in males and usually presents in childhood or early adulthood, with a peak between 10 and 20 years of age. Patients usually present with bone pain. Radiological findings are a permeative lytic

lesion with periosteal reaction. The classic description of lamellated or 'onion skin' type periosteal reaction is often associated with this lesion.

13. Nerve root/nerve injuries

B&L **For further reading, see *Bailey and Love*, Chapter 27, 'Extremity trauma'.**

55 C

Compression of the first sacral nerve root results in pain in the posterior leg and ankle, reduced plantar flexion, reduced sensation in the lateral aspect of the foot and loss of the ankle reflex.

Table 10 Lumbar radiculopathy secondary to lumbar disc protrusions

	L4/L4	L4/L5	L5/S1
Disc	5%	45%	50%
Root	L4	L5	S1
Reflex	Knee	–	Ankle
Motor	Knee extension	Extensor hallucis longus Tibialis anterior	Plantar flexion
Sensory	Medial calf	Lateral calf	Lateral foot
Pain	Anterior thigh	Posterior leg	Posterior leg Ankle

56 H

The superficial peroneal nerve supplies the peroneal muscles, hence the loss of ankle eversion. It should be differentiated from the common peroneal nerve injury, which involves loss of function in both superficial and deep peroneal nerves. The deep peroneal nerve supplies the anterior compartment of the leg; injury causes inability to dorsiflex the foot.

14. Skin conditions

B&L **For further reading, see *Bailey and Love*, Chapter 39, 'Skin and subcutaneous tissue'.**

57 A

Basal cell carcinoma is the most common type of skin cancer. It is considered malignant because it can cause significant local destruction by invading into the surrounding tissues. Most lesions are located on the patient's head and neck (80 per cent). It occurs more often in men than in women. Most basal cell carcinomas are seen in patients over the age of 40 years. Patients present with a shiny and pearly white nodule on sun-exposed areas.

58 E

Keratocanthoma is a benign lesion that originates in the pilosebaceous glands and closely resembles squamous cell carcinoma. In most cases, a keratocanthoma is characterized by rapid growth over a few weeks to months, followed by spontaneous resolution over 4–6 months. It usually appears as a volcano-like bump on the sun-exposed skin of middle-aged and elderly individuals. Most lesions cause minimal skin destruction, but a few behave more aggressively and can spread to regional lymph nodes.

59 B

Malignant melanoma is a tumour of melanocytes. The cells are found in the skin, bowel and eye. There are five types of malignant melanoma of the skin:

- superficial spreading (most common) – usually palpable with an irregular edge
- lentigo maligna (least common) – least malignant, usually located on the face of the elderly (Hutchinson's freckle)

- nodular – most malignant, affects the young and may ulcerate and bleed
- acral – affects palms and soles (includes subungual tumours) and has poor overall prognosis
- amelanotic – pink in colour but usually pigmented at base; poor prognosis.

Patients present with changes to the shape or colour of existing moles or appearance of new skin lesions. They cause pruritus, ulceration or bleeding. Urgent excisional biopsy is recommended.

Resection on a malignant melanoma is based on Breslow staging (Table 11).

Table 11 Breslow staging of melanoma

Depth of lesion (mm)	Recommended width of excision (mm)
< 0.75	2
0.76–1.5	20
1.6–3.0	50
> 3.0	50

15. Trauma patient

B&L **For further reading, see *Bailey and Love*, Chapter 22, 'Early assessment and management of trauma'.**

60 D

This patient is presenting with a ruptured spleen (left lower rib fractures with associated hypotension) secondary to trauma. Patients present with abdominal pain, left shoulder tip pain (Kehr's sign), hypotension and tachycardia. Bruising may present over the left upper abdomen, left chest, or left lower back and is associated with underlying haemorrhage.

61 B

The patient has a cardiac (pericardial) tamponade. The clinical syndrome is caused by accumulation of fluid in the pericardial space, which results in reduced ventricular filling and subsequent haemodynamic compromise. Cardiac tamponade presents with Beck's triad: quiet and muffled heart sounds, hypotension and distended neck vein (jugular venous distention). An emergency pericardiocentesis is the life-saving treatment of choice.

16. Lower leg ulceration

B&L **For further reading, see *Bailey and Love*, Chapter 54, 'Venous disorders'.**

62 B

Venous ulcers are commonly secondary to venous stasis from varicose veins and/or deep vein thrombosis. They invariably begin after the skin of the leg has been injured. However, the patient may not recall the initial insult. Chronic venous insufficiency may occur secondary to longstanding high pressure in the veins. This high venous pressure results in reflux (reverse flow) in the veins. Characteristic changes occur at the medial gaiter area of the leg. The classical changes include ulceration, haemosiderin deposition, thrombophlebitis, venous eczema and scars, lipodermatosclerosis,'inverted champagne bottle leg', pitting oedema, healed ulceration (atrophie blanche), ankle flare (corona phlebectatica), and loss of hair.

63 E

A chronic venous ulcer may rarely undergo metaplasia to form an ulcerating squamous cell carcinoma, which is called a Marjolin's ulcer. In 1828, Dr Jean Nicolas Marjolin first described the occurrence of ulcerating lesions within scar tissue. Marjolin's ulcer is the term given to these aggressive epidermoid tumours that arise from areas of chronic injury (burn injuries, osteomyelitis, post-radiotherapy).

17. Aneurysms

B&L **For further reading, see *Bailey and Love*, Chapter 54, 'Venous disorders'.**

64 B

An aneurysm is an abnormal, permanent dilation of a blood vessel, to 1.5–2 times its normal diameter. Patients who present with back pain and shock should be managed as a high index of suspicion as having a leaking abdominal aortic aneurysm (AAA). They need immediate resuscitation and reconstruction surgery, as 50 per cent of patients die before reaching hospital, and of those who arrive, 50 per cent die either of shock before theatre and renal failure after surgery. An elective operation has under 6 per cent mortality rate. Thus, asymptomatic aneurysms are regularly followed up with ultrasound or CT scan. This is because an AAA with a diameter of more than 6 cm has a high chance of rupture within 1 year. The immediate management of this patient is to insert intravenous lines, cross-match and transfer to theatre.

65 D

A patient with a widened mediastinum on chest X-ray needs to have the diagnosis of a thoracic aortic aneurysm excluded. The gold standard investigation to detect this abnormality is an angiogram. However, a CT scan is easier, time-efficient and non-invasive. Both investigations will demonstrate whether the aneurysm is secondary to an aortic dissection. As this patient is cardiovascularly stable, there is time to undergo formal investigations.

66 C

The patient's history is suggestive of a subarachnoid haemorrhage secondary to an aneurysmal bleed. In general, patients present with a sudden onset of a severe headache coupled with neck pain, vomiting and photophobia. The diagnosis of a subarachnoid haemorrhage is confirmed with a CT head scan. The Fisher grade classifies the appearance of the subarachnoid haemorrhage on a CT head scan (Table 12).

Table 12 Fisher grading for subarachnoid haemorrhage

Grade	Appearance
1	None evident
2	Less than 1 mm thick
3	More than 1 mm thick
4	Any thickness with intraventricular haemorrhage or parenchymal extension

The World Federation of Neurosurgeons (WFNS) classification uses the Glasgow Coma Scale (GCS) score and focal neurological deficit to classify the severity of symptoms (Table 13). A cerebral angiogram will identify the underlying aneurysm.

Table 13 World Federation of Neurosurgeons (WFNS) classification

Grade	GCS score	Focal neurological deficit
1	15	Absent
2	13–14	Absent
3	13–14	Present
4	7–12	Present or absent
5	< 7	Present or absent

18. Metabolic disorders of adrenal dysfunction

B&L **For further reading, see *Bailey and Love*, Chapter 49, 'Adrenal gland and other endocrine disorders'.**

67 D

In 60 per cent of cases, Addison's disease, an adrenocortical insufficiency, is caused by an autoimmune disorder. There is an association with other autoimmune conditions (i.e. chronic thyroiditis, Graves' disease, hypoparathyroidism, hypopituitarism, myasthenia gravis or pernicious anaemia). Other causes include tuberculosis, metastases (lung cancer), amyloidosis and bleeding. Patients present with muscle weakness, fatigue, loss of appetite, weight loss, dizzy spells (low blood pressure), nausea, diarrhoea, vomiting, irritability and depression. Routine investigations may reveal hypercalcaemia, hypoglycaemia, hyponatraemia, hyperkalaemia, eosinophilia, lymphocytosis and metabolic acidosis.

68 E

Multiple endocrine neoplasia is due to neoplasia of APUD cells (amine precursor uptake and decarboxylation). Inheritance may be sporadic or autosomal dominant. They are classified into three types:

- MEN 1 – parathyroid gland, pancreatic islet cells and pituitary gland (common), thyroid and adrenal cortex (rare)
- MEN 2a – parathyroid hyperplasia, medullary thyroid carcinoma and phaeochromocytoma
- MEN 2b – MEN 2a and neurofibromatosis.

This patient is suffering from MEN1. Her signs and symptoms can be classified by organ system.

- *Parathyroid*. Hyperparathyroidism is present in 90 per cent or more of patients.
- *Pancreas*. Pancreatic islet cell tumours occur in 60–70 per cent of patients. Approximately 40 per cent of islet tumours originate from beta-cells, secrete insulin (insulinoma) and cause hypoglycaemia. Most islet tumour cells secrete pancreatic polypeptides. Gastrin is secreted by many non-B-cell tumours (increased gastrin secretion is linked to the duodenum). Increased gastrin secretion increases gastric acid production, which may inactivate pancreatic lipase leading to diarrhoea and steatorrhoea. Increased gastrin secretion also leads to peptic ulcer formation in more than 50 per cent of MEN 1 patients.
- *Pituitary*. Pituitary tumours can occur In MEN 1. The majority are prolactinomas, followed by tumours that secrete growth hormone and prolactin, and ACTH. Excess hormones may lead to other clinical syndromes (i.e. excess prolactin: galactorrhoea; excess growth hormone: acromegaly; excess ACTH: Cushing's disease).

Overall, this patient's symptoms may be associated with the following:

- hypercalcaemia from hyperparathyroidism
- excess steroid production from Cushing's disease
- Zollinger–Ellison syndrome.

19. Paediatric urogenital conditions

B&L **For further reading, see *Bailey and Love*, Chapter 6, 'Principles of paediatric surgery, Part 12: Genetourinary'.**

69 C

Hypospadias is a common congenital abnormality in which the external urethral meatus is located on the ventral aspect of the penis. Epispadias occurs when the meatus is located on the dorsal aspect of the penis. Chordee is a condition in which the head of the penis curves downward or upward at the junction of the head and shaft of the penis.

70 E

The testis descends from the posterior wall of the abdomen into the scrotum via the inguinal canal. It carries a pouch of peritoneum called the processus vaginalis. In a child's first year, the

processus vaginalis becomes obliterated, leaving the tunica vaginalis surrounding the testis. If this does not occur, the scrotal sac fills with peritoneal fluid via a communicating hydrocele. Owing to the continuity with the peritoneal cavity, the swelling will increase in size during standing and resolve when lying down. If the sac fills with bowel contents, an inguinal hernia will be present. A non-communicating hydrocele occurs when the processus vaginalis has closed, but the reabsorption of fluid from the tunica vaginalis is incomplete. This condition is present at birth and does not change in size.

20. Vomiting

B&L **For further reading, see *Bailey and Love*, Chapter 57, 'Hernias, umbilicus and abdominal wall', and Chapter 60, 'Stomach and duodenum'.**

71 D

A hernia is a protrusion of an organ or the fascia through the wall of the cavity that normally contains it. An incisional hernia occurs when the defect is the result of an incompletely healed surgical wound. The small bowel has herniated through a defect in the linea alba, which was not closed adequately during her diagnostic laparoscopy. A strangulated hernia occurs when pressure on the hernial contents may compromise blood and may cause ischaemia, and later necrosis and gangrene. Clinically, strangulated hernias are painful. The pain is coupled with abdominal tenderness. Nausea, vomiting and a fever may also be noted.

72 B

This patient has haematemesis (vomiting blood) secondary to oesophageal varices. Oesophageal varices are dilated submucosal veins in the lower oesophagus. They are often a consequence of portal hypertension. Cirrhosis is a common cause of portal hypertension. The patient's history of alcohol use, hepatomegaly, and peripheral stigmata of liver disease (spider naevi and palmar erythema) is in keeping with this underlying diagnosis. His portal hypertension is a result of enlarged collateral channels between the portal and systematic circulation (at points of portal systemic anastomosis: Table 14).

Table 14 Sites of portosystemic anastomosis

Site	Portal circulation	Systemic circulation
Oesophagus	Left gastric vein	Azygous vein
Paraumbilical	Paraumbilical vein	Superior epigastric vein
Retroperitoneal	Right, left and middle colic veins	Renal, suprarenal, paravertebral and gonadal veins
Patent ductus venosus	Left branch of portal vein	Inferior vena cava
Rectal	Superior rectal vein	Middle and inferior rectal veins

21. Paediatric gastrointestinal disorders

B&L **For further reading, see *Bailey and Love*, Chapter 6, 'Principles of paediatric surgery, Part II: Abdominal'.**

73 B

Intussusception is an invagination of one segment of bowel into another segment of bowel. Peristalsis lengthens the invaginated portion and each peristaltic wave results in a bout of colic. A viral illness is thought to enlarge Peyer's patches, resulting in an intussusception. In the adult population, this may also be associated with intestinal polyps or tumours. Early symptoms are nausea, vomiting and abdominal pain. Later, rectal bleeding ('redcurrant stool') and a sausage-shaped mass may be palpable in the abdominal examination. An ileocaecal intussusception is the most common type. The investigations of choice are an ultrasound and barium enema. A barium

enema can be diagnostic and therapeutic (inflation of air). Further treatment includes an urgent laparotomy for reduction with or without bowel resection.

74 D

This child is presenting with mesenteric adenitis. This condition is a self-limiting inflammatory process that affects the mesenteric lymph nodes in the right lower quadrant of the abdomen. It is frequently caused by a viral pathogen. The patient has a history of fever, enlarged lymph nodes and generalized abdominal pain. The abdominal pain and tenderness are often centred in the right lower quadrant, but they may be more diffuse than appendicitis. The site of tenderness may shift when the position of the patient changes. The clinical presentation of mesenteric adenitis may mimic appendicitis. With appendicitis, children often present with pyrexia, facial flushing and localized abdominal pain.

75 E

Meckel's diverticulum is the most common congenital abnormality of the small intestine. It is caused by an incomplete obliteration of the vitelline duct. It is present in approximately 2 per cent of the population, with a male predominance. The rule of 2s may be applied:

- 2 per cent of the population
- 2 types of ectopic tissue (gastric and pancreatic)
- 2 years of age at time of presentation
- 2 times more common in males to be affected.

The most common presenting symptom is painless rectal bleeding followed by intestinal obstruction, volvulus and intussusception.

76 A

Hypertrophic pyloric stenosis is an obstruction of the pyloric lumen due to pyloric muscular hypertrophy. It affects 1 in 250 infants, is more common in firstborn males and occurs at age 2–6 weeks. The typical infant presents with non-bilious projectile vomiting and dehydration. On examination, gastric peristaltic waves may be present and a discrete 2–3 cm firm movable 'olive-like' mass may be palpable. The classic laboratory finding is a hypochloraemic, hypokalaemic metabolic alkalosis. Repeated vomiting results in a loss of HCl, causing the hypochloraemic metabolic alkalosis. The patient is likely to be dehydrated from repeated gastrointestinal loss and poor oral intake. The diagnosis is confirmed by abdominal ultrasound. Initial treatment is correction of the dehydration and electrolyte abnormality. Definitive treatment is a longitudinal pyloromyotomy.

22. Rectal pain

B&L **For further reading, see *Bailey and Love*, Chapter 68, 'The rectum'.**

77 D

A fissure-in-ano is a split or tear in the mucosa lining the lower rectum (anus). Common causes include Crohn's disease, iatrogenic (post-haemorrhoidectomy) and chronic constipation (passing dry hard stools). Patients suffer from pain during bowel movement, spasm of the anal sphincter coupled with bright-red rectal bleeding.

78 E

Proctalgia fugax is a sudden, severe and episodic pain in the rectum lasting several seconds to minutes. It is associated with cramps in the pubococcygeus or levator ani muscles. It often presents in the middle of the night and lasts less than 20 minutes. Of note, levator ani syndrome presents with pain and lasts longer than 20 minutes.

23. Diarrhoea

B&L **For further reading, see *Bailey and Love*, Chapter 67, 'The vermiform appendix', Chapter 65, 'The small and large intestines', and Chapter 69, 'The anus and anal canal'.**

79 D

Appendicitis is a result of acute inflammation of the appendix. The main symptom is abdominal pain. The pain is generalized and then localizes to the right lower quadrant (McBurney's point). On clinical examination, rebound tenderness is noted. Rectal examination may also illicit tenderness. Patients also present with loss of appetite, which can progress to nausea and vomiting. Other symptoms include constipation or diarrhoea, low-grade fever and abdominal swelling. The diagnosis is based on patient history and physical examination supported by an elevated neutrophilic white cell count.

80 E

Amoebic dysentery is transmitted through contaminated food and water sources and is caused by the amoeba *Entamoeba histolytica*. Patients can present with frequent, loose and bloodstained stools, weight loss, dehydration, indigestion, colic abdominal pain and rectal bleeding. The most frequent sites of infection are the caecum, ascending colon and sigmoid colon. The amoebae affect the underlying mucosa causing inflammation and ulceration.

81 B

Anal carcinoma, typically a squamous cell carcinoma, arises near the squamocolumnar junction. The adult population is most commonly affected (average age of presentation is 60 years). Right-sided colon cancer commonly presents with anaemia and weight loss, whereas transverse and left-sided colon cancer presents with change in bowel habit, blood mixed with stool, and weight loss. Risk factors for this condition include human papillomavirus, smoking, immunosuppression, benign anal lesions (inflammatory bowel disease, haemorrhoids, fistulae) and sexual activity (multiple sexual partners and anal intercourse).

24. Dysphagia

B&L **For further reading, see *Bailey and Love*, Chapter 59, 'The oesophagus'.**

82 B

Oesophageal cancer can be divided into various subtypes based on anatomical location. In general, a cancer in the upper two-thirds is a squamous cell carcinoma and one in the lower third is an adenocarcinoma. In cases of squamous cell carcinoma, which are similar to head and neck cancers, there is an association with tobacco and alcohol excess. Cases of adenocarcinoma are often associated with gastro-oesophageal reflux disease and Barrett's oesophagus. Patients present with dysphasia, odynophagia and weight loss. Initially, patients have difficulty with swallowing hard and bulky substances, but will progress to having difficulty with soft foods and liquids.

83 A

Achalasia is an oesophageal motility disorder involving the smooth muscle layer of the oesophagus and the lower oesophageal sphincter. The oesophageal sphincter fails to relax owing to a defect of the parasympathetic Auerbach's myenteric plexus. Patients present with difficulty swallowing fluids and solids. The patient will eat slowly and may employ the Valsalva manoeuvre to force food boluses from the oesophagus into the stomach. Regurgitation may lead to aspiration pneumonia.

84 C

Pharyngeal pouches occur most commonly in patients aged over 70 years. Typical symptoms include dysphagia, regurgitation, chronic cough, aspiration and weight loss. The aetiology remains unknown, but many theories centre upon a structural or physiological abnormality of the oesophageal muscles. The pharyngeal pouch is thought to be due to a mucosal out-pouching between the two parts of the inferior constrictor: thyropharyngeus above and cricopharyngeus below. The potential gap is called Killian's dehiscence. Food is propelled from the pharynx to the oesophagus by a series of sequential contractions of the superior, middle and thyropharyngeus constrictors. Then the cricopharyngeus, which as a sphincter, relaxes to allow food to enter the oesophagus. If it fails to relax, the pressure above will produce a posterior out-pouching through the weak Killian's dehiscence. It cannot expand posteriorly because of the adjacent vertebrae, so it descends down the back of the oesophagus to present as a lump in the posterior triangle of the neck. This is usually on the left as the oesophagus lies in the left side of the vertebral bodies. The diagnosis is confirmed on barium studies.

25. Testicular conditions

B&L **For further reading, see *Bailey and Love*, Chapter 75, 'Testis and scrotum'.**

85 B

Teratomas are germ cell tumours commonly composed of multiple cell types derived from one or more of three germ layers. They belong to a class known as non-seminomatous germ cell tumours (NSGCTs). All of this class are the result of abnormal development of pluripotent cells: germ cells and embryonic cells. Histologically, teratomas have contained hair, teeth and bone. The age of onset is 20–30 years. Formal investigations include blood tests (α-fetoprotein and β-hCG) and radiological imaging (ultrasound and CT scan of abdomen and pelvis). Surgical treatment is the mainstay, but teratomas are also chemosensitive.

86 D

A cyst of the hydatid of Morgagni is also known as an 'appendix testis'. It is a remnant of the Mullerian duct and located at the top of the testis. It is comparable to the fimbriated end of the fallopian tube in females. It may become twisted upon itself, causing a painful lump, which remains in a similar anatomical position. In cases of testicular torsion, the testicle will reside in a higher position and may be rotated.

26. Jaundice

B&L **For further reading, see *Bailey and Love*, Chapter 61, 'The liver'.**

87 I

Primary sclerosing cholangitis (PSC) is a chronic liver disease caused by progressive inflammation and scarring of the bile ducts of the liver. The inflammation impedes the flow of bile to the gut, which can ultimately lead to liver cirrhosis, liver failure and liver cancer. The underlying cause of the inflammation is believed to be autoimmunity. Patients present with fatigue, lethargy, jaundice, malabsorption, steatorrhoea, cirrhosis and dark urine. There is an association of PSC with ulcerative colitis: as many as 5 per cent of patients with ulcerative colitis may progress to develop primary sclerosing cholangitis, and about 70 per cent of people with primary sclerosing cholangitis have ulcerative colitis. The following blood studies may suggest the diagnosis of primary sclerosing cholangitis:

- elevated alkaline phosphatase or γ-glutamyltransferase (GGT)
- elevated serum transaminase level (but may be normal)
- elevated serum bilirubin level (in advanced stages)
- serum albumin and prothrombin time abnormal (with advanced disease)

- immunoglobulin IgG and IgM levels elevated in 48 and 80 per cent of cases, respectively
- the presence of perinuclear antineutrophil cytoplasmic autoantibodies (p-ANCAs) in 60–82 per cent of patients.

Radiological imaging can aid diagnosis: endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP).

88 A
Gilberts' syndrome is a common hereditary cause of increased unconjugated bilirubin in the bloodstream. Mild jaundice may appear with exertion, stress, fasting and infections (but there may be no symptoms). It has an autosomal dominant pattern of inheritance.

89 C
Acute alcoholic hepatitis is an acute inflammation of the liver secondary to alcohol excess. Symptoms include jaundice, hepatomegaly, ascites, fatigue and hepatic encephalopathy. Peripheral stigmata of cirrhosis also include spider naevi, scleral icterus, palmar erythema, gynaecomastia and asterixis. The diagnosis is made by taking a full medical history, physical examination, ultrasound, and bloods tests (abnormal liver and clotting function tests: aspartate aminotransferase (AST) and alanine aminotransferase (ALT), prothrombin time (PT)).

90 G
Hepatic metastases is a malignant neoplasm that has spread to the liver from a primary site. Colon cancer can spread to other organs in the body including the lungs and liver (stage III disease). Between 20 and 25 per cent of patients with colorectal cancer have liver metastases at the time of their diagnosis. Patients present with jaundice, anorexia, nausea, fevers, pain in the upper right part of the abdomen, and weight loss. Blood tests demonstrate elevated plasma alkaline phosphatase and carcinoembryonic antigen. An ultrasound and CT scan of the abdomen will confirm the diagnosis.

27. Haematuria

B&L **For further reading, see *Bailey and Love*, Chapter 71, 'The kidneys and ureter' and Chapter 72, 'The urinary bladder'.**

91 C
Renal cell carcinoma is also known as hypernephroma, Grawitz tumour or clear cell carcinoma. The classical triad of presentation occurs in 10–15 per cent of patients: haematuria, flank pain and a loin mass. Patients can also present with malaise, weight loss, anorexia, polycythaemia (secondary to excess erythropoietin production), anaemia (secondary to depression of erythropoietin), varicocele (secondary to obstruction of the testicular vein), hypertension (secondary to renin secretion by the tumour), hypercalcaemia (secondary to ectopic parathormone production by the tumour), cannonball metastases (which may disappear after nephrectomy), pyrexia of unknown origin and nephritic syndrome.

92 E
March haemaglobinuria occurs when blood (haemoglobin from red cells) is seen in the urine after strenuous exercise. The repetitive nature of severe exercise caused by mechanical trauma may result in haemolysis. Free haemoglobin released from lysed red blood cells is filtered into the urine. Defects in red blood cell membrane have been identified in selected patients.

93 A
Transitional cell carcinoma of the bladder is the most common cause of painless haematuria. Transitional epithelium lines the entire urinary tact, so these tumours may arise from the renal pelvis to the end of the urethra in females and to the end of the prostatic urethra in males.

Patients commonly present with haematuria, dysuria, polyuria and nocturia. If left untreated, local invasion of the bladder neck may lead to incontinence. Obstructive hydronephrosis and clot retention are also recognized complications. There are recognized *risk factors*:

- *Cigarette smoking*. Smoking increases the risk of developing bladder cancer nearly 5-fold. As many as 50 per cent of all bladder cancers in men and 30 per cent in women are linked to cigarette smoke.
- *Chemical exposure at work*. About one in four cases of bladder cancer are caused by exposure to carcinogens. Dye workers, rubber workers, aluminium workers, leather workers, truck drivers and pesticide applicators are at the highest risk. Arylamines are the chemicals most responsible.
- *Radiation and chemotherapy*. Women who received radiation therapy for the treatment of cervical cancer have an increased risk of developing transitional cell bladder cancer. Some patients who have received chemotherapy with cyclophosphamide (Cytoxan) are also at an increased risk.
- *Parasite infection*. In developing countries, infection with schistosomiasis has been linked to bladder cancer.

28. Prostate cancer

B&L **For further reading, see *Bailey and Love*, Chapter 73, 'The prostate and seminal vesicles'.**

94 E

Staging is one of the most important factors in determining the best way to treat prostate cancer. This patient has stage T4 disease. The cancer has spread to the bladder, rectum, lymph nodes, or distant organs (bone). This cancer is not curable, but treatment is directed at improving the patient's quality of life. Treatment options may include:

- hormone therapy
- external-beam radiation (in selected cases: radiotherapy for pain from bone metastases)
- surgery (TURP) to relieve symptoms such as bleeding or urinary obstruction
- watchful waiting – for older men whose cancer causes no symptoms or for those who have another serious illness.

95 A

This patient has stage T1 disease (intracapsular tumour surrounded by a normal prostate). This patient is well. Surgery coupled with radiotherapy offers the best chance for a cure. Treatment options include the following.

- For elderly men without any symptoms and/or having other serious health problems, watchful waiting and radiation therapy (external beam or brachytherapy) are reasonable options.
- Men who are younger and healthy may consider watchful waiting, surgery to remove the prostate (radical prostatectomy), or radiation therapy (external-beam or brachytherapy).

96 D

This patient has stage T4 disease. The cancer has spread to the bladder, rectum, lymph nodes, or distant organs (bone). This cancer is not curable, but treatment is directed at improving the patient's quality of life. The patient is suffering from lumbar back pain, which is not responding to medical treatment. Treatment options include:

- hormone therapy
- external-beam radiation (in selected cases: radiotherapy for pain from bone metastases)
- surgery (TURP) to relieve symptoms such as bleeding or urinary obstruction
- watchful waiting for older men whose cancer is causing no symptoms or for those who have other serious illness.

29. Wound infections

B&L **For further reading, see *Bailey and Love*, Chapter 3, 'Wounds, tissue repair and scars'.**

See Table 15.

97 D
This patient has a dirty wound. Examples are wounds made in the presence of pus, a perforated viscus or traumatic wounds. The infection rate is 40 per cent.

98 C
This patient has a contaminated wound. Examples are incisions contaminated by opening the colon, open fractures or animal bites. The infection rate is 20 per cent.

99 A
This patient has a clean wound. Examples are incisions through uninfected skin that do not breach any hollow viscus (inguinal hernia repair). The infection rate is 2 per cent.

100 B
This patient has a clean contaminated wound. Examples are incisions that breach a hollow viscus other than the colon (open cholecystectomy). The infection rate is below 10 per cent.

Table 15 Classification of wounds

Classification	Description	Infective risk (%)
Clean (class I)	Uninfected operative wound No acute inflammation Closed primarily Respiratory, gastrointestinal, biliary and urinary tracts not entered No break in aseptic technique Closed drainage used if necessary	< 2
Clean contaminated (class II)	Elective entry into respiratory, biliary, gastrointestinal, urinary tracts and with minimal spillage No evidence of infection or major break in aseptic technique Example: appendectomy	< 10
Contaminated (class III)	Non-purulent inflammation present Gross spillage from gastrointestinal tract Penetrating traumatic wounds <4 hours Major break in aseptic technique	About 20
Dirty (class IV)	Purulent inflammation present Preoperative perforation of viscera Penetrating traumatic wounds >4 hours	About 40

30. Endocrine

B&L **For further reading, see *Bailey and Love*, Chapter 49, 'Adrenal glands and other endocrine disorders'.**

101 J
The diagnosis is primary hyperparathyroidism. This patient has symptomatic hypercalcaemia with polyuria and polydipsia. The high calcium fails to suppress PTH secretion, making a parathyroid adenoma most likely. This is an important point – a normal PTH in this instance is *abnormal*, since in normal individuals a high calcium would suppress PTH secretion and one should expect in such

instances a *low* PTH. The low phosphate fits with primary hyperparathyroidism since PTH has a phosphaturic effect at the level of the renal tubules.

Other symptoms of hypercalcaemia may be remembered by 'bones, stones, abdominal moans and psychotic groans' (i.e. bony pains, renal stones, constipation, abdominal pains and psychiatric disturbances).

Management consists of control of calcium with fluids, furosemide and bisphosphonates. An ultrasound and/or Sestamibi scan may be used to localize the parathyroid adenoma. Definitive treatment is surgical: neck exploration and parathyroidectomy.

102 L

The diagnosis is secondary hyperparathyroidism. This patient demonstrates symptomatic hypocalcaemia with acroparasthesia (pins and needles in the peripheries) and an elevated PTH. Chvostek's sign (gentle tapping over the facial nerve causing twitching of the facial muscles) and Trousseau's sign (carpopedal spasm) would be expected to be positive.

Secondary hyperparathyroidism is physiological compensatory hypertrophy of all parathyroid glands because of hypocalcaemia, such as occurs in renal failure or vitamin D deficiency. PTH levels are raised due to loss of the inhibitory feedback effect of calcium on the parathyroid glands. PTH levels fall to normal on correction of the cause of hypocalcaemia where this is possible.

103 A

This patient has Addison's disease (primary hypoadrenalism), as manifested by hypotension, hypoglycaemia, hyponatraemia and hyperkalaemia, as a result of mineralocorticoid and glucocorticoid deficiency. Diagnosis is confirmed by a short synACTHen (synthetic ACTH) test, whereby the endocrine response of the adrenal gland (cortisol production) is measured in response to a given bolus of synthetic ACTH. An absent or impaired cortisol response in seen in Addison's disease.

31. Rheumatology

B&L **For further reading, see *Bailey and Love*, Chapter 37, 'Inflammation and infection and musculoskeletal tumours'.**

104 F

Crystal-related arthropathy defines a syndrome of synovitis in response to crystal deposition/formation in the joint. There are two main forms: gout and pseudogout. Gout is the more common entity. The main distinguishing features are given in Table 16.

Table 16 Gout and pseudogout

Gout	Pseudogout
Affects smaller joints	Affects large joints
Pain intense	Pain moderate
Joint inflamed	Joint swollen
Hyperuricaemia	Chondrocalcinosis
Uric acid (monosodium urate) crystals: • Needle-like • 5–20 μm long • Exhibit strongly negative birefringence under plane polarized light • Often associated with increased polymorphs	Calcium pyrophosphate crystals: • Rhomboid • Slightly smaller than urate crystals (<10 μm) • Show positive birefringence under plane polarized light
Treatment is analgesia and prophylaxis	Treatment is analgesia; no prophylaxis available

105 K

The diagnosis is septic arthritis until proven otherwise. The organism responsible in this particular instance is *Neisseria gonorrhoeae* (gonococcal arthritis), although the most common organism implicated in septic arthritis over all age groups is *Staphyloccoccus aureus*. Gonococcal arthritis may cause a septic arthritis (as illustrated here with the presence of organisms within joint aspirate), or a reactive arthritis with sterile joint fluid. The treatment consists of oral penicillin, ciprofloxacin or doxycycline for 2 weeks, and joint rest.

32. Hepatology

B&L **For further reading, see *Bailey and Love*, Chapter 61, 'The liver'.**

106 G

The diagnosis is Gilbert's syndrome, which affects some 2–3 per cent of the population. The clinical features are mild, fluctuant unconjugated hyperbilirubinaemia.

The jaundice is typically mild and presents only intermittently, often noticed after an infection or a period of fasting. This is possibly because fasting increases plasma concentrations of free fatty acids which compete with bilirubin for transport by albumin and uptake into liver cells. Bilirubin rarely exceeds 100 μmol/L. There may be mild malaise and hepatic tenderness, but there are no other abnormal physical signs. The liver is histologically normal and individuals have a normal lifespan.

The hyperbilirubinaemia is due to a defect in the regulatory part of the gene coding for bilirubin UDP-glucuronyl transferase; in some cases there is also decreased hepatic uptake of bilirubin. In cases where there is a family history, the pattern of inheritance is autosomal dominant.

107 L

The symptoms, signs and liver function tests are consistent with a mixed cholestatic/obstructive and hepatocellular picture. A high titre of antimitochondrial antibodies is characteristic of primary biliary cirrhosis, which is an autoimmune condition that typically affects middle-aged women.

Antimitochondrial antibodies are found in the serum of over 95 per cent of patients with primary biliary cirrhosis, and of the mitochondrial proteins involved, the antigen M2 is specific to the condition. Diagnosis can be confirmed by liver biopsy.

The course and prognosis is very variable, although the median survival is only 7–10 years. Once jaundice develops, survival is below 2 years. Liver transplantation should therefore be offered when the serum bilirubin reaches 100 μmol/L. Post-transplantation 5-year survival is above 75 per cent.

108 H

The history and liver function tests are characteristic of acute hepatitis, with a predominantly raised ALT reflecting hepatocellular damage ('transaminitis'). The travel history and the timing of the events make viral hepatitis A the most likely cause in this particular case.

Serum transaminases rise 22–40 days after exposure, IgM rises from day 25 and signifies recent infection; IgG remains detectable for life. Infection with hepatitis A virus never progresses to chronic liver disease and only rarely causes fulminant hepatitis, so the mortality rate associated with hepatitis A infection is about 0.1 per cent.

33. Abdominal trauma

B&L **For further reading, see *Bailey and Love*, Chapter 26, 'Chest and abdomen'.**

109 A

Gunshot wounds are a clear indication for laparotomy even if the patient is not clinically shocked. The trajectory and projectile of a bullet is unpredictable and the damage is difficult to assess from inspection.

110 B
The patient is stable enough to undergo DPL, but not to be transferred to the radiology department for a CT scan ('doughnut of death').

111 C
This patient appears stable and if his peritoneum is intact he may be a suitable candidate for conservative management (routine observations).

34. Lumps

B&L **For further reading, see *Bailey and Love*, Chapter 45, 'Pharynx, larynx and neck', Chapter 25, 'Trauma to the face and mouth', Chapter 36, 'Foot and ankle', Chapter 27, 'Extremity trauma' and Chapter 37, 'Inflammation and infection and musculoskeletal disorders'.**

112 F
A dermoid cyst is a subcutaneous lump that develops mostly in the midline along the lines of fusion in the face and neck. It is a result of the inclusion of epidermal cells deep to the skin, which can be congenital or secondary to trauma.

113 D
This is also known as a dermatofibroma. They often occur on the lower limbs and like implantation dermoid cysts, often follow trauma. They are skin-coloured in appearance and woody-hard in consistency.

114 G
This is an ivory osteoma, a benign swelling which results from an osteoma (benign bone tumour) of the outer table of the skull.

35. Intestinal polyps

B&L **For further reading, see *Bailey and Love*, Chapter 65, 'The small and large intestines', Chapter 68, 'The rectum' and Chapter 69, 'The anus and anal canal'.**

115 G
This operation involves excision of the entire colon and rectum, with an ileo-anal anastomosis. It is a complex operation but aims to preserve continence.

116 H
These polyps do not have a malignant potential and can be left alone.

117 C
It is not possible to establish adequate clearance distally and preserve the anal sphincter. The whole of the colon is required to be excised to avoid potential future malignancy.

36. Cancer staging

B&L **For further reading, see *Bailey and Love*, Chapter 68, 'The rectum'.**

118 F

119 I
Clarke's levels are defined as:

- I – confined to the epidermis
- II – extends to the papillary dermis
- III – extends to the papillary-reticular junction

- IV – extends to the reticular dermis
- V – invades the subcutaneous tissue.

120 B

121 D

- Dukes' A – limited to the colonic wall
- Dukes' B – extends through the muscularis propria (muscle layer of wall)
- Dukes' C – mesenteric lymph node involvement
- Dukes' D – spread beyond regional lymph nodes, or involvement of adjacent structures.

37. Anaemia

B&L **For further reading, see *Bailey and Love*, Chapter 13, 'Perioperative care'.**

122 G
Glucose-6-phosphate dehydrogenase deficiency is a hereditary condition in which red blood cells break down, or haemolyse, when the body is exposed to certain drugs, stress, or infection. Risk factors include aspirin, antimalarials, non-steroidal anti-inflammatory drugs; and it is more common in patients of African American, or Middle Eastern descent, with a male predominance.

123 B
This condition is inherited in an autosomal dominant pattern, mostly seen in northern Europeans. The defect in the cell membrane leads to premature cell destruction.

124 D
The diagnosis is sickle cell crisis. The definitive diagnosis is made through haemoglobin electrophoresis.

38. Complications of blood transfusions

B&L **For further reading, see *Bailey and Love*, Chapter 2, 'Shock and blood transfusion'.**

125 F
The risk is highest in blood maintained in suboptimal conditions where the blood is not stored properly prior to transfusion.

126 B
This occurs secondary to a leucocyte antigen and may be treated with anti-pyretics and antihistamines.

127 G
The patient is usually immunized to the antigen at previous transfusion, but the concentration of the antibodies are too low to produce an immediate reaction. Production of a further IgG usually one week later leads to delayed haemolysis.

39. Fractures

B&L **For further reading, see *Bailey and Love*, Chapter 27, 'Extremity trauma'.**

128 C
This is also known as a 'march' fracture.

129 G
This is an incomplete, or 'greenstick', fracture because it involves one of the cortices.

130 D
The patient has Paget's disease as evidenced by thickening of the bone and a bowed tibia. It is associated with an isolated elevated alkaline phosphatase, in the presence of normal calcium, phosphate and aminotransferases. A bone scan is useful for determining the activity and extent of this condition.

40. Acid–base balance

B&L **For further reading, see *Bailey and Love*, Chapter 13, 'Perioperative care'.**

131 F
The pH reveals acidosis which must be respiratory in origin in view of the elevated carbon dioxide. The elevated bicarbonate indicates a metabolic alkalosis in an attempt to correct the abnormality. This scenario occurs in chronic respiratory disease.

132 A
Respiratory compensation occurs within minutes. The carbon dioxide rises in an attempt to compensate for a metabolic alkalosis, as in pyloric stenosis.

133 D
This is an uncompensatory respiratory acidosis as the bicarbonate is within normal limits. This occurs in acute ventilatory compromise, as in a flail chest.

41. Informed consent

B&L **For further reading, see *Bailey and Love*, Chapter 9, 'Surgical ethics'.**

134 C
An adolescent has the right to accept surgery, but those under 18 cannot refuse life-saving surgery and the parents can consent for this procedure.

135 D
The surgeon has a legal and moral duty to treat the patient in an emergency under these circumstances.

136 A
Even those 'under section' to receive psychiatric treatment cannot be forced to have a surgical procedure for a physical condition if they are deemed to be competent.

42. Neck anatomy

B&L **For further reading, see *Bailey and Love*, Chapter 45, 'Pharynx, larynx and neck'.**

137 D
Acral parasthesia is a common manifestation of hypocalcaemia secondary to damage to the parathyroid glands.

138 F
Injury to the external laryngeal nerve, which supplies the important cricothyroid muscle (that controls voice pitch), produces this deficit.

139 B
These are the manifestations of Horner's syndrome.

43. Innervation of lower limb muscles

140 F
The deep peroneal nerve is also known as the anterior tibial nerve. It supplies the muscles of the anterior compartment of the leg, extensor hallucis longus, extensor digitorum longus, extensor digitorum brevis, peroneus tertius and, most importantly, tibialis anterior.

141 C
Quadratorus femoris is composed of three vastus muscles and rectus femoris. The femoral nerve also innervates iliacus, pectineus and sartorius.

142 A
The obturator nerve supplies the muscles of the medial compartment of the thigh.

44. Brachial plexus injuries

B&L **For further reading, see *Bailey and Love*, Chapter 24, 'Neck and spine' and Chapter 33, 'The spine'.**

143 B
This is an Erb's palsy, caused by injury to the upper trunk of the brachial plexus (C5–6). The hand takes on the 'waiter's-tip' position.

144 E
This is Dejerine–Klumpke palsy, caused by injury to the lower roots of the brachial plexus (C8, T1). It gives the typical appearance of a 'claw-hand'.

145 G
The patient has lost all innervation to his right upper limb.

45 Herniae

B&L **For further reading, see *Bailey and Love*, Chapter 57, 'Hernias, umbilicus and abdominal wall'.**

146 C
Obturator hernias protrude through the obturator foramen which is bounded by the superior pubic ramus, anterior acetabular wall and ischio-pubic ramus. Irritating the obturator nerve can lead to referred knee pain, or parasthesia in the inner thigh.

147 F
Umbilical hernias in the adult population are rare. They are secondary to increased intra-abdominal pressure. A para-umbilical hernia is seen more commonly.

148 D
Femoral hernias pass through the femoral canal which is below and lateral to the pubic tubercle. The femoral canal is medial to the femoral vein and contains fat and lymphatics ('Cloquet's lymph node').

46 Tumour markers

B&L **For further reading, see *Bailey and Love*, Chapter 76, 'Gynaecology', Chapter 61, 'The liver' and Chapter 68, 'The rectum'.**

149 A
CA-125 is used for the diagnosis, response to treatment and follow-up for recurrence in ovarian tumours.

150 F
Alpha-fetoprotein is often raised in hepatocellular carcinoma. It is the most widely used tumour marker for the condition and is an independent prognostic indicator.

151 D
CEA (carcino-embryonic antigen) is the tumour marker of choice for patients with colorectal cancer.

47 Adrenal pathology

B&L **For further reading, see *Bailey and Love*, Chapter 49, 'Adrenal glands and other endocrine disorders'.**

152 E
MEN 1:

- parathyroid gland adenomas
- pancreatic islet cell tumours
- pituitary gland adenomas.

MEN 1 patients can have duodenal ulcers secondary to:

- Hypercalcaemia secondary to hyperparathyroidism
- Excess steroid production from Cushing's disease
- Zollinger–Ellison syndrome (gastrinoma)

153 A
An ACTH-secreting lung tumour produces adrenal cortical hyperplasia and Cushing's syndrome. This is separate from Cushing's disease which is produced from hypersecretion of ACTH from the anterior pituitary gland.

154 D
Addison's disease is adrenocortical insufficiency. Sixty per cent are autoimmune in aetiology (pernicious anaemia and Hashimoto's thyroiditis). Other causes include TB, lung metastases and amyloidosis.

48. Chest pain

B&L **For further reading, see *Bailey and Love*, Chapter 50, 'The breast' and Chapter 51, 'Cardiac surgery'.**

155 E
Tietze's syndrome, or costochondritis, presents with pain and swelling over the sternocostal junction. It is usually evident on palpation and perceived pain is exacerbated with respiration.

156 F
The condition should be suspected in the absence of cardiac pathology. Oesophageal manometry is used to make the diagnosis.

157 C
The symptoms of a pulmonary embolus include sudden-onset dyspnoea, tachypnoea, pleuritic chest pain, cough and haemoptysis. On clinical examination, a pleural friction rub may be auscultated. Risk factors are attributed to Virchow's triad. Her risk factors include recent pregnancy which changes blood flow dynamics and increases the risk of a pulmonary embolus developing.

49. Metabolic abnormalities

158 A
Both loop diuretics and corticosteroids cause hypokalaemia.

159 E
Hypophosphataemia occurs during acute alcohol withdrawal. It is also a risk when giving carbohydrates after fasting ('refeeding syndrome').

160 B
Burns cause the release of myoglobin secondary to rhabdomyolysis. This blocks the renal tubules, resulting in acute renal failure and consequently hyperkalaemia.

50. Lung volumes

B&L **For further reading, see *Bailey and Love*, Chapter 52, 'The thorax'.**

See Figure 6.

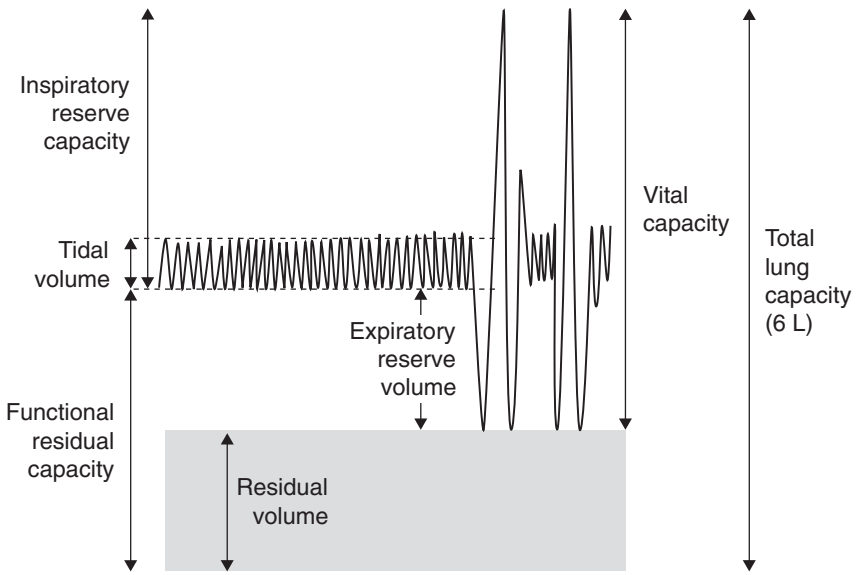

Figure 6 Lung spirometry.

161 C
■ Functional residual capacity.

162 F
■ Residual volume.

163 B
■ Tidal volume.

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