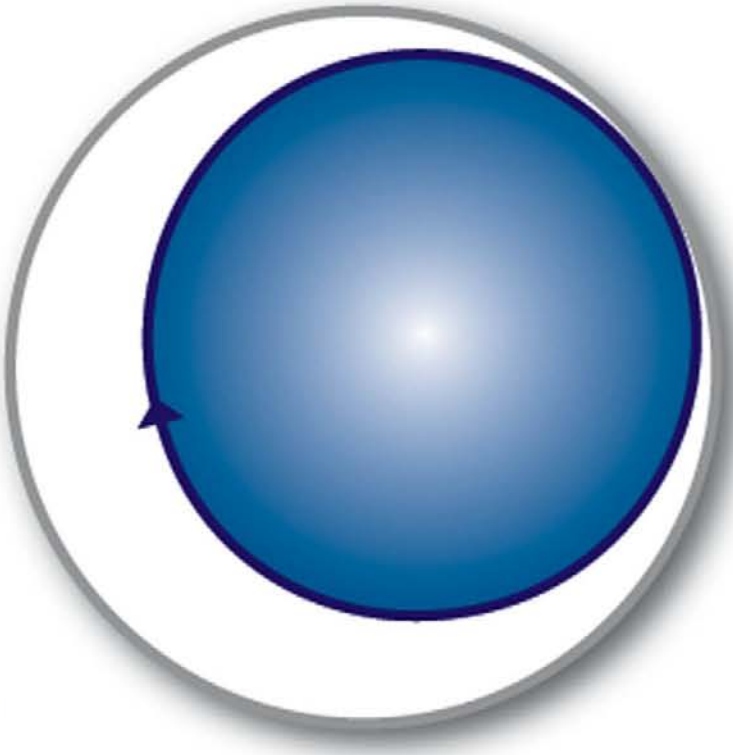

Core Clinical Cases

Medicine and Medical Specialties

Second edition

Steve Bain and Jeffrey Stephens
Series editor: Janesh K Gupta

Core Clinical Cases in Medicine and Medical Specialties

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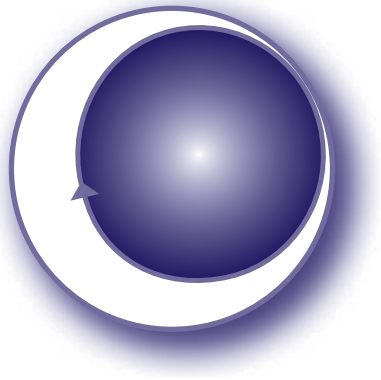

Core Clinical Cases in Medicine and Medical Specialties

Second edition

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Series preface

‘A history lesson’

Between about 1916 and 1927 a puzzling illness appeared and swept around the world. Dr von Economo first described encephalitis lethargica (EL), which simply meant ‘inflammation of the brain that makes you tired’. Younger people, especially women, seemed to be more vulnerable, but the disease affected people of all ages. People with EL developed a ‘sleep disorder’, fever, headache and weakness, which led to a prolonged state of unconsciousness. The EL epidemic occurred during the same period as the 1918 influenza pandemic, and the two outbreaks have been linked ever since in the medical literature. Some people confused it with the epidemic of Spanish flu at that time, while others blamed weapons used in the First World War.

Encephalitis lethargica was dramatized by the film *Awakenings*, based on the book written by Oliver Sacks, an eminent neurologist from New York, and starring Robin Williams and Robert De Niro. Professor Sacks treated his patients with l-dopa, which temporarily awoke his patients, giving rise to the belief that the condition was related to Parkinson’s disease.

Since the 1916–1927 epidemic, only sporadic cases of EL have been described. Pathological studies have revealed an encephalitis of the midbrain and basal ganglia, with lymphocyte (predominantly plasma cell) infiltration. Recent examination of archived EL brain material has failed to demonstrate influenza RNA, adding to the evidence that EL was not an invasive influenza encephalitis. Further investigations found no evidence of viral encephalitis or other recognized causes of rapid-onset parkinsonism. Magnetic resonance imaging of the brain was normal in 60 per cent but showed inflammatory changes localized to the deep grey matter in 40 per cent.

As late as the end of the twentieth century, it seemed that the possible answers lay in the clinical presentation of the patients in the 1916–1927 epidemic. It had been noted by the clinicians at that time that the central nervous system (CNS) disorder had presented with pharyngitis. This led to the possibility of a post-infectious autoimmune CNS disorder similar to Sydenham’s chorea, in which group A beta-haemolytic streptococcal antibodies cross-react with the basal ganglia and result in abnormal behaviour and involuntary movements. Anti-streptolysin-O titres have subsequently been found to be elevated in the majority of these patients. It seemed possible that autoimmune antibodies may cause remitting parkinsonian signs subsequent to streptococcal tonsillitis as part of the spectrum of post-streptococcal CNS disease.

Could it be that the 80-year-old mystery of EL has been solved by relying on the patient’s clinical history of presentation rather than focusing on expensive investigations? More research in this area will give us the definitive answer. This scenario is not dissimilar to the controversy about the idea that streptococcal infections were aetiologically related to rheumatic fever.

With this example of a truly fascinating history lesson, we hope you will endeavour to use the patient’s clinical history as your most powerful diagnostic tool to make the correct diagnosis. If you do, you are likely to be right 80–90 per cent of the time. This is the basis of the Core Clinical Cases series, which will make you systematically explore clinical problems through the clinical history of presentation, followed by examination and then the performance of appropriate investigations. Never break those rules!

Janesh Gupta

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Abbreviations

AAFB	acid- and alcohol-fast bacilli
ABGs	arterial blood gases
ACE	angiotensin-converting enzyme
ACh	acetylcholine
ACTH	adrenocorticotrophic hormone
A&E	accident and emergency
AED	anti-epileptic drug
AF	atrial fibrillation
AIDP	acute inflammatory demyelinating polyneuropathy
AIDS	acquired immunodeficiency syndrome
AKI	acute kidney injury
ALP	alkaline phosphatase
ALS	advanced life support
ANA	antinuclear antibody
ANCA	anti-neutrophil cytoplasmic antigen
ARDS	adult respiratory distress syndrome
ARF	acute renal failure
5-ASA	5-acetylsalicylic acid
AST	aspartate aminotransferase
ATN	acute tubular necrosis
AV	atrioventricular
BCC	basal cell carcinoma
BMI	body mass index
cANCA	cytoplasmic anti-neutrophil cytoplasmic antigen
CEA	carcinoembryonic antigen
CFA	cryptogenic fibrosing alveolitis
CIDP	chronic inflammatory demyelinating polyneuropathy
CKD	chronic kidney disease
CMV	cytomegalovirus
CNS	central nervous system
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease

CPAP continuous positive airway pressure
CPK creatine phosphokinase
CPR cardiopulmonary resuscitation
CRH corticotrophin-releasing hormone
CRP C-reactive protein
CSF cerebrospinal fluid
CT computed tomography
CTPA computed tomography pulmonary angiogram
CVP central venous pressure
CVVH continuous veno-venous haemofiltration
DC direct current
DEXA dual-energy X-ray absorptiometry
DIC disseminated intravascular coagulation
DKA diabetic ketoacidosis
DMARD disease-modifying anti-rheumatoid drug
DOT directly observed therapy
dsDNA double-stranded DNA
DVLA Driver and Vehicle Licensing Agency
DVT deep vein thrombosis
EAA extrinsic allergic alveolitis
ECG electrocardiogram
eGFR estimated glomerular filtration rate
EGFR epidermal growth factor receptor
EL encephalitis lethargica
ENA extractable nuclear antigen
ENT ear, nose and throat
ERCP endoscopic retrograde cholangiopancreatography
ESR erythrocyte sedimentation rate
ESRF end-stage renal failure
FBC full blood count
FEV_1 forced expiratory volume in 1 s
FSGS focal segmental glomerulosclerosis
FSH follicle-stimulating hormone
FT4 free thyroxine
5FU 5-fluorouracil

FVC forced vital capacity
GAD glutamate decarboxylase
GBM glomerular basement membrane
GCS Glasgow coma score
G-CSF granulocyte colony-stimulating factor
GH growth hormone
GI gastrointestinal
GLP-1 glucagon-like peptide 1
GP general practitioner
GTN glyceryl trinitrate
Hb haemoglobin
HbA1c glycated haemoglobin
HBGM home blood glucose monitoring
HbS haemoglobin S
HIV human immunodeficiency virus
HLA human leucocyte antigen
HONK hyperosmolar non-ketotic pre-coma or coma
HPLC high-performance liquid chromatography
HRT hormone replacement therapy
IBD inflammatory bowel disease
IBS irritable bowel syndrome
ICD implantable cardioverter defibrillation
IFG impaired fasting glycaemia
IgA immunoglobulin A
IgE immunoglobulin E
IGF-I insulin-like growth factor I
IGT impaired glucose tolerance
IHD ischaemic heart disease
IUCD intrauterine contraceptive device
IV intravenous
IVIG intravenous immunoglobulin
JVP jugular venous pressure
LDH lactate dehydrogenase
LDL low-density lipoprotein
LEMS Lambert–Eaton myasthenic syndrome

LFTs	liver function tests
LGV	large goods vehicle
LH	luteinizing hormone
LHRH	luteinizing hormone-releasing hormone
LMW	low molecular weight
LV	left ventricular
LVEF	left ventricular ejection fraction
MAOI-B	monoamine oxidase type B
MCH	mean cell haemoglobin
MCV	mean cell volume
MEN-1	multiple endocrine neoplasia type 1
MI	myocardial infarction
MMSE	Mini-Mental State Examination
MND	motor neuron disease
MRA	magnetic resonance angiography
MRCP	magnetic resonance cholangiopancreatography
MRI	magnetic resonance imaging
MRSA	methicillin-resistant *Staphylococcus aureus*
MS	multiple sclerosis
MSH	melanocyte-stimulating hormone
MSU	midstream urine specimen
NASH	non-alcoholic steatohepatitis
NICE	National Institute of Health and Clinical Excellence
NSAID	non-steroidal anti-inflammatory drug
NYHA	New York Heart Association
OGTT	oral glucose tolerance test
pANCA	perinuclear anti-neutrophil cytoplasmic antigen
PaO_2	partial pressure of oxygen in arterial blood
PCI	percutaneous coronary angioplasty
PCV	passenger-carrying vehicle
PE	pulmonary embolism
PEF	peak expiratory flow
PPI	proton pump inhibitor
PRV	polycythaemia rubra vera
PSA	prostate-specific antigen

PT	prothrombin time
PTE	pulmonary thromboembolism
PTH	parathyroid hormone
PUVA	psoralen and ultraviolet A
QCT	qualitative computed tomography
RAS	renal arterial stenosis
RAST	radioallergosorbent
RF	rheumatoid factor
RRT	renal replacement therapy
rTPA	recombinant tissue plasminogen activator
RV	right ventricular
RVH	right ventricular hypertrophy
SCC	squamous cell carcinoma
SIADH	syndrome of inappropriate antidiuretic hormone secretion
SIRS	systemic inflammatory response syndrome
SLE	systemic lupus erythematosus
SUDEP	sudden unexplained death in epilepsy
SVCO	superior vena cava obstruction
SVT	supraventricular tachycardia
TB	tuberculosis
TIA	transient ischaemic attack
TNF	tumour necrosis factor
TSH	thyroid-stimulating hormone
TSS	toxic shock syndrome
TTP	thrombotic thrombocytopenic purpura
U&Es	urea and electrolytes
UKPDS	UK Prospective Diabetes Study
UTI	urinary tract infection
VF	ventricular fibrillation
VT	ventricular tachycardia
VTE	venous thromboembolism
WBC	white blood cell
WCC	white cell count
WHO	World Health Organization

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1 Diabetes

Steve Bain

DIAGNOSIS

GLUCOSE CONTROL FOR PATIENTS WITH DIABETES MELLITUS

DIABETIC SMALL VESSEL COMPLICATIONS

DIAGNOSIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What specific questions would you ask the patient?
Q2: What investigations would you request to confirm a diagnosis?
Q3: What examination would you perform?
Q4: What would be the initial management?
Q5: What are the long-term sequelae?
Q6: What issues need to be addressed apart from blood glucose control?

CASE 1.1 – A 73-year-old man with glycosuria and a finger-prick glucose of 11.4 mmol/L.

A 73-year-old man is found to have glycosuria on urine testing as part of a new patient assessment. A random finger-prick test by the practice nurse using a modern calibrated glucose meter gives a level of 11.4 mmol/L. Arrangements are made for a repeat blood test after an overnight fast; this plasma glucose level is analysed by the local hospital clinical chemistry department and is reported at 6.7 mmol/L.

CASE 1.2 – A 57-year-old woman with lethargy and thrush and a fasting plasma glucose of 8.2 mmol/L.

A 57-year-old woman presents to the surgery with lethargy. She has a long history of recurrent episodes of vaginal irritation, which had been formally diagnosed as candidal thrush on one occasion. Treatment with clotrimazole leads to a short amelioration of symptoms. A fasting plasma glucose level has been reported by the laboratory to be 8.2 mmol/L.

CASE 1.3 – A 21-year-old woman with a random finger-prick glucose of 18.9 mmol/L and urinary ketones.

A 21-year-old woman who has always been fit and well visits you shortly after her honeymoon. She has been profoundly thirsty and noticing blurring of her vision. A finger-prick test in the surgery shows a blood glucose level of 18.9 mmol/L and a fresh urine specimen has both glycosuria and heavy ketones (+++).

OSCE counselling cases

OSCE COUNSELLING CASE 1.1 – **'Will I always have diabetes?'**

A 53-year-old man is diagnosed with type 2 diabetes mellitus. He is treated with diet and subsequently oral agents. A couple of years after diagnosis, he begins to take his diet more seriously and takes up regular exercise. He loses weight and his glucose levels fall to such an extent that he is experiencing frequent hypoglycaemia. He is keen to reduce his medication and wants to know if the diabetes is disappearing.

OSCE COUNSELLING CASE 1.2 – **'Does having diabetes affect my driving licence?'**

A 48-year-old man is admitted to hospital with newly diagnosed diabetes. He is discharged on twice-daily insulin and after 6 weeks has established reasonable diabetic control with no hypoglycaemia. He has previously driven heavy goods vehicles and is keen to return to work. He asks your advice about driving.

Key concepts

To work through the core clinical cases in this chapter, you will need to understand the following key concepts.

DIAGNOSTIC CRITERIA FOR TYPE 2 DIABETES PUBLISHED BY THE WORLD HEALTH ORGANIZATION (WHO) AND RECOMMENDED BY DIABETES UK (2000)

Diagnostic tests should use plasma glucose measurements from a venous sample and performed in an accredited laboratory. Diagnosis should never be made on the basis of glycosuria or stick testing of a finger-prick blood glucose alone (although these may be useful for screening).

If symptoms are present (i.e. polyuria, polydipsia, unexplained weight loss), the diagnosis can be made on the basis of a single:

- random plasma glucose ≥11.1 mmol/L
- fasting plasma glucose ≥7.0 mmol/L.

If symptoms are not present, two abnormal results (as above) on separate days are needed.

A fasting plasma glucose of 6.1–6.9 mmol/L is termed *impaired fasting glycaemia* (IFG) and should be followed up by a formal glucose tolerance test to exclude diabetes.

Impaired glucose tolerance (IGT) is defined by a formal glucose tolerance test as a 2-h plasma glucose of 7.8–11.0 mmol/L. This should lead to assessment of vascular risk factors and yearly screening of fasting plasma glucose.

More recently, the WHO (2011) has updated its criteria to include glycated haemoglobin (HbA1c) testing, a value >6.5% being diagnostic of diabetes in the presence of symptoms (two values are required in asymptomatic patients). Although this has been widely welcomed in the UK, there has not been a formal adoption at the time of printing, largely because of the uncertainty surrounding a lower cut-off for the diagnosis of impaired glucose tolerance (‘pre-diabetes’).

Answers

Clinical cases

CASE 1.1 – A 73-year-old man with glycosuria and a finger-prick glucose of 11.4 mmol/L.

A1: What specific questions would you ask the patient?

The detection of glycosuria has led to two tests to investigate the possibility of diabetes. The random glucose is elevated (≥11.1 mmol/L) but, as a single test, is diagnostic only when it satisfies two criteria: it must be a venous sample (not finger-prick) analysed in an accredited laboratory, and it must be in association with symptoms of hyperglycaemia. The patient should be quizzed about typical symptoms, which will include lethargy, weight changes (gain or loss is possible), polydipsia, polyuria, visual disturbance and infections (e.g. thrush, balanitis, boils). Even in the presence of symptoms, a diagnosis of diabetes would not be made because this has not been confirmed by the fasting plasma glucose, which is <7.0 mmol/L.

A2: What investigations would you request to confirm a diagnosis?

This patient has IFG because his fasting plasma glucose is in the range 6.1–6.9 mmol/L. The guidelines suggest that IFG should be followed up by a formal oral glucose tolerance test (OGTT). This may confirm a diagnosis of: IFG, if the 2-h glucose is <7.8 mmol/L; IGT, if the 2-h level is 7.8–11.0 mmol/L; or diabetes, if the 2-h glucose is ≥11.1 mmol/L.

A3: What examination would you perform?

Given the provisional diagnosis of IFG, there should be no evidence of diabetes-specific small vessel complications (retinopathy, neuropathy, nephropathy); however, large vessel complications are possible and indeed likely. The cardiovascular system should be examined for evidence of large vessel disease (e.g. carotid auscultation, palpation of peripheral pulses).

A4: What would be the initial management?

Assuming that diabetes is not subsequently diagnosed by an OGTT, the patient would receive general health-care advice about diet and exercise. The advice on diet is also appropriate for the treatment of diabetes (i.e. high carbohydrate, high fibre, low saturated fat, low refined carbohydrate), with weight reduction if appropriate. A target body mass index (BMI) of 25 kg/m^2 is generally quoted. Recommended levels of exercise are regular moderate physical activity for sedentary individuals and 30 min on 5 days a week for people who already take some moderate activity. Patients with IGT would be followed annually by means of a fasting plasma glucose level.

A5: What are the long-term sequelae?

Neither IFG nor IGT imparts any risk of specific small vessel complications and glycosuria related to a low renal threshold for glucose is a benign condition. A diagnosis of IGT increases the future risk of type 2 diabetes, however, and is associated with significant cardiovascular risk (in some studies, equivalent to the diagnosis of diabetes itself). It is assumed that IFG carries similar prognoses.

A6: What issues need to be addressed apart from blood glucose control?

Cardiovascular risk factors need to be addressed, specifically smoking, lipid levels, blood pressure, exercise and obesity. Aspirin is not currently considered appropriate in this scenario.

CASE 1.2 – A 57-year-old woman with lethargy and thrush and a fasting plasma glucose of 8.2 mmol/L.

A1: What specific questions would you ask the patient?

In this case, the presence of symptoms (lethargy, recurrent thrush) and the elevated fasting plasma glucose (≥7.0 mmol/L) are sufficient to make the diagnosis of diabetes, which, given her age, is almost certain to be type 2. She should be questioned for other symptoms of hyperglycaemia (polyuria, polydipsia, visual disturbance, weight change) and symptoms relating to small vessel disease (tingling, burning of the feet) and large vessel disease (e.g. angina, claudication). A family history should be elicited along with a drug history to exclude the use of diabetogenic drugs (e.g. steroids, beta-blockers, thiazide diuretics).

A2: What investigations would you request to confirm a diagnosis?

The diagnosis is already confirmed and additional tests are not necessary. Most clinicians would request a measure of long-term glycaemic control (e.g. HbA1c) as a baseline for future comparison.

A3: What examination would you perform?

The UK Prospective Diabetes Study (UKPDS) showed that 40 per cent of patients with type 2 diabetes have evidence of complications at diagnosis; examination should, therefore, focus on small and large vessel diabetic complications. For small vessel complications, this would involve examination of the ocular fundi through dilated pupils (or arrangement for this to be performed via a formal screening programme), and examination of the feet for evidence of peripheral neuropathy, in addition to their general condition and the presence of pulses. There should also be a thorough examination of the cardiovascular system. The patient should be weighed and a BMI calculated (weight (kg)/[height (m)]^2).

A4: What would be the initial management?

In the UK most patients with type 2 diabetes are given a period of non-pharmacological management. Dietary advice, preferably from a state-registered dietitian, should promote a diet high in complex carbohydrates but low in fat and refined sugars. If the patient is overweight (BMI >27 kg/m^2), calorific reduction should also be advised. The benefits of regular exercise should be stressed where appropriate. The patient should be taught how to monitor the impact of these changes by testing their blood (finger-prick testing), although the long-term value of this type of monitoring is uncertain.

These conservative measures are usually continued for at least 3 months, unless the patient becomes more symptomatic, in which case oral medication should be started. Current advice in the United States would lead to the immediate use of metformin alongside these lifestyle modifications.

A5: What are the long-term sequelae?

The patient is at risk of both small vessel and large vessel disease. Regular screening (at least yearly) should be performed for diabetic retinopathy, diabetic neuropathy and diabetic nephropathy. Blood pressure and lipids should be monitored and treated if necessary.

A6: What issues need to be addressed apart from blood glucose control?

Other cardiovascular risk factors include the following.

- *Smoking:* advise complete cessation.

- *Lipid levels:* in a patient over 40 years of age with type 2 diabetes, the target lipid levels according to the National Institute of Health and Clinical Excellence (NICE; Clinical Guideline 66, 2008) are total cholesterol <4.0 mmol/L and low-density lipoprotein (LDL) cholesterol <2.0 mmol/L ('<4&2'), with the use of simvastatin recommended as first-line therapy in patients above these targets.
- *Blood pressure:* treat initially with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker when over 140/80 mmHg.

CASE 1.3 – **A 21-year-old woman with a random finger-prick glucose of 18.9 mmol/L and urinary ketones (+++).**

A1: What specific questions would you ask the patient?

In this case, the diagnosis is type 1 (insulin-dependent) diabetes until proved otherwise. This diagnosis is based on the age of the patient and the presence of ketones in the urine. Answers to further questions will probably support this view but should not dissuade you from it. One might expect there to have been a short duration of symptoms (days to weeks), such as profound weight loss, polyuria, nocturia, lethargy and recurrent infection.

In the absence of ketonuria, especially in obese Asian people, there is the possibility of early-onset type 2 diabetes, although this is by no means the 'epidemic' suggested by the medical journals. A strong family history of early-onset type 2 diabetes (affecting siblings, parents and grandparents) may also point to one of the rare autosomal dominant forms of diabetes (maturity-onset diabetes of the young), but again ketonuria effectively excludes this.

A2: What investigations would you request to confirm a diagnosis?

No laboratory confirmation is necessary. Blood should be taken for a laboratory plasma glucose, but this must not delay initial treatment. A baseline level of glycaemic control would usually be requested (HbA1c) and a screen for associated autoimmune disease (especially thyroid function) may be checked. Autoantibodies (e.g. islet cell, anti-insulin, antibodies to glutamate decarboxylase [GAD]) are negative in 20–30 per cent of newly diagnosed patients and so are of little clinical use (they will also take some time to be reported). Insulin levels, likewise, are of little help and are rarely performed.

A3: What examination would you perform?

In a typical case of type 1 diabetes, there will be no evidence of diabetic complications at diagnosis because the duration of hyperglycaemia will have been short. Assessment should focus on the conscious level and circulatory state of the patient because she could easily be acidotic, despite the relatively modest level of hyperglycaemia. Near-patient plasma ketone testing is now available and should be performed to exclude diabetic ketoacidosis (DKA) and to inform the patient of this possibility as part of their initial education.

A4: What would be the initial management?

The patient needs to be treated with insulin and so should be in a setting where the necessary expertise is available (in the UK, typically a hospital). If the patient is fit, insulin can be started without the need for admission. Patients will need to be taught how to monitor blood glucose using finger-prick tests and to understand the concepts of hypo- and hyperglycaemia. They will also need to be shown how to test blood or urine for ketones and understand the significance of these. Dietary advice will be needed and appropriate targets for blood glucose levels agreed. Frequent contact over the early days and weeks after diagnosis will be essential, ideally with an experienced diabetes nurse specialist.

A5: What are the long-term sequelae?

By virtue of her younger age at onset, this patient is at particular risk of the small vessel complications of diabetes, specifically diabetic retinopathy, diabetic neuropathy and diabetic nephropathy. The minority of patients who go on to develop diabetic nephropathy (which usually manifests clinically after 15–25 years of disease) are prone to premature cardiovascular disease and are more susceptible to the other small vessel complications.

A6: What issues need to be addressed apart from blood glucose control?

The risks of specific diabetic complications and large vessel disease can be dealt with over the following months and years. Of a higher priority are matters that may have an immediate impact. The first of these is hypoglycaemia, which can occur from the moment that insulin injections are commenced. Patients need to be able to recognize the symptoms of 'hypos' and take appropriate action (see Case 1.15 and OSCE counselling case 1.10). Patients should also be aware that rapid lowering of blood glucose level can induce these symptoms, even when the blood glucose levels are within the 'normal' range. This patient should be given counselling about future pregnancy (exemplary diabetic control is necessary in the periconception period to reduce the risk of fetal abnormality) and driving.

OSCE counselling cases

OSCE COUNSELLING CASE 1.1 – 'Will I always have diabetes?'

The answer is, unfortunately, 'yes'. This is certainly the case as far as medical and insurance matters are concerned. By strict adherence to diet and regular exercise, however, it may be possible to reduce or even eliminate the need for medication. This applies to both oral agents and insulin in patients with type 2 diabetes. In the case presented, medication should be decreased or withheld to reduce the risk of hypoglycaemia.

Glucose levels tend to rise with age, and so patients with type 2 diabetes who control their diabetes with diet alone will ultimately need oral medication (often labelled 'diet failures') and patients on tablets may well need to go on to insulin.

People with type 1 diabetes may go through a period in the weeks to months after diagnosis where insulin can be withheld. This is labelled the 'honeymoon period' and is thought to reflect the removal of the influence of hyperglycaemia, which depresses β-cell function (so-called 'glucose toxicity'). The continued (autoimmune) β-cell destruction ultimately means that insulin will be required.

The prospect for a cure of diabetes is some way off in type 2 diabetes but may be possible for type 1 diabetes. Pancreas transplantation is becoming a feasible option in type 1 diabetes but is typically limited to patients with advanced complications, such as patients who will need to take anti-rejection drugs for a renal transplant or patients with hypoglycaemia unawareness. Recent advances in islet cell transplantation have allowed patients to become independent of insulin for more than 2 years, but long-term independence from insulin is uncommon. Unfortunately, problems surrounding islet availability and preparation mean that this therapy is limited to small numbers of patients.

OSCE COUNSELLING CASE 1.2 – 'Does having diabetes affect my driving licence?'

The answer in this case is currently 'yes'. The Driver and Vehicle Licensing Agency (DVLA) issues regular guidance on the medical standards of fitness to drive. Licences are split into two groups (groups 1 and 2), with group 2 including heavy goods vehicles, now termed large goods vehicles (LGVs), and passenger-carrying vehicles (PCVs). This patient should be advised to notify the DVLA that he is taking insulin and that, while he does so, he is barred in law from driving LGVs. If the use of insulin is temporary, he may reapply for a licence when he has been transferred to another treatment.

Regarding his group 1 (motor car and motor cycle) licence, he must notify the DVLA but he can retain his licence as long as he can recognize the warning symptoms of hypoglycaemia and is not experiencing disabling hypos. He should also advise his insurance company of his change in health status.

Note that regulations are changing at the time of going to print and readers are advised to avail themselves of the most recent DVLA guidance from its website. These may allow for patients treated with insulin to drive LGVs but with frequent monitoring and regular specialist review.

Notes about group 1 entitlement (motor cars and motor cycles) in the UK

- Patients with type 2 diabetes managed on diet alone need not notify the DVLA unless they develop relevant complications (e.g. retinopathy affecting visual acuity or visual fields).
- Patients with type 2 diabetes treated with oral hypoglycaemic medication should notify the DVLA but will be allowed to retain their licence until the age of 70 years, unless complications cause disability (such as vision loss).
- Patients on insulin should notify the DVLA and must be able to recognize the warning symptoms of hypoglycaemia. There are the same provisos regarding visual complications. Licences are granted for 1-, 2- or 3-year periods.

GLUCOSE CONTROL FOR PATIENTS WITH DIABETES MELLITUS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What are the treatment options?
Q2: What factors influence the choice of therapy?
Q3: What would be the preferred choice of treatment?
Q4: How would the impact of treatment be assessed?
Q5: What are the potential complications?
Q6: What issues need to be addressed when the patient has fully recovered?

CASE 1.4 – A 72-year-old man with newly diagnosed type 2 diabetes.

A 72-year-old man has recently been diagnosed with type 2 diabetes. He is mildly symptomatic with lethargy, thirst and polyuria. A random blood glucose level is 13 mmol/L and dipstick urine testing revealed +++ glucose but no ketones. He is known to have hypertension and takes bendroflumethiazide 5 mg once a day. His weight is stable at 94 kg (BMI 32 kg/m^2). On examination, there is no evidence of large or small vessel complications.

CASE 1.5 – An 84-year-old woman with type 2 diabetes has been treated with gliclazide for 4 years.

A fit 84-year-old woman with type 2 diabetes had been started on metformin after strict dietary adherence failed to control her symptoms. She now presents with persistently high glucose levels (home blood glucose monitoring [HBGM] 12–15 mmol/L) and has an elevated HbA1c level (9.0%, 73 mmol/mol) despite taking metformin 1 g twice a day. She is symptomatic with lethargy, frequency and dysuria. Random finger-prick glucose is 15 mmol/L and urine dipstick shows ++++ glucose, ++ albumin and + haematuria. Her blood pressure is normal, her weight is 67 kg (BMI 24 kg/m^2) and she has no evidence of retinopathy. There is early peripheral neuropathy and foot pulses are absent.

CASE 1.6 – A 57-year-old man treated with gliclazide 160 mg twice a day and metformin 500 mg three times a day, who has suboptimal glycaemic control.

A 57-year-old man with type 2 diabetes is currently treated with gliclazide 160 mg twice a day and metformin 500 mg three times a day, but his glycaemic control is suboptimal. He reports blood glucose levels between 12 mmol/L and 20 mmol/L and has an elevated HbA1c level (11.0%, 97 mmol/mol). He claims good dietary adherence but is overweight (110 kg, BMI 33 kg/m^2). He denies any symptoms and has previously refused to consider insulin. He has normal visual acuity but fundal photography shows hard exudates encroaching on the left macula.

OSCE counselling cases

OSCE COUNSELLING CASE 1.3 – **'I have been diagnosed as having maturity-onset diabetes. Does this mean that I will never need go on to injections?'**

OSCE COUNSELLING CASE 1.4 – **'I hate doing injections and painful blood tests for my diabetes. Can I try an insulin pump instead?'**

Key concepts

To work through the core clinical cases in this chapter, you will need to understand the following key concepts.

GLUCOSE CONTROL FOR PATIENTS WITH DIABETES MELLITUS

Type 2 diabetes is a condition caused by a combination of resistance to the action of circulating insulin (insulin resistance) and β-cell failure (lack of insulin). The loss of β-cell function is a progressive disorder and is not modified by commonly used hypoglycaemic therapies (although more modern agents may have this benefit). This means that diet and then tablet and injectable therapies will ultimately fail and, if the patient lives for long enough, rising blood glucose levels will eventually require insulin therapy.

In the UK, the usual approach to glycaemic management is to start with modification of diet and exercise, often in the hope of achieving weight reduction (obesity is associated with insulin resistance). Unless the patient is very symptomatic or glucose levels are particularly high, this would be tried for at least 3 months. The target would be a HbA1c level below 7.0%, 53 mmol/mol, although some people would advocate lower levels (e.g. NICE suggests an initial target below 6.5%, 48 mmol/mol). If the target is not achieved, oral medication is added. Metformin is the first-line agent, especially in obese people, because it does not promote weight gain and in monotherapy should not render patients hypoglycaemic. Unfortunately, metformin has significant side effects, including anorexia, nausea, abdominal discomfort, constipation and diarrhoea. These side effects are less pronounced if the dose is increased slowly, so 500 mg once a day is commonly prescribed, building up to 1 g twice a day with meals, with weekly dose increases of 500 mg.

If metformin is ineffective or not tolerated, sulphonylureas are used. Gliclazide is the most commonly prescribed sulphonylurea in the UK, starting at 80 mg once a day with breakfast and increasing to a maximum of 320 mg, usually in two divided doses. More modern preparations of this and other sulphonylureas allow for single daily dosing. As sulphonylureas act by increasing endogenous insulin secretion, they can promote both hypoglycaemia and weight gain as side effects.

In patients who do not achieve target with metformin and a sulphonylurea, triple oral therapy may be initiated. The options include pioglitazone, a thiazolidinedione, which reduces insulin resistance, or a gliptin (e.g. saxagliptin, linagliptin), which enhances insulin secretion in a glucose-dependent way. These third-line agents do not induce hypoglycaemia but their side effects differ. Pioglitazone often induces weight gain and can cause oedema, leading to heart failure. Pioglitazone also increases the risk of bone fracture and may be associated with a small increase in bladder cancer. The gliptins are weight-neutral and have a placebo-like side-effect profile.

Before the initiation of insulin, use of injectable glucagon-like peptide 1 (GLP-1) therapies may be considered. Like the gliptins, these drugs have a glucose-dependent mechanism of action (i.e. they lower glucose only when levels are high) and so do not cause hypoglycaemia. They also induce weight loss in a significant number of patients. Their major side effect is nausea, occasionally with vomiting, but this tends to diminish over time.

There are various ways of starting insulin in type 2 diabetes. Insulin can be added to oral therapy, usually as a single dose of long-acting insulin (either isophane insulin or analogues such as glargine or detemir). This regimen has the advantages of simplicity but is ultimately doomed to fail with patients needing fast-acting insulin to prevent postprandial hyperglycaemia. This can either involve the addition of three pre-meal injections (a standard basal bolus regimen) or a change to two pre-meal injections of premixed insulin. As far as reaching HbA1c targets is concerned (NICE suggests 7.5%, 58 mmol/mol), the twice-daily and add-on regimens are equally (in)effective and one can argue there is less activity going straight to twice-daily insulin when tablets fail. This also has the advantage that patients can stop taking many tablets, although metformin is often continued to try to reduce the weight gain that can be associated with insulin use. Gliptins can be used with insulin but GLP-1 injections are currently unlicensed for this combination, a situation that is likely to change soon.

Answers

Clinical cases

CASE 1.4 – **A 72-year-old man with newly diagnosed type 2 diabetes.**

A1: What are the treatment options?

The treatment options are wide and include the following:

- dietary review and manipulation
- exercise
- weight loss (achieved by diet and exercise)
- change of antihypertensive agent
- oral hypoglycaemic agents (metformin).

A2: What factors influence the choice of therapy?

The choice of therapy is influenced by factors including the level of symptoms, the degree of hyperglycaemia, the patient's weight and the fact that there has been no weight loss, and the patient's age. This patient is said to have type 2 diabetes, and this fits with his age, symptoms, obesity and hypertension. His symptoms are mild, his glucose level is moderately elevated, and there are no ketones in the urine. He currently takes a high-dose thiazide diuretic, which in some cases can cause glucose intolerance, and so the dose should be reduced or the drug should be replaced by an ACE inhibitor.

A3: What would be the preferred choice of treatment?

A reasonable course of action would be to advise on diet (see answer A4 to Case 1.1), with the aim of reducing daily calorie intake and increasing exercise. The bendroflumethiazide could be stopped and replaced with an ACE inhibitor. Assuming that he does not become more symptomatic, this regimen could be followed for 3 months, at which point oral hypoglycaemic agents may be considered. The first-line agent would be metformin, based on his obesity.

A4: How would the impact of treatment be assessed?

The patient should be made aware of the symptoms of hyperglycaemia and should make contact if these worsen, especially if weight loss is marked. The technical options to assess the glycaemic response are near-patient (usually self-) testing of blood glucose and laboratory testing (HbA1c levels).

Home blood glucose monitoring is commonly taught to patients in this scenario, but critics argue that it is of little value and is very expensive. Unless a patient or the clinician is going to manipulate therapy based only on the results of HBGM (and this is unlikely to be the case here), one can argue that it should not be routine practice. On the other hand, HBGM will provide immediate feedback to the patient on which aspects of the diet worsen his glucose levels and can be seen to be an essential aspect of patient empowerment. HbA1c levels provide a long-term indication of glycaemic control (typically quoted to be 2–3 months) and, if compared with a baseline value, will give a good indication as to whether conservative measures are being effective. HbA1c also allows for targets to be set, initially aiming for a level below 6.5%, 48 mmol/mol.

Do not forget that a change in blood pressure therapy means that blood pressure monitoring will need to be performed on a monthly basis and, if an ACE inhibitor is used, electrolytes will need to be checked before treatment and after 7–14 days of treatment.

CASE 1.5 – **An 84-year-old woman with type 2 diabetes has been treated with gliclazide for 4 years.**

A1: What are the treatment options?

The treatment options include:

- further dietary review and manipulation
- add another oral hypoglycaemic agent (sulphonylurea, pioglitazone, gliptin)
- add insulin
- exclude urinary tract infection (UTI) or treat if this is confirmed.

A2: What factors influence the choice of therapy?

The choice of therapy is influenced by the natural history of the patient's condition, her weight, her current therapy and her age. Type 2 diabetes is a progressive disease and so failure of diet and then oral monotherapy to control her symptoms should be anticipated (and not attributed to failure on the part of the patient). Although a dietary assessment is reasonable (and should be performed as part of the annual diabetes review), she has previously been strict and is not currently overweight. In this setting, it is unlikely that dietary change will make a significant impact. Her current dose of metformin is not at the maximum recommended; however, the dose–response curve tends to be flattened at higher doses (and a further increase is likely to induce side effects), and so additional therapy would be instituted. UK guidelines suggest a sulphonylurea as second-line, but many clinicians prefer to add a gliptin, as the combination with metformin will not put the patient at risk of hypoglycaemia. Given her age, tight glycaemic control is not a priority and symptomatic relief with low risk of hypoglycaemia is the main aim of therapy. Note that the possibility of diabetic foot complications does not influence the treatment choices.

Although hyperglycaemia causes lethargy and frequency, dysuria with proteinuria and haematuria on dipstick testing suggest the possibility of a UTI (common in hyperglycaemia and a cause of worsened diabetic control). If UTI is confirmed by urine culture, a course of antibiotics would be indicated.

A3: What would be the preferred choice of treatment?

Add a second oral agent to the patient's current dose of metformin. Options include a gliptin, pioglitazone and a sulphonylurea. The reduction achieved with any of these therapies is likely to be the same; side effects, especially the risk of hypoglycaemia, are the major reason for opting for a gliptin rather than a sulphonylurea. If the patient remains symptomatic and her HbA1c remains very high, then insulin (in combination with metformin) may have to be considered, but again this would increase the risk of hypoglycaemia.

A4: How would the impact of treatment be assessed?

Given that the patient is already performing HBGM, it is not unreasonable for her to continue this practice. Fasting, pre-meal and pre-bed glucose testing is the norm, with targets below 10 mmol/L without hypoglycaemia being reasonable in this case. HbA1c testing could also be performed for comparison with the pretreatment level. Symptomatic improvement is the main aim of therapy, and the HbA1c target needs to be individualized since the benefits of tight control in this age group are unproven and the side effects of treatment (especially hypoglycaemia) are dangerous.

CASE 1.6 – **A 57-year-old man treated with gliclazide 160 mg twice a day and metformin 500 mg three times a day, who has suboptimal glycaemic control.**

A1: What are the treatment options?

The treatment options include:

- further dietary review and manipulation
- increasing the dose of metformin
- adding another oral hypoglycaemic agent (pioglitazone or a gliptin)
- add a GLP-1 injectable therapy
- add insulin.

A2: What factors influence the choice of therapy?

The choice of therapy is influenced by the natural history of the condition, the patient's current therapy, age and weight, and the presence of retinopathy. The progressive nature of type 2 diabetes is such that almost all patients will end up on insulin if they survive for long enough. Although he is not on maximal doses of metformin, further increases are unlikely to achieve glycaemic targets. Addition of pioglitazone or a gliptin (triple therapy) is an alternative but is often a disappointing combination in this type of scenario. Use of a GLP-1 injectable therapy would now be a popular option in the UK, although current NICE guidelines suggest that this should be offered to patients only where the BMI is over 35 kg/m^2. Insulin thus becomes a leading option, especially given the patient's young age and the development of diabetic retinopathy. Clearly the patient is not keen to go on insulin and the reasons for this need to be explored, because many patients are pleasantly surprised at how painless insulin injections are (compared with HBGM) and feel much better when their glycaemic control improves. A dietary assessment is reasonable because weight gain is highly likely with insulin; for this reason, metformin should be continued (while the sulphonylurea may be withheld).

A3: What would be the preferred choice of treatment?

Suggest to the patient that he tries insulin for a period. This will allow him to see how simple the procedure can be and if, like many patients, he feels better on insulin, he may well wish to stay on it. Twice-daily insulin using fixed mixtures before breakfast and evening meal is a simple regimen that may seem less daunting than basal bolus (where the patient injects fast-acting insulin before each meal and a night-time injection of long-acting insulin). Given the risk of weight gain, the patient should continue on metformin but can cease taking his sulphonylurea.

If a GLP-1 receptor agonist is preferred by the patient (many people hate the idea of insulin, not because of the injections but due to a bad family experience or to fears of hypoglycaemia), then the current options are exenatide or liraglutide. Exenatide can be prescribed as a twice-daily or once-weekly preparation, and liraglutide is given once a day. Both can cause nausea and vomiting. UK guidelines suggest their impact on glycaemic control and weight should be assessed after 6 months, with treatment failure (HbA1c reduction of less than 1% and weight loss of less than 3%) leading to drug withdrawal.

A4: How would the impact of treatment be assessed?

Symptomatic improvement (he may recognize and admit to symptoms in retrospect, especially lethargy) and HBGM will provide feedback on the patient's progress. He should also monitor his weight. HbA1c will be the ultimate assessment with a lower target (7.0–7.5%, 53–58 mmol/mol) given his young age.

OSCE counselling cases

OSCE COUNSELLING CASE 1.3 – 'I have been diagnosed as having maturity-onset diabetes. Does this mean that I will never need go on to injections?'

The short answer is 'no'. Maturity-onset diabetes is the old term for non-insulin-dependent diabetes, now called type 2 diabetes mellitus. The natural history of this condition has been convincingly demonstrated and is one of progressive deterioration in blood glucose control. This is felt to reflect progressive loss of β-cell function over time. Insulin resistance, the other contributing metabolic abnormality, appears to deteriorate before the diagnosis of type 2 diabetes but then remains relatively fixed.

As a result of β-cell failure, dietary change is likely to have a limited and temporary impact, leading to the introduction of oral hypoglycaemic agents and GLP-1 receptor agonists. Ultimately these agents will fail and the patient may need insulin to achieve reasonable glycaemic control. One can argue that if an individual with type 2 diabetes lives for long enough, then insulin is inevitable. This can be used as a justification for early exposure to the use of insulin (handling injection devices, experiencing the injection) so that, when insulin is needed, it is not delayed by unjustified anxieties.

The exception to this rule of progressive glycaemic deterioration may be patients who are obese at diagnosis and manage to lose vast amounts of weight, thereby restoring insulin sensitivity. There are also preliminary data that gliptins and GLP-1 agents can slow the progression of β-cell dysfunction, but these data need to be confirmed.

Learning points

- Type 2 diabetes is the modern name for maturity-onset (non-insulin-dependent) diabetes.
- The natural history of this condition is for blood glucose control to deteriorate over time as a result of β-cell failure.
- If survival is prolonged, insulin treatment will be needed in most cases of type 2 diabetes.
- It is the treatment, not the patient, that fails; this should be expected and anticipated. Patients can be introduced to the concept of insulin at an early stage and should not be 'threatened' with its introduction.

OSCE COUNSELLING CASE 1.4 – 'I hate doing injections and painful blood tests for my diabetes. Can I try an insulin pump instead?'

Insulin pumps (also known as continuous subcutaneous insulin infusions, CSII) are available in the UK but this is not a good reason for using one because the amount of finger-prick testing is typically increased.

The use of an insulin pump involves the insertion of a cannula into the subcutaneous tissue, through which small amounts of insulin are continuously delivered. In addition, bolus doses can be administered by the same equipment, to coincide with meals. The pump is a small device and can easily be carried in a belt or holster.

NICE has advised that pump therapy can be made available to people with type 1 diabetes where multiple insulin dose therapy has failed to achieve good glycaemic control. Type 2 diabetes is not currently regarded as an indication for pump use. Patients should be able to maintain 'a high order of personal hygiene' (to avoid catheter site infection) and test finger-prick blood glucose four times

a day. In addition, patients should be capable of estimating carbohydrate and calorie consumption, programming the pump and changing the cannula site every 2–3 days.

Learning points

- Insulin pumps are available for therapy of type 1 diabetes in the UK.
- Insulin pumps are indicated where control remains poor despite multiple insulin injection regimens.
- Patients need to be motivated and technically competent.

DIABETIC SMALL VESSEL COMPLICATIONS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What questions would you ask the patient and why?
Q2: What investigations would you request?
Q3: What examination would you perform?
Q4: What are the differential diagnoses related to diabetes?
Q5: What are the potential complications?
Q6: What issues need to be addressed when the patient has fully recovered?

CASE 1.7 – **A 75-year-old man with long-standing type 2 diabetes complains of difficulty in seeing television programmes.**

A 75-year-old man with diabetes of 15 years' standing complains of difficulty in seeing programmes on the television. There has been no pain or redness affecting his eyes and he has not had headaches. His diabetic control is poor but stable.

CASE 1.8 – **A 31-year-old man with type 1 diabetes has albuminuria on urine dipstick testing.**

A 31-year-old man with type 1 diabetes has joined your practice. He was diagnosed at age 12 years. Having attended the clinic regularly as a child, he defaulted from the adult clinic, attending only when he needed replacement equipment (e.g. injection devices). He takes no other medication and has had no treatment for complications. Blood pressure is 160/80 mmHg. Dipstick urine testing shows +++ glucose, ++ albumin and + blood, but no ketones. Visual acuity is 6/6 in both eyes.

CASE 1.9 – **A 56-year-old man with newly diagnosed type 2 diabetes complains of pins and needles in his feet.**

A 56-year-old man is diagnosed with type 2 diabetes by his local optometrist. He attends your practice and during diabetic review complains of 'pins and needles' affecting both of his feet and his right hand. The symptoms are worse at night when he is in bed. Discomfort in his hand often disturbs his sleep. There is no discomfort in his feet during the day and his exercise tolerance has been unaffected.

OSCE counselling cases

OSCE COUNSELLING CASE 1.5 – **'Do all people with diabetes end up on kidney dialysis treatment?'**

OSCE COUNSELLING CASE 1.6 – **'My friend has diabetes and she says that all people with diabetes should go to a chiropodist. Is this true?'**

Key concepts

To work through the core clinical cases in this chapter, you will need to understand the following key concepts.

Long-term complications of diabetes are traditionally divided into diabetes-specific small vessel complications (meaning that only patients with diabetes are at risk) and diabetes-non-specific large vessel complications (increased risk in diabetes but not limited to patients with diabetes). The small vessel complications are:

- *eye disease:* diabetic retinopathy – the most common cause of blindness in the working population of the UK
- *nerve disease:* diabetic neuropathy – usually a progressive peripheral neuropathy that presents with tingling and burning affecting the feet and progresses to complete sensory loss
- *kidney disease:* diabetic nephropathy – the most common cause of end-stage renal failure in western countries.

There is crossover between the small and large vessel complications – e.g. patients with diabetic nephropathy have a greatly increased risk of ischaemic heart disease, and most will succumb to this rather than end-stage renal failure.

The diabetes annual review aims to detect diabetes complications at an early stage and institute therapy before there has been irreversible damage (e.g. laser treatment for retinopathy to prevent loss of visual acuity).

Answers

Clinical cases

CASE 1.7 – A 75-year-old man with long-standing type 2 diabetes complains of difficulty in seeing television programmes.

A1: What questions would you ask the patient and why?

Symptoms of cataract progression include halos around bright lights, such as car headlights. The symptoms are usually slow in progression but patients may report abrupt changes. Maculopathy may give either a slow or a sudden loss of vision in one eye, whereas a bleed related to proliferative diabetic retinopathy classically causes sudden painless visual loss in one eye. Note that patients may be unaware of the extent of loss of vision if the good eye compensates. Changes in vision related to poor glycaemic control (usually enhanced long vision and difficulty reading) may affect both eyes and can be variable over short periods. During periods of poor glycaemic control (e.g. at diagnosis), patients should be advised against changing their lens prescription.

A2: What investigations would you request?

In the vast majority of cases, the history and examination will be sufficient.

A3: What examination would you perform?

Visual acuity should be tested, with correction with spectacles if the patient normally uses these for distance vision. Pinhole correction should be performed if the visual acuity is 6/9 or less. Examination of the fundi through dilated pupils (1% tropicamide) is mandatory. This will allow detection of a cataract by examination of the red reflex and also detection of retinal abnormalities by direct visualization, including those concerning diabetes and related medical disorders. Ideally, binocular stereomicroscopy should be performed (usually in the setting of an ophthalmic clinic), which facilitates the detection of macular oedema. Digital images may also be requested.

A4: What are the differential diagnoses related to diabetes?

The major possibilities related to the patient's diabetes are:

- cataract
- diabetic retinopathy (more likely maculopathy than proliferative diabetic retinopathy)
- change in blood glucose levels leading to alteration in lens shape
- related retinal disorders such as central retinal vein or artery occlusion.

CASE 1.8 – A 31-year-old man with type 1 diabetes has albuminuria on urine dipstick testing.

A1: What questions would you ask the patient and why?

He should be asked about symptoms of UTI (e.g. frequency, dysuria, nocturia, haematuria). Although his attendance at clinic has been sporadic, he should have had urine testing previously, so he should be quizzed as to whether he had been told about urinary abnormalities (especially albuminuria) before. Previous blood pressure assessments would also be of value because this one-off reading may reflect anxiety-induced ('white-coat') hypertension. A family history of hypertension and ischaemic heart disease are also more common in patients at risk of diabetic nephropathy.

A2: What investigations would you request?

A midstream urine specimen should be sent for culture to exclude a UTI. If UTI is excluded, formal assessment of the albumin excretion is needed; this can be by one of the following, depending on the patient's expected compliance: 24-h urine collection for albumin; timed overnight urine collection for albumin excretion rate; first voided urine for albumin/creatinine ratio. Blood should be sent for HbA1c to assess glycaemic control, lipids should be checked (total and high-density lipoprotein [HDL]-cholesterol), and creatinine should be checked to estimate the glomerular filtration rate (eGFR). Haematuria is not typical of diabetic nephropathy and so renal ultrasonography should be arranged to exclude other causes (rare in this setting).

A3: What examination would you perform?

People with type 1 diabetes and diabetic nephropathy are at high risk of other complications. The feet should be examined for evidence of peripheral neuropathy and reduced circulation. Coexisting diabetic retinopathy is almost inevitable and so arrangements for dilated fundoscopy should be made. Blood pressure should be repeated after a period of rest and then follow-up arrangements for more blood pressure checks over the next 2–3 months to establish whether there is a persistent elevation. If diabetic nephropathy is confirmed, a target systolic pressure of 130 mmHg is recommended.

A4: What are the differential diagnoses related to diabetes?

The following major possibilities are related to the patient's diabetes.

- Diabetic nephropathy: the duration of disease (19 years) is typical, and it is likely that his control has been poor, given the poor clinic attendance. In addition to the albuminuria, he has a raised blood pressure, which is part of the syndrome.
- UTI (in view of the + blood).

CASE 1.9 – **A 56-year-old man with newly diagnosed type 2 diabetes complains of pins and needles in his feet.**

A1: What questions would you ask the patient and why?

Peripheral neuropathy symptoms (to which burning dysaesthesiae may be added) are of gradual onset, typically worse at rest and in bed, when bedclothes can be particularly irritating. Autonomic neuropathy (rare) may also be present, with symptoms including gustatory sweating (facial sweating after meals) and postural hypotension.

Carpal tunnel syndrome is common at night, patients often being awoken with discomfort and typically shaking the hand to relieve symptoms. Excessive use of the hands (e.g. in painting) may also induce symptoms. It may be associated with loss or change of sensation in the hand, and symptoms may be referred to the whole forearm. Again, gradual onset of symptoms would be expected and the other hand may also be affected.

Given the association of carpal tunnel syndrome with myxoedema, acromegaly, rheumatoid arthritis and osteoarthritis, symptoms of these conditions may be elicited.

A2: What investigations would you request?

Nerve conduction studies will confirm a diagnosis of both peripheral diabetic neuropathy and carpal tunnel syndrome. They are most useful in the latter, where surgical intervention can be considered when entrapment is confirmed. Bloods to exclude hypothyroidism and vitamin B12 deficiency (more common with metformin treatment) should also be requested.

A3: What examination would you perform?

Examination of the feet for abnormal sensation using monofilaments and vibration sensation as screening tools can be done. Ulceration (painless) should be excluded and skin care assessed. Peripheral pulses should be examined, which may be enhanced ('bounding') in the neuropathic foot.

In carpal tunnel syndrome there may be sensory loss over the palmar aspects of the first three and a half fingers and wasting of the thenar eminence. In advanced cases, there can be weakness of abduction, flexion and apposition of the thumb. Symptoms can be worsened by various manoeuvres such as percussion of the carpal tunnel (Tinel's sign), flexion of the wrist (Phalen's sign) and hyperextension of the wrist.

Given the association of carpal tunnel syndrome with myxoedema, acromegaly, rheumatoid arthritis and osteoarthritis, signs of these conditions may be looked for.

A4: What are the differential diagnoses related to diabetes?

The major possibilities related to the patient's diabetes are:

- peripheral diabetic neuropathy affecting the feet and possibly the right hand – although diagnosed only recently, the patient has clearly had diabetes for some time to manifest retinal changes. Hence other long-term complications of diabetes may also be present
- carpal tunnel syndrome affecting the right hand
- mononeuropathy affecting the right hand
- vascular insufficiency is an *unlikely* cause of symptoms given the absence of claudication.

OSCE counselling cases

OSCE COUNSELLING CASE 1.5 – 'Do all people with diabetes end up on kidney dialysis treatment?'

No. There may appear to be a paradox in that diabetes is now the most common cause of end-stage renal failure in the western world and renal dialysis as a result of diabetes is becoming more frequent. This relates, however, to the massive increase in the number of people diagnosed with type 2 diabetes, and the vast majority will never need dialysis treatment.

Taking the example of type 1 diabetes, studies from the 1960s and 1970s show that only a minority (at most, 40 per cent) of patients will develop diabetic nephropathy, irrespective of their glycaemic control. This is likely to represent a genetic predisposition to diabetic nephropathy, which means that most patients are protected from this complication (contrast with diabetic retinopathy, where all patients continue to be at risk). Continued improvements in blood pressure, lipids and glucose control will inevitably reduce this proportion.

In type 2 diabetes, the major risk associated with abnormal albumin excretion is cardiovascular disease, which tends to cause premature death long before renal dialysis becomes a possibility.

Learning points

- Diabetes is the most common cause of end-stage renal disease in the western world.
- The number of people with diabetes going on to renal dialysis programmes is likely to increase as a result of the rise in prevalence of diabetes.
- Susceptibility to diabetic nephropathy is partly genetically determined, with most patients protected from this complication.
- With advances in blood pressure, lipid and glucose management, the proportion of people with diabetes, especially type 1, needing renal replacement therapy is likely to fall.
- Diabetic nephropathy greatly increases the risk of other diabetic complications, including premature coronary heart disease.

OSCE COUNSELLING CASE 1.6 – 'My friend has diabetes and she says that all people with diabetes should go to a chiropodist. Is this true?'

No. The level of resource directed towards diabetic foot care should be dictated by the individual needs. This has led to a risk categorization with varying levels of input.

Normal feet (low risk) – all newly diagnosed patients should receive basic foot health advice and subsequently be reviewed on an annual basis. This assessment can be carried out by a doctor, diabetes nurse specialist or practice nurse (with the appropriate level of training). If at any stage the patient is found to be 'at risk' or to have active foot disease, then referral should be made as follows.

- *At risk:* patients with reduced sensation or reduced pedal pulses or unable to perform nail chiropody (or have it provided by a responsible carer) should be seen every 3–6 months for review by a chiropodist. Foot care advice should be given and the need for vascular assessment reviewed.
- *High risk:* patients with a risk factor for foot disease and either foot deformity or a previous ulcer should be seen every 1–3 months by a senior podiatrist. Specialist foot care treatment and advice should be given, as per the published guidelines. There should be easy access to a shoe-fitter, surgical appliances and, where necessary, a limb-fitting centre.
- *Active foot disease:* patients with active ulceration, cellulitis, osteomyelitis, a Charcot joint or foot discoloration should be seen urgently in a multidisciplinary diabetic foot clinic.

Learning points

- All people with diabetes need foot assessment and advice at diagnosis and at least yearly thereafter.
- This can be performed by different health-care professionals, so long as they have been adequately trained.
- The intensity of clinical input depends on the risk categorization of each individual case.

DIABETIC LARGE VESSEL COMPLICATIONS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: Are further assessments required before the italicized finding provokes a drug intervention?
Q2: If drug therapy were indicated, which would be the most appropriate choice of agent?
Q3: What sort of follow-up is indicated?
Q4: What other issues need to be addressed with regard to cardiovascular risk?
Q5: What are the potential complications?
Q6: What issues need to be addressed when the patient has fully recovered?

CASE 1.10 – **A 68-year-old man with type 2 diabetes and *a total cholesterol of 5.6 mmol/L*.**

A 68-year-old man with type 2 diabetes has a new person check in primary care. He has no significant medical history apart from diabetes and he does not smoke. His BMI is 32 kg/m^2 and he has no evidence of diabetic retinopathy or foot complications. His blood pressure is 170/96 mmHg and urinalysis shows glycosuria ++ but no protein. A random total cholesterol is 5.6 mmol/L and triglycerides 2.3 mmol/L. He takes metformin 1 g twice a day and has an HbA1c level of 7.5%, 58 mmol/mol.

CASE 1.11 – **A 76-year-old woman with type 2 diabetes and *a stable blood pressure of 166/70 mmHg*.**

A 76-year-old woman with type 2 diabetes is under regular review. She has a history of angina, which is well controlled, and does not smoke. Her BMI is 28 kg/m^2 and she has background diabetic retinopathy and absent foot pulses. Her blood pressure is 166/70 mmHg and urinalysis shows persistent + albuminuria in the absence of infection. Blood pressure recordings over the previous 6 months have shown similar levels. She takes gliclazide 80 mg twice a day, and isosorbide mononitrate 60 mg, simvastatin 10 mg and aspirin 75 mg once a day. A random total cholesterol is 4.8 mmol/L, triglycerides 2.3 mmol/L and HbA1c 7.8%, 62 mmol/mol.

CASE 1.12 – **A 21-year-old woman with type 1 diabetes and *microalbuminuria (urinary albumin/creatinine ratio 3.7)*.**

A 21-year-old woman with type 1 diabetes of 15 years' standing has an annual review of her diabetes. She injects insulin using a basal bolus regimen and does not smoke. Her BMI is 22 kg/m^2, her blood pressure is 120/60 mmHg and she has good pedal pulses. She has minimal background diabetic retinopathy and slightly diminished sensation in her feet. Random total cholesterol is 5.7 mmol/L, triglycerides 1.1 mmol/L and HbA1c 6.5%, 48 mmol/mol. Analysis of a random urine shows an albumin/creatinine ratio of 2.7, which is reported as 'microalbuminuria'. Previously, urinalysis had been negative for dipstick proteinuria.

OSCE counselling cases

OSCE COUNSELLING CASE 1.7 – **'As someone with diabetes, should I be taking aspirin?'**

OSCE COUNSELLING CASE 1.8 – **'Why is my blood pressure so difficult to control?'**

Key concepts

To work through the core clinical cases in this chapter, you will need to understand the following key concepts.

People with diabetes get the same large vessel disease as people who do not have diabetes, but they get it earlier and it is more widespread.

- *Cardiovascular disease:* 75 per cent of people with type 2 diabetes will die as a result of ischaemic heart disease. Some studies suggest that IGT carries a similar cardiovascular prognosis to overt type 2 diabetes. This implies that glucose control is not the dominant issue and is consistent with the limited impact of glycaemic control in many studies. This is in stark contrast to the major impact of blood pressure and lipid control on cardiovascular outcomes in patients with type 2 diabetes.
- *Peripheral vascular disease:* diabetes is the most common cause of non-traumatic lower limb amputation in the UK.
- *Cerebrovascular disease:* stroke is two to four times more common in diabetic cohorts.

There is a focus on coronary heart disease prevention (both primary and secondary) in diabetes management, with attention to lipids, blood pressure control (and, to a lesser extent, aspirin) and a sound evidence base. Microalbuminuria screening is also recommended in this context (as a marker of early vascular disease), but the rationale for this is less convincing.

Answers

Clinical cases

CASE 1.10 – **A 68-year-old man with type 2 diabetes and a *total cholesterol of 5.6 mmol/L*.**

A1: Are further assessments required before the italicized finding provokes a drug intervention?

The total cholesterol warrants consideration in terms of primary prevention of cardiovascular disease. Issues include whether fasting lipids are required, the potential impact of diet, and what level of cholesterol justifies drug treatment.

Total cholesterol is not altered by recent food intake (unlike triglycerides), and so a fasting sample is not mandatory. Most clinicians would, however, repeat the lipids to include an HDL-cholesterol, allowing for calculation of the LDL-cholesterol. This allows for assessment of the patient's 10-year coronary heart disease risk using the Framingham or similar calculation. For most patients, diet has little impact on total cholesterol levels; this is borne out by the large statin trials, which show a reduction of only 2–4 per cent in diet-treated patients.

The generally quoted targets for lipids in patients with type 2 diabetes are total cholesterol <4.0 mmol/L and LDL-cholesterol <2.0 mmol/L.

A2: If drug therapy were indicated, which would be the most appropriate choice of agent?

Simvastatin should be prescribed, aiming for a daily dose of 40 mg. If the lipid targets are not achieved with this dose, then a more potent statin should be introduced and consideration given to the co-prescription of ezetimibe (although the evidence base supporting this agent is much less). There is currently no evidence that fibrates produce cardiovascular benefits in patients with diabetes.

A3: What sort of follow-up is indicated?

Liver function tests (LFTs) and creatine kinase should be checked before initiation of statin treatment but probably do not need to be checked again. At the same time, thyroid function tests could be requested to exclude underlying hypothyroidism, which can raise cholesterol levels. Patients should be aware of the risk of muscle pains, which are rarely the result of myositis; creatine kinase should be checked if the patient experiences this symptom. Lipids should be repeated after 3 months of treatment and, if targets have been hit, checked on a yearly basis thereafter.

A4: What other issues need to be addressed with regard to cardiovascular risk?

One needs to give consideration to glycaemic control, smoking, BMI, blood pressure and drug therapy, although not necessarily in that order. The evidence that improving blood glucose control and reducing weight would have a major impact on coronary heart disease risk in this case is weak. In contrast, blood pressure control is crucial; however, one needs to know that the reading taken on this visit is representative and not anxiety induced (so-called 'white coat hypertension'). An electrocardiogram (ECG) may be helpful because evidence of left ventricular hypertrophy would imply long-standing hypertension; however, if this were normal, then repeated blood pressure checks should be arranged. A

minimum of three recordings over a 3-month period would be appropriate, with consideration of drug therapy if the level remains above 140/80 mmHg. Aspirin is not currently recommended at this stage.

CASE 1.11 – **A 76-year-old woman with type 2 diabetes and a stable *blood pressure of 166/70 mmHg*.**

A1: Are further assessments required before the italicized finding provokes a drug intervention?

This patient with diabetes, ischaemic heart disease and peripheral vascular disease has isolated systolic hypertension confirmed by multiple assessments over time. The literature strongly supports reduction of her systolic pressure using drugs to a target of less than 130 mmHg. Further attention to weight, exercise and glycaemic control would be beneficial, but these will have minimal impact on her blood pressure. Apart from baseline urea and electrolytes (U&Es), no further investigations are required at this point.

A2: If drug therapy were indicated, which would be the most appropriate choice of agent?

The first-line antihypertensive agent in a person with diabetes and proteinuria should be an inhibitor of the renin–angiotensin system. This would typically be an ACE inhibitor, with consideration of an angiotensin II receptor blocker if side effects (most often cough) are experienced. In either case, check that U&Es have been performed before initiation and 7–10 days thereafter. For a substantial proportion of people with diabetes, monotherapy is not sufficient to achieve blood pressure targets, and additional classes of blood pressure medication will be needed. A typical second-line agent in this case would be a calcium channel blocker or a low-dose diuretic.

A3: What sort of follow-up is indicated?

The effect of drug therapy may take 2 months to become apparent. An interim target blood pressure of 160 mmHg is appropriate; if the patient feels well having achieved this, further increases in medication should be made, aiming for systolic blood pressure below 130 mmHg. Once stabilized, blood pressure can be checked every 3–6 months. Patients on ACE inhibitors and angiotensin II receptor blocker should have renal function and electrolytes checked at regular intervals (every 6 months) because renal function can deteriorate at any time. Additional tests are required if the dose of ACE inhibitor or angiotensin II receptor blocker is increased, additional medication is added, or there is intercurrent illness.

A4: What other issues need to be addressed with regard to cardiovascular risk?

Attention to glycaemic control, weight and exercise is justified but unlikely to have a significant impact on the risk of coronary heart disease. The patient's other medications should be reviewed: the simvastatin dose should be increased to 40 mg once a day (the dose on which most of the evidence for this agent is based), and the dose of aspirin should be increased to 150 mg once a day, given her known ischaemic heart disease (i.e. secondary prevention).

CASE 1.12 – **A 21-year-old woman with type 1 diabetes and *microalbuminuria* (urinary albumin/creatinine ratio 3.7).**

A1: Are further assessments required before the italicized finding provokes a drug intervention?

Screening for microalbuminuria in patients with type 1 diabetes is part of the diabetes annual review. It aims to detect the early stage of diabetic nephropathy before the onset of dipstick-positive proteinuria

(so-called macroalbuminuria). Diabetic nephropathy is a clinical syndrome of persistent proteinuria, hypertension and declining renal function. Patients with this complication have increased premature morbidity and mortality as a result of end-stage renal failure, cardiovascular disease and other diabetes complications, which cluster in this cohort. In well-controlled patients, the discovery of microalbuminuria after 15 years of diabetes would be typical of the natural history of this complication.

The issue surrounds the validity of this screening result. Urinary albumin excretion rates are highly variable, being affected by infection, posture and exercise, and this means that sampling procedures are very important. The test should be performed on a first-voided urine sample and, if positive, infection should be excluded by culture. If microalbuminuria is confirmed, then a timed overnight collection should be arranged for assessment of the albumin excretion rate; if this is also positive, a further two overnight collections should be organized. No treatment should be instituted on the basis of this one-off finding.

A2: If drug therapy were indicated, which would be the most appropriate choice of agent?

Evidence supports the use of ACE inhibitors to delay the progression of microalbuminuria towards diabetic nephropathy, even in the presence of normal blood pressure. A further consideration in this case, however, is that ACE inhibitors should not be used in pregnancy and so appropriate contraceptive measures should be instituted before prescription is considered.

A3: What sort of follow-up is indicated?

Once a definitive diagnosis has been made, annual screening is probably satisfactory. This is definitely the case if the repeat urine tests are negative. If a diagnosis of persistent microalbuminuria is made and the patient opted to take an ACE inhibitor, sequential urine testing is unlikely to alter management – hence, yearly screening as part of the annual review would be appropriate.

A4: What other issues need to be addressed with regard to cardiovascular risk?

This person has no evidence of coronary heart disease and she is currently normotensive, non-smoking and lean. In this age group there is no evidence to support the use of long-term lipid-lowering therapy or aspirin, and she has good glycaemic control. Apart from advice on keeping her weight under control and taking regular exercise, no other issues need to be addressed.

OSCE counselling cases

OSCE COUNSELLING CASE 1.7 – **'As someone with late-onset diabetes, should I be taking aspirin?'**

'Late-onset diabetes' is an old term for non-insulin-dependent diabetes, now termed type 2 diabetes mellitus. The short answer to the question is 'probably no'. This advice, however, is based more on consensus expert opinion than on trial evidence.

Patients with known coronary heart disease should receive secondary prevention with aspirin prescribed at a dose of 150 mg once daily. For patients with no evidence of coronary heart disease, primary prevention with aspirin 75 mg once daily used to be the norm but the risk of bleeding is now thought to outweigh the benefits. The outcome of a large trial (called ASCEND) assessing the use of aspirin in 'low-risk' type 2 diabetes is awaited.

OSCE COUNSELLING CASE 1.8 – **'Why is my blood pressure so difficult to control?'**

Hypertension is commonly associated with type 2 diabetes but is difficult to treat to target. This difficulty is made worse by the lowering of target levels, based on results of large clinical trials. In the UKPDS, blood pressure targets were less stringent than those that are now advocated for routine primary care (140/80 mmHg in type 2 diabetes); nevertheless, more than one-third of patients required three or more antihypertensive drugs. Added to this is the tendency for blood pressure to rise with age and obesity.

All of the major classes of antihypertensive agent can be used in patients with diabetes and raised blood pressure, and all classes produce an equivalent antihypertensive action and achieve target levels in a similar proportion of patients. Current guidelines support the use of ACE inhibitors as first-line in diabetes, followed by calcium channel blockers and low-dose diuretics.

DIABETES EMERGENCIES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely diagnosis?
Q2: What investigations would be performed?
Q3: How would the diagnosis be confirmed?
Q4: What would be the initial management?
Q5: What are the potential complications?
Q6: What issues need to be addressed when the patient has fully recovered?

CASE 1.13 – A 77-year-old man who is drowsy and dehydrated and with a plasma glucose of 84 mmol/L.

A 77-year-old man has been found collapsed at home by a care assistant. He was previously independent but known to have hypertension, angina and osteoarthritis. His regular medication is bendroflumethiazide 5 mg once a day, atenolol 50 mg once a day and aspirin. He had been noted to be lethargic over the previous few weeks and had been incontinent of urine on a couple of occasions. On arrival in the accident and emergency (A&E) department he is drowsy but oriented. Vital signs are normal but he is clinically dehydrated. Urinalysis shows ++++ glucose, ++ protein and + ketones. Plasma glucose is 84 mmol/L.

CASE 1.14 – A 32-year-old woman with abdominal pain and vomiting and a plasma glucose of 22 mmol/L and urinary ketones.

A previously well 32-year-old woman presents to the general practice surgery with a 24-h history of abdominal pain and vomiting. On direct questioning, she admits to weight loss over the previous 2 weeks, associated with thirst, polydipsia and polyuria. A finger-prick glucose is 22 mmol/L and urine dipstick testing shows +++ ketones.

CASE 1.15 – A 18-year-old man, known to have type 1 diabetes, who is unconscious.

An 18-year-old man who is known to have type 1 diabetes is found unconscious in his front garden. He had been playing football earlier in the day but had not complained of symptoms at that time. The diabetes is treated with four injections of insulin a day and his control is regarded as excellent.

OSCE counselling cases

OSCE COUNSELLING CASE 1.9 – **'What should I do with my insulin if I develop a vomiting illness that stops me eating?'**

OSCE COUNSELLING CASE 1.10 – **'What advice do I give to my partner if they witness me having a "hypo" reaction?'**

Key concepts

To work through the core clinical cases in this chapter, you will need to understand the following key concepts.

HYPOGLYCAEMIA

Hypoglycaemia in diabetes is caused by an imbalance of insulin (too much), exercise (too much) and glucose (too little). Patients usually experience warning symptoms and signs of hypoglycaemia, which prompt them to take treatment in the form of glucose. These are often listed as adrenergic (related to autonomic nervous system) and neuroglycopenic (brain hypoglycaemia); however, in reality patients will have warnings that are a combination of the two.

- *Adrenergic:* sweating, palpitations, hunger, tachycardia.
- *Neuroglycopenic:* dizzy, faint, confused, abnormal behaviour, unconsciousness.

HYPERGLYCAEMIA

Hyperglycaemia in type 1 diabetes may develop into diabetic ketoacidosis (DKA), while in type 2 diabetes it may develop into hyperosmolar non-ketotic pre-coma or coma (HONK).

Hyperglycaemic coma may be a presenting feature of diabetes or the result of intercurrent illness, manipulation of insulin (usually DKA) or concomitant medication (HONK). In many cases, the cause remains unknown.

Symptoms include lethargy, thirst, polydipsia, polyuria, nocturia, blurred vision and diminished conscious level, although unconsciousness is uncommon (below 5 per cent). Patients with DKA hyperventilate (as a result of the acidosis) and have sweet-smelling ketones on their breath. They may also have mildly raised plasma glucose levels, so the severity of their condition should not be judged on this measure. Abdominal pain, masquerading as an acute abdomen, is frequently present.

In HONK, patients are severely dehydrated and glucose levels are always very high. The prognosis in HONK is poor as a result of the concomitant illnesses (coronary heart disease, renal disease, cardiovascular disease) seen in this usually elderly cohort.

Answers

Clinical cases

CASE 1.13 – **A 77-year-old man who is drowsy and dehydrated with a plasma glucose of 84 mmol/L.**

A1: What is the likely diagnosis?

The likely diagnosis is hyperosmolar non-ketotic coma, which usually affects older people with type 2 diabetes and can be the presenting feature (as in this case). Precipitating causes include concurrent medication, including thiazide diuretics, and intercurrent illness (a UTI being possible in this scenario). Although termed 'coma', it is unusual for patients to be unconscious. Although this patient has + ketones, this is unlikely to represent acidosis, where more than ++ urinary ketones would be expected. Extremely high plasma glucose levels may be seen, as in this case.

A2: What investigations would be performed?

- venous blood for plasma glucose, U&Es, osmolality, bicarbonate, amylase and full blood count (FBC)
- arterial blood gases (ABGs)
- culture of urine and venous blood (and sputum if available)
- chest radiograph
- ECG.

A3: How would the diagnosis be confirmed?

Hyperglycaemia has already been demonstrated. Hyperosmolality can be confirmed after U&Es results are available using the formula $[2(Na^+ + K^+) + \text{urea} + \text{glucose}] > 350$ mmol/L. Plasma ketones should be within normal limits, and there should be no acidosis confirmed by ABGs or venous bicarbonate.

A4: What would be the initial management?

- Attention to airways, breathing and circulation, as necessary.
- Gain intravenous access and set up an intravenous infusion.
- Cardiac monitor.
- Treatment should then be given with intravenous insulin and intravenous fluids while monitoring electrolytes (Box 1.1).
- A nasogastric tube should be inserted and the patient should be fully anticoagulated with heparin.
- Consideration should be given to central venous pressure monitoring, urinary catheterization and broad-spectrum antibiotics.

A5: What are the potential complications?

The prognosis for HONK remains poor (20–30 per cent). Patients are at high risk of thromboembolism and congestive cardiac failure as a result of the fluid regimen. As a result of age and comorbidity, ischaemic heart disease, renal failure and stroke are common. Aspiration of gastric contents may occur in the setting of reduced consciousness.

Box 1.1 Hyperosmolar non-ketotic coma (HONK)

Insulin management of HONK

- Insulin 3 units/h via intravenous (IV) pump.
- Monitor glucose every hour using meter and laboratory testing.
- Aim for fall in glucose level of 3–6 mmol/h.
- At plasma glucose < 12 mmol/L, reduce to 1.5 units/h.
- Continue insulin infusion for at least 2 h.

Fluid management of HONK guided by central venous pressure line

- IV 0.9% saline if Na^+ < 160 mmol/L:
  - 1 L in 1 h hour 1: 1 L
  - 1 L in 2 h hour 3: 2 L
  - 1 L in 2 h hour 5: 3 L
  - 1 L in 4 h hour 9: 4 L
- Then every 4 h.
- Change to 5% dextrose when plasma glucose < 12 mmol/L.

Electrolyte (K^+) management of HONK

- No K^+ in litre 1, pending laboratory reading:
  - usually K^+ 3.5–5.5 mmol/L: add 20 mmol/L
  - recheck every 2 h and then every 4 h
  - if K^+ > 5.5 mmol/L: no K^+ and then recheck in 1 h
  - if K^+ < 3.5 mmol/L: add 40 mmol/L and then recheck in 1 h.
- If Na^+ > 160 mmol/L, use half 0.9% saline.

A6: What issues need to be addressed when the patient has fully recovered?

Despite the level of presenting glycaemia, management of the diabetes often does not involve insulin and some patients manage on diet only. The patient needs to be given dietary advice and specific diabetes education on issues such as monitoring and foot care. This would usually involve the specialist diabetes nurse and a dietitian. Other aspects of cardiovascular risk need to be assessed and, in this case, blood pressure medication may be changed from a high-dose thiazide to an ACE inhibitor.

CASE 1.14 – A 32-year-old woman with abdominal pain and vomiting and a plasma glucose of 22 mmol/L and urinary ketones.

A1: What is the likely diagnosis?

The likely diagnosis is diabetic ketoacidosis. This is an emergency complication of type 1 diabetes and can be the presenting feature, as in this scenario. Precipitating causes include intercurrent illness (e.g. UTI) and withholding insulin (in an established case of type 1 diabetes). Abdominal pain and vomiting are common and can lead to the erroneous diagnosis of an acute abdomen.

A2: What investigations would be performed?

- Venous blood for plasma glucose (to confirm the finger-prick test), U&Es, osmolality, bicarbonate, amylase and FBC.
- Plasma ketones may become a more widely used test with the arrival of near-patient analyses.
- ABGs (will be performed less frequently as plasma ketone testing becomes available).

- Culture of urine and venous blood.
- Chest radiograph.
- ECG.

A3: How would the diagnosis be confirmed?

Confirmation of hyperglycaemia with ketonuria and acidosis (pH <7.2, H^+ >63 mmol/L). Note that the hyperglycaemia is often not pronounced.

A4: What would be the initial management?

A4: The patient should be admitted to hospital. Intravenous access should be established for blood tests and infusion, and a cardiac monitor attached. Treatment should then be given with intravenous insulin and intravenous fluids while monitoring electrolytes (Box 1.2).

A5: What are the potential complications?

The prognosis for DKA should be good, given that it affects young people who rarely have other significant comorbidities. Cerebral oedema may occur during treatment, although the cause of this complication is unknown. Aspiration of gastric contents may occur in the setting of reduced consciousness.

A6: What issues need to be addressed when the patient has fully recovered?

The diagnosis of DKA implies that the patient has type 1 diabetes and will require life-long insulin. She will therefore need to be educated about the condition, and taught to inject insulin and how to

Box 1.2 Diabetic ketoacidosis (DKA)

Insulin management of DKA

- Insulin: 6 units/h via intravenous (IV) pump.
- Monitor glucose every hour using meter and laboratory testing.
- Aim for fall in glucose level of 3–6 mmol/h.
- At plasma glucose <12 mmol/L, reduce to 2–3 units/h.
- Continue insulin infusion for at least 24 h and no urinary ketones.

Fluid management of DKA

- IV 0.9% saline:
  - 1 L in 1 h hour 1: 1 L
  - 1 L in 1 h hour 2: 2 L
  - 1 L in 2 h hour 4: 3 L
  - 1 L in 2 h hour 6: 4 L
  - 1 L in 4 h hour 10: 5 L.
- Then every 4 h.
- Change to 5% dextrose when plasma glucose <12 mmol/L.

Electrolyte (K^+) management of DKA

- No K^+ in litre 1, pending laboratory reading:
  - if K^+ >5.5 mmol/L: no K^+ and recheck in 1 h
  - if K^+ <3.5 mmol/L: add 40 mmol/L and recheck in 1 h
  - if K^+ 3.5–5.5 mmol/L: add 20 mmol/L and recheck every 2 and then every 4 h.

self-monitor using finger-prick testing. She will need to be given information about the immediate complications of her condition (hypoglycaemia, DKA) and advised to avoid pregnancy until good glycaemic control is achieved. Ultimately she will need to understand the long-term risks of small and large vessel disease. These issues are best addressed by a diabetes nurse specialist and a formal education programme.

CASE 1.15 – **A 18-year-old man, known to have type 1 diabetes, who is unconscious.**

A1: What is the likely diagnosis?

The likely diagnosis is hypoglycaemia. As a general rule, an unconscious person with diabetes is hypoglycaemic until proved otherwise. This diagnosis is very likely in an otherwise fit young person who takes insulin. Precipitating factors in this case may be the exercise earlier in the day (the effects of exercise can last for many hours) and tight glycaemic control, which may provoke hypoglycaemia unawareness.

A2: What investigations would be performed?

See the answer to A3.

A3: How would the diagnosis be confirmed?

Treatment can be initiated without any investigation and before the hypoglycaemia has been confirmed (indeed, a satisfactory response to treatment will itself confirm the diagnosis). Finger-prick blood glucose testing will confirm a low blood glucose level.

A4: What would be the initial management?

In an unconscious patient the two main options are administration of glucagon or intravenous dextrose. Glucagon may be available because patients with type 1 diabetes are encouraged to keep a supply for this type of emergency. It comes as a powder that must be dissolved in water (a vial of sterile water is part of the kit). One vial = 1 mg = 1 unit, which is the standard injection, usually into muscle (but it can be subcutaneous or intravenous).

Intravenous dextrose is given by diluting 50% dextrose to half-strength and injecting 50 mL via a cannula. An infusion of 5% dextrose is then set up to reduce the risk of phlebitis.

A5: What are the potential complications?

Patients can suffer injury if they have lost their warnings of hypoglycaemia. In older patients, hypoglycaemia may present with neurological signs typical of stroke. Death is thought to be uncommon in this setting, although hypoglycaemia has been implicated in the higher incidence of the 'dead-in-bed' syndrome seen in type 1 diabetes. There is increasing evidence to implicate frequent hypoglycaemia as a risk factor for cardiovascular disease. With regard to the treatments, intravenous dextrose can cause phlebitis and glucagon is associated with nausea and vomiting.

A6: What issues need to be addressed when the patient has fully recovered?

You need to find out the cause of the event (too much insulin, too much exercise or too little food) and then provide education to prevent future recurrence. In this case, the active issues would be manipulation of the treatment regimen to be able to cope with exercise and possibly a relaxing of glycaemic control to reduce the risk of hypoglycaemia and decrease hypoglycaemia unawareness.

OSCE counselling cases

OSCE COUNSELLING CASE 1.9 – 'What should I do with my insulin if I develop a vomiting illness that stops me eating?'

The issue here is what most people with diabetes refer to as 'sick day rules'. Patients will understandably be concerned that they may become hypoglycaemic by taking insulin without food. Any intercurrent illness can cause blood glucose levels to rise, however, probably by increasing insulin resistance – hence the advice that '*You should never stop insulin!*'.

The patient should perform more frequent finger-prick testing, at least every 4 hours. This will allow detection of hypoglycaemia; if, as is likely, glucose levels rise, additional insulin (rapid acting) may then be needed.

For patients with type 1 diabetes, vomiting should raise the possibility of DKA and urine ketones should be checked at least twice a day. If these are positive to +++ or more, medical advice, and probably admission to hospital, must be sought. Near-patient plasma ketone testing is now more frequently performed by patients with type 1 diabetes, and they should be educated on the levels that may need medical intervention. In young people with type 1 diabetes, dehydration can develop very quickly and a low threshold for seeking medical advice should be promoted.

Patients should be aware of the actions to take during illness and how to access appropriate advice (probably not NHS Direct). This will mean telephone numbers of the diabetes specialist nurse team and agreed guidelines for out-of-hours management of diabetes emergencies

OSCE COUNSELLING CASE 1.10 – 'What advice do I give to my partner if they witness me having a "hypo" reaction?'

Symptoms of hypoglycaemia include lack of concentration, bad temper, change in behaviour, confusion and pallor, all of which are easily (perhaps more easily) recognized by a third party. It is vital that the partner of a person with diabetes is aware of the symptoms and signs of hypoglycaemia and is able to take appropriate action.

If the person's partner suspects hypoglycaemia, ideally he or she should encourage the patient to check a finger-prick glucose level. There is little to be lost by instituting treatment without confirmation of the diagnosis, however. Assuming the patient is alert, this involves taking food by mouth, usually in the form of glucose tablets: 10 g glucose is equivalent to three sugar lumps or one Dextrosol tablet. Patients with diabetes should always carry some form of glucose replacement; Dextrosol tablets are recommended because they are less palatable than sweets (and so less likely to be consumed as treats). Alternatives include 200 mL milk or 100 mL Coca-Cola (not Diet Coke). A longer-acting carbohydrate such as bread or biscuits should then be consumed.

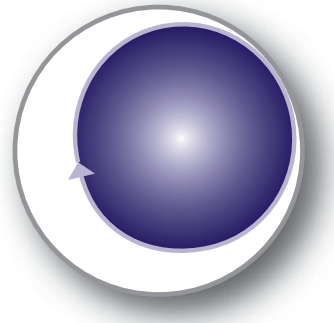
If the patient is semiconscious, a glucose gel can be administered via the buccal membrane. Glucostop is a glucose gel supplied in a plastic bottle with a nozzle. The gel can be squeezed into the mouth between the teeth and cheek and is absorbed into the circulation without the need for swallowing.

If the patient is unconscious, he or she should be placed into the recovery position. If the person's partner has been trained, glucagon can be administered (see above), otherwise medical aid should be summoned.

Perhaps the most important advice to the partner is not to panic and to be reassured that the normal outcome of a 'hypo' is that blood glucose levels rise in response to the body's natural adrenergic response.

REVISION PANEL

- Diagnostic guidelines for diabetes are revised every 10 years or so and are based on consensus opinion rather than absolute cut-offs for symptoms or complications. These typically apply to type 2 diabetes. The diagnosis of type 1 diabetes, if suspected, should never be delayed by requesting investigations such as a glucose tolerance test or HbA1c, which may take days to be reported.
- A diagnosis of diabetes should never be casually applied to a patient, since it is likely that this can never be erased from their medical record and will have a major impact on their insurance premiums (e.g. life assurance, travel insurance). This shows the importance of laboratory testing rather than near-patient testing in type 2 diabetes.
- Diabetes has major implications for driving, the authorities being particularly interested in hypoglycaemia and the presence of complications such as retinopathy and peripheral neuropathy. The regulations are constantly changing, and readers should refer to the relevant website for the latest situation for their country.
- Targets for glycaemic control, typically measured by HbA1c, should be tailored according to the circumstances of the individual, bearing in mind the downsides of treatment (hypoglycaemia, weight gain).
- There are several therapeutic options that may be used to lower blood glucose (currently seven classes). The choice will be guided by considerations of cost, safety, efficacy and patient preference. Cost pressures have had a major impact on national guidelines, such as those of NICE.
- Small vessel, diabetes-specific complications affect the eyes, feet and kidneys. Screening for these complications forms part of the diabetes review, with prevention being far more effective than 'cure'.
- Large vessel complications, affecting the coronary, cerebral and peripheral arteries, are more common in people with diabetes, and hence there are aggressive blood pressure and lipid targets. The impact of tight glycaemic control, especially in people with established large vessel disease, is a controversial topic.
- An unconscious person with diabetes should always be suspected of being hypoglycaemic. In a person with diabetes who has abdominal pain and vomiting, diabetic ketoacidosis should be excluded.



2 Endocrinology

Andrew Levy

HYPERTHYROIDISM

ADDISON'S DISEASE (AUTOIMMUNE ADRENAL FAILURE)

CUSHING'S DISEASE

ACROMEGALY

HYPERTHYROIDISM

Questions

Clinical case

For the case scenario given, consider the following:

Q1: What do you think the likely diagnosis is?
Q2: What tests could you do to confirm this?
Q3: What tests would help establish the cause?
Q4: What is the initial management?
Q5: What are the long-term complications/sequelae?

CASE 2.1 – **A 26 year-old-receptionist presents with palpitations and weight loss.**

Although pleased about the weight loss, the patient is concerned that her menstrual periods have stopped and it is the anxiety related to this, she believes, that is responsible for disturbing her sleep. Her partner has insisted that she seek a medical opinion.

OSCE counselling cases

OSCE COUNSELLING CASE 2.1 – **'Do I have to have surgery?'**

OSCE COUNSELLING CASE 2.2 – **'Will I be able to have children after radioiodine treatment?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Graves' disease is an autoimmune condition characterized by thyroid overactivity, eye changes (Graves' infiltrative ophthalmopathy or, more specifically, 'orbitopathy') and skin changes (pretibial myxoedema and finger clubbing, known as thyroid acropachy). The three components may occur in isolation, in any combination or not at all. Their clinical courses are usually independent and unpredictable. Skin changes are rare. Note that 'myxoedema' was an old term for thyroid underactivity but is now reserved for the skin changes that sometimes occur in Graves' disease.

In all patients with hyperthyroidism (even if iatrogenic), sympathetic overactivity leads to retraction of the upper lid, with widening of the gap between the upper and lower lids when the eyes are open (the palpebral fissure). Increased exposure of the cornea and conjunctiva leads to grittiness and soreness of the eyes.

In Graves' orbitopathy, which can occur without hyperthyroidism, autoimmune-mediated infiltration of the contents of the orbit and periorbital tissue leads to non-pitting and boggy soft tissue swelling, with increased volume of extraocular muscles, connective tissue and fat. This pushes the globe of the eye forward and can interfere with the function of the extraocular muscles, optic nerves and eyelids, reducing protection afforded by the tear film and leading to double vision and even blindness.

People with hyperthyroidism tend to be sweaty, tremulous, anxious and sometimes rather aggressive. Proximal myopathy (weakness of the thigh and arm muscles) makes their muscles ache and, although tired, sleeping is often difficult. Appetite is increased, weight tends to decrease and stools are often softened but not frankly diarrhoeal. Fertility is reduced, and menstrual periods become lighter or stop altogether. Patients often find that their short-term memory is impaired, and it may become difficult for them to make rational decisions.

In addition to sore eyes, the patient may complain of fast palpitations. If present, a thyroid bruit (the sound of blood rushing through the highly vascular overactive gland) is a useful sign because it excludes thyroiditis and exogenous thyroid hormone as causes of hyperthyroidism.

Answers

Clinical case

CASE 2.1 – **A 26-year-old receptionist presents with palpitations and weight loss.**

A1: What do you think the likely diagnosis is?

Hyperthyroidism would fit all of the symptoms here and, as it is very common, it is certainly an important diagnosis to confirm or refute. There are differential diagnoses: panic attacks, agitated depression, tachyarrhythmias (e.g. paroxysmal supraventricular tachycardia, atrial fibrillation or flutter) and excessive caffeine or other stimulant ingestion could be responsible for some, if not all, of the symptoms. Anyone taking thyroxine surreptitiously or being prescribed an excessive dose for the treatment of hypothyroidism may also present in this way. Much rarer endocrine conditions such as phaeochromocytoma should also be kept in mind.

A2: What tests could you do to confirm this?

Laboratories vary in the thyroid function tests that they are willing to run for screening, but all provide a measure of thyroid-stimulating hormone (TSH), which is suppressed by most causes of thyrotoxicosis. A free thyroxine (FT4) is also useful and will be raised above the upper limit of normal in hyperthyroidism. Unusually for tests of endocrine function, the TSH and FT4 are very reliable, and single samples taken at any time of day will be representative of thyroid function.

A3: What tests would help establish the cause?

Clinically, the presence of Graves' eye disease establishes the diagnosis in a patient presenting with thyrotoxicosis, and no further investigations need to be done. Similarly, if a thyroid bruit is present, this is unequivocal evidence of primary hyperthyroidism and excludes thyroiditis and the effects of exogenous thyroid hormones. Thyroid autoantibodies (antimicrosomal antibodies) are usually present, but this test is not often particularly helpful.

Imaging the thyroid using ultrasonography or isotope scans is not often required in patients presenting with hyperthyroidism. Confirming the presence of a solitary 'hot nodule', however, can be useful because radioiodine is a more appropriate treatment than anti-thyroid medication, which, although effective, would have to be continued in the long term to maintain euthyroidism.

A4: What is the initial management?

In this case, after suitable explanation of the various options, treatment with carbimazole 40 mg daily, to which thyroxine (100 μg daily) is added after a couple of weeks, is probably the most secure route to rapid restoration of euthyroidism. The patient must be warned that carbimazole can cause dangerous neutropenia idiosyncratically, and that the first sign of this is a sore throat. If this symptom occurs, the patient must be advised to stop the drug immediately and seek medical advice.

An alternative to the block and replace regimen described above is to treat with carbimazole alone and repeat thyroid function tests every 3–4 weeks, and to reduce the dose of carbimazole as the condition comes under control, aiming for a dose of 5–10 mg daily after 2–3 months.

A5: What are the long-term complications/sequelae?

Abnormalities of thyroid function are very common and highly amenable to treatment. We often forget, however, just how uncomfortable these conditions can be for the patient. Graves' eye disease, for example, can produce major cosmetic problems, even if vision remains entirely unaffected. Primary hyperthyroidism often takes well over a year or longer to treat effectively, and during this time the patient's ambient thyroid hormone levels, symptoms and mood often fluctuate uncomfortably.

Persistent hyperthyroidism is associated with osteoporosis, proximal myopathy and cardiomyopathy, manifesting as atrial fibrillation and its associated increase in thromboembolic risk.

OSCE counselling cases

OSCE COUNSELLING CASE 2.1 – **'Do I have to have surgery?'**

In the past, subtotal thyroidectomy was extensively used to treat hyperthyroidism. Radioiodine is a very effective treatment and anti-thyroid drugs are also safe to use as a long-term therapy if the patient objects to radioiodine or if there is concern that radioiodine might worsen Graves' orbitopathy. Thyroid surgery is reserved for patients in whom very rapid and permanent control of hyperthyroidism is required, or in whom a goitre is causing compressive or cosmetic problems.

It is hoped that early and aggressive immunosuppressive treatment, principally with prednisolone, will reduce the frequency and extent of surgery required to correct problems associated with Graves' orbitopathy.

OSCE COUNSELLING CASE 2.2 – **'Will I be able to have children after radioiodine treatment?'**

It is a commonly held misconception that radioiodine has an adverse effect on fertility or that having children is inadvisable after radioiodine treatment. Neither is true. The only caveats to radioiodine use in this respect are that radioiodine has exactly the same effect on the thyroid of the developing fetus as it does on the mother. It is therefore vital that radioiodine is not inadvertently given to a woman who is pregnant. Health and safety regulations also seek to limit third-party exposure to irradiation and, for that reason, it is not an ideal treatment for anyone who cannot at least temporarily escape spending a great deal of time in close proximity to young children.

ADDISON'S DISEASE (AUTOIMMUNE ADRENAL FAILURE)

Questions

Clinical case

For the case scenario given, consider the following:

Q1: What do you think the likely diagnosis is?
Q2: What tests could you do to confirm this?
Q3: What tests would help establish the cause?
Q4: What is the initial management?
Q5: What are the long-term complications/sequelae?

CASE 2.2 – **A 19-year-old student presents with an 18-month history of progressive tiredness, weight loss and lethargy.**

One year before presentation she had a common cold that forced her to stay away from lectures for 2 days. Three months before presentation, another common cold laid her low for almost 2 weeks, during which time she lost 3 kg in weight. The local student health doctors assured her that the symptoms were the result of either being pregnant or taking drugs. On examination, she was noted to have darker skin than her mother and pigmented palmar creases.

OSCE counselling cases

OSCE COUNSELLING CASE 2.3 – **'Why did this happen to me?'**

OSCE COUNSELLING CASE 2.4 – **'How will it affect my life?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Before steroids (glucocorticoids) became available, autoimmune destruction of both adrenal glands invariably led to death from circulatory collapse. In much the same way that the autoimmune destruction of pancreatic islets, which characterizes type 1 diabetes mellitus, does not become apparent until many months after it starts, autoimmune destruction of the adrenal glands has usually been advancing for many months by the time it is recognized. In retrospect, the patient may have noticed progressive impairment of the ability to respond appropriately to acute stress and that it is taking longer to recover from trivial illnesses such as the common cold.

Both adrenal glands, including the zona glomerulosa, the aldosterone-producing and the angiotensin II responsive layer, are entirely destroyed in primary adrenal failure. Consequently, the patient becomes critically deficient in both glucocorticoids (cortisol) and mineralocorticoids (aldosterone), resulting terminally in profound hyperkalaemia and hyponatraemia. Lack of glucocorticoid feedback at the level of the hypothalamus and pituitary leads to a marked increase in adrenocorticotrophic hormone (ACTH) and associated melanocyte-stimulating hormone (MSH), which stimulates skin melanocytes. By making the patient look suntanned, the increase in skin pigmentation (including parts that are not exposed to the sun and new scars) tends to disguise the fact that the patient is gravely ill, and it can be surprisingly easy to overlook or ascribe the associated history of weakness, weight loss and intermittent vomiting to other causes.

In secondary adrenal failure (i.e. resulting from pituitary failure), lack of glucocorticoids is not as absolute, and catastrophic inability to respond to stress is rare. In addition, as ACTH levels are low rather than high, pigmentation does not occur and mineralocorticoid production is impaired only modestly because it is controlled by the renin–angiotensin–aldosterone pathway rather than the pituitary. As secondary adrenal failure is often associated with hypogonadotrophic hypogonadism, adrenal pre-androgens and gonadal testosterone are both low and secondary sexual hair is often lost.

Answers

Clinical case

CASE 2.2 – **A 19-year-old student presents with an 18-month history of progressive tiredness, weight loss and lethargy.**

A1: What do you think the likely diagnosis is?

This is a fairly classic presentation of Addison's disease. It is relatively easy in retrospect to put together the symptoms and signs of Addison's disease, but it can be very difficult to recognize, particularly in its early stages, when adrenal function is only suboptimal under stress. Delay in diagnosis is therefore very understandable.

A2: What tests could you do to confirm this?

The characteristic biochemical changes of hyperkalaemia and hyponatraemia tend to occur relatively late and, if the diagnosis is suspected, it is perfectly acceptable to start treatment with glucocorticoids immediately, pending an opportunity to carry out a diagnostic test. The confirmatory test (Synacthen) is described below in OSCE counselling case 2.3.

A3: What tests would help establish the cause?

In the developed world at least 80 per cent of cases of Addison's disease are caused by autoimmune destruction of the adrenal glands. Tuberculosis (TB) remains a relatively common cause of Addison's disease in the absence of autoimmune disease and is suggested by the presence of enlarged adrenal glands with necrotic areas and often dots of calcification visible on computed tomography (CT). In boys under 16 years of age, X-linked adrenoleukodystrophy, diagnosed by measuring an increase in circulating very-long-chain fatty acids, is an important cause of adrenal failure. In older patients, measurement of anti-cardiolipin antibodies, a marker of primary antiphospholipid syndrome, is useful if features such as recurrent venous thrombosis suggest that the condition is not idiopathic.

In primary adrenal failure, a random plasma ACTH will be high. In secondary adrenal failure, the symptoms and signs related to the condition are usually much more subtle and the biochemical signs do not appear. ACTH will be low or low-normal and the cortisol response to exogenous ACTH will be suboptimal.

A4: What is the initial management?

Glucocorticoid replacement (usually with 10–15 mg hydrocortisone first thing in the morning and another 5 mg hydrocortisone at around 4pm) is required immediately. In primary Addison's disease, mineralocorticoid replacement with fludrocortisone 50–100 μg/day is also required. As Addison's disease is often disclosed by an episode of acute stress, it is not uncommon for glucocorticoid treatment to be given parenterally and at a higher dose at least initially.

A5: What are the long-term complications/sequelae?

Patients with autoimmune Addison's disease are more likely to have other autoimmune diseases, and a proportion of them claim to 'not feel right' despite what appears to be adequate replacement therapy. Under conditions of stress, patients should be asked to step up their glucocorticoid dose two- or threefold for a few days; they are asked to wear a MedicAlert bracelet or necklace and carry an injectable form of glucocorticoid to use if they find themselves unable to take oral steroids. For some patients, a longer-acting glucocorticoid such as prednisolone seems to be more comfortable than the short-acting hydrocortisone.

OSCE counselling cases

OSCE COUNSELLING CASE 2.3 – **'Why did this happen to me?'**

All patients with autoimmune Addison's disease have detectable adrenal cortex or steroid 21-hydroxylase autoantibodies. The specific human leucocyte antigen (HLA) subtypes HLA-A1, HLA-B8 and HLA-DR3 predispose to developing the condition. It is not clear, however, why some patients develop the condition and others do not. The risk of developing other autoimmune conditions such as type 1 diabetes mellitus, primary gonadal failure, hypoparathyroidism, Hashimoto's thyroiditis, vitiligo and pernicious anaemia is modestly increased in patients with Addison's disease.

If the diagnosis is suspected in an ill patient, formal diagnosis can wait and immediate treatment with glucocorticoids is usually appropriate. A high plasma ACTH in the presence of low random cortisol is often sufficient to confirm the diagnosis. If doubt remains, a cortisol response of less than 495 nmol/L 1 h after a 250 μg intravenous bolus of synthetic ACTH (Synacthen) confirms the diagnosis.

OSCE COUNSELLING CASE 2.4 – **'How will it affect my life?'**

For most patients the diagnosis of Addison's disease has no adverse long-term effects on life or lifestyle. Some patients, however, claim not to feel as well as they did before the onset of overt disease, despite optimized glucocorticoid and mineralocorticoid replacement. For some of these patients, additional replacement of adrenal pre-androgens has been advocated, but there is little good evidence to support this at the present time.

The long-term outlook for Addison's disease is good, provided that the patient is fully aware of the implications of the condition and the need to respond to stressful situations by temporarily increasing the glucocorticoid dose.

CUSHING'S DISEASE

Questions

Clinical case

For the case scenario given, consider the following:

Q1: What do you think the likely diagnosis is?
Q2: What tests could you do to confirm this?
Q3: What tests would help establish the cause?
Q4: What is the initial management?
Q5: What are the long-term complications/sequelae?

CASE 2.3 – **A 56-year-old woman presents with depression, hirsutism, weight gain and muscle weakness.**

On examination, her general practitioner found her to be hypertensive and to have wide purple striae on her abdomen and thighs. Her visual fields were full to confrontation and there was no bruising.

OSCE counselling cases

OSCE COUNSELLING CASE 2.5 – **'Will "the tumour" spread to other parts of my body?'**

OSCE COUNSELLING CASE 2.6 – **'Can I have tablets instead of an operation?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Hypercortisolaemia (Cushing's syndrome) is in most cases iatrogenic, an unavoidable side effect of the high-dose glucocorticoid treatment required for many immune and autoimmune conditions. Rarely, hypercortisolaemia is pituitary dependent (Cushing's disease) and is the result of a pituitary adenoma secreting ACTH. Cushing's syndrome can also result from other sources of ACTH such as carcinoid tumours of the lung or gut or from adrenal adenomas and carcinomas secreting inappropriate amounts of cortisol. It is often surprisingly difficult to identify the source of the problem with certainty and to treat it adequately, because even the most careful battery of well-organized investigations can be misleading. The first task is to confirm the presence of hypercortisolaemia and, if that can be confirmed, investigations are redirected to identify the source.

In hypercortisolaemia of malignancy, there may be insufficient time for the typical phenotype to develop. In more chronic cases, patients characteristically gain weight, develop neuropsychiatric problems (often accentuation of premorbid personality – miserable people become more miserable and vice versa), proximal myopathy (difficulty standing from sitting without using the arms), muscle wasting, central accumulation of fat (filling in the temporal fossae and development of the characteristic 'moon face' and 'buffalo hump'), and weakening of the skin leading to the formation of wide purple stretch marks (striae) and easy bruisability (although bruises are not often evident in the clinic). Hypertension, hirsutism (caused by increased ACTH drive to adrenal androgen production) and glucose intolerance are also common. In Cushing's disease the ACTH-induced increase in production of adrenal pre-androgens (responsible for the hirsutism) tends to protect against steroid-induced thinning of the skin.

Answers

Clinical case

CASE 2.3 – **A 56-year-old woman presents with depression, hirsutism, weight gain and muscle weakness.**

A1: What do you think the likely diagnosis is?

Although Cushing's syndrome is suggested by the combination of mental and physical changes listed, the only one that is specific in the circumstances is the presence of wide purple striae rather than pale striae. Simple gross obesity could be responsible for everything else. Obese people are often depressed about their inability to lose weight, and the sheer mass of tissue to carry around can make them feel weak, even though they tend to be much stronger than an equivalent patient with hypercortisolaemia. The fat tissue can aromatize pre-androgens to androgens and oestrogens, leading to hirsutism, and there is an association between obesity and hypertension, both of which are extremely common. Cushing's syndrome is an important diagnosis to make, but it is as well to remember that Cushing's disease is extremely rare compared with simple obesity.

A2: What tests could you do to confirm this?

If hypercortisolaemia is suspected, one of the most reliable screening tests currently available in the UK is to measure 24-h urinary free cortisol, three samples of which should be assayed along with creatinine clearance to ensure that the patient has managed to produce complete collections. Pregnancy, pain, heavy alcohol ingestion or alcohol withdrawal and vigorous exercise, particularly if the patient gets up very early every morning to run, will increase urinary free cortisol to above the normal range. As cortisol is metabolized by the kidneys during filtration, if the patient drinks more than 5 L of fluid daily, urinary free cortisol will be high. In addition, some drugs unexpectedly increase urinary free cortisol (e.g. statins) or interfere with analytical methods, such as co-eluting with cortisol on high-performance liquid chromatography (HPLC) (e.g. carbamazepine). The best test to distinguish Cushing's from pseudo-Cushing's is the dexamethasone suppressed corticotrophin-releasing hormone (CRH) test. Eight 0.5 mg doses of dexamethasone are given orally at strict 6-h intervals from midday, ending at 6am on the morning of the test. Two hours later, the patient is given 100 μg CRH (strictly 1 μg/kg); 15 min later a single cortisol above 38 nmol/L suggests hypercortisolaemia.

A3: What tests would help establish the cause?

Establishing the cause of Cushing's syndrome can be difficult. Delays associated with various investigations can make it difficult to carry them out in a logical order without taking an excessive time to reach a conclusion. A peripheral ACTH measurement is useful because a very high level suggests ectopic ACTH syndrome and a very low level suggests adrenal disease. Pituitary magnetic resonance imaging (MRI) may show a macroadenoma (a tumour greater than 10 mm in diameter or distorting the sella turcica), in which case it is very likely to be responsible for the Cushing's syndrome. Conversely, as the prevalence of incidental pituitary adenomas under 4 mm in diameter in the general population is very high (probably around 10 per cent), an MRI scan is insufficient evidence to send a neurosurgeon in after it. Computed tomography or MRI of the adrenal glands showing a unilateral nodule with contralateral atrophy suggests a primary adrenal lesion. For many patients, petrosal sinus sampling, i.e. sampling the venous outflow of the pituitary, is necessary to confirm or refute a pituitary source of excess ACTH. The level of ACTH should be at least double the level found in peripheral samples taken simultaneously and should increase further (to at least three times peripheral levels) in response to CRH.

A4: What is the initial management?

The initial management of Cushing's disease (i.e. pituitary-dependent Cushing's syndrome) is trans-sphenoidal microadenomectomy by a skilled neurosurgeon. If the problem is a carcinoid tumour of the lungs secreting ACTH, or an adrenocortical tumour producing too much cortisol, the respective tumours should be removed by an appropriate specialist.

A5: What are the long-term complications/sequelae?

Unfortunately, cure of Cushing's disease is difficult to achieve and a large minority of patients relapse at some time or have only a partial remission and end up with persistent hypercortisolaemia. Improvements in trans-sphenoidal surgery and endoscopic adrenal surgery should allow a higher percentage of 'long-term remissions' in the future and a reduction in the prevalence of patients suffering the consequences of persistent hypercortisolaemia, principally osteoporosis and the risks associated with impaired glucose tolerance or frank diabetes mellitus, hypertension and obesity.

OSCE counselling cases

OSCE COUNSELLING CASE 2.5 – 'Will "the tumour" spread to other parts of my body?'

Metastatic spread of pituitary tumours has been documented but is extremely rare. The word 'benign' is, however, a little misleading in that some corticotrophic adenomas can infiltrate locally, particularly after bilateral adrenalectomy, which removes endogenous feedback inhibition of tumour growth (Nelson's syndrome). It is not unusual for corticotrophic adenomas to be so small that, despite causing dramatic symptoms and signs, they are not visible on pituitary MRI. Even stranger is the relatively high remission rate when unaffected pituitary tissue is excised at surgery.

Cushing's disease has such a high risk of recurrence or failure of initial treatment that the word 'remission' rather than 'cure' is used.

Standard fractionated linear accelerator pituitary radiotherapy to the remnant reduces recurrence rate about fivefold but is associated with a small increased risk of other tumour formation in the radiation field and an increase in the risk of stroke. It is an important treatment, particularly if the patient has had bilateral adrenalectomy as part of the management of the condition.

Appropriate treatment of the primary disease does result in weight loss, but many patients find that it is difficult to shed all of the extra weight they accumulated before effective treatment was instigated.

OSCE COUNSELLING CASE 2.6 – 'Can I have tablets instead of an operation?'

Tablets tend not to be used first-line because surgery offers the chance of immediate remission, confirmation of the diagnosis histologically, and an opportunity to debulk an adenoma that may subsequently be associated with space-occupying problems if allowed to continue to grow in situ. Drugs are sometimes used in preparation for surgery or if the patient has very aggressive disease causing severe neuropsychiatric symptoms, but they are often not very well tolerated. In the UK, metyrapone is used to inhibit adrenal hormone synthesis competitively. Ketoconazole, an imidazole antifungal agent, is also a useful adrenocortical hormone synthesis inhibitor. Etomidate at low dose is useful if rapid intravenous control of excessive glucocorticoid levels is required, as is sometimes the case in Cushing's syndrome secondary to malignant disease.

ACROMEGALY

Questions

Clinical case

For the case scenario given, consider the following:

Q1: What do you think the likely diagnosis is?
Q2: What tests could you do to confirm this?
Q3: What tests would help establish the cause?
Q4: What is the initial management?
Q5: What are the long-term complications/sequelae?

CASE 2.4 – **A 44-year-old woman presents with excessive sweating and an increase in hat size over a 3-year period.**

She comments that her face and hands just seem 'bigger' than before.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Acromegaly is caused by the presence of a growth hormone (GH)-secreting tumour of the anterior pituitary (somatotroph adenoma) that develops after puberty. Coarsening of the facial features, headaches, drenching sweats and a progressive increase in jaw, glove, ring and shoe sizes are well-known features of excess GH. The most common and troublesome symptoms are, however, carpal tunnel syndrome, obstructive sleep apnoea and osteoarthritis, caused by persistent growth of soft tissue and cartilage. These changes can be partially reversed in some patients when the condition is treated, but unfortunately many of the changes remain and widespread arthritis, caused by disruption of joint cartilage, can be disabling.

If a somatotroph adenoma occurs before increased sex hormones cause the epiphyses of long bones to fuse at puberty, the patient has the potential to become a giant. In true gigantism, the somatotroph adenoma not only arises early in life but also impairs the function of pituitary gonadotrophs, giving rise to hypogonadotrophic hypogonadism. Without gonadotrophins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]), puberty cannot proceed, and if the epiphyses remain open persistent growth of long bones can continue throughout life, leading in exceptional cases to remarkably tall stature.

As GH is involved primarily in the growth of the long bones, whereas sex hormones are responsible for growth of the axial skeleton, patients with gigantism tend to have very long limbs but relatively short backs. These so-called 'eunuchoid' proportions, where span exceeds standing height, also tend to be found in other conditions associated with low sex hormone levels such as Klinefelter's syndrome (XXY).

Thickening of the tissues of the nasopharynx predisposes to severe snoring and frequent episodes of complete obstruction of the airways during the night. This leads to arterial blood oxygen desaturation and increasing respiratory efforts, causing partial wakefulness until eventually airflow resumes. Consequently, patients frequently complain of tiredness in the morning. Obstructive sleep apnoea has also been implicated in the pathogenesis of hypertension, which affects over one-third of people with acromegaly.

Treatment of acromegaly involves trans-sphenoidal debulking of the tumour and in some cases pituitary radiotherapy. Drug treatment is also used, with long-acting parenteral somatostatin (GH-release inhibiting hormone) analogues such as octreotide LAR or lanreotide, dopamine (D2) analogues such as cabergoline or bromocriptine, which reduce GH and insulin-like growth factor I (IGF-I) levels in about 10 per cent of patients, and GH-receptor blockers (pegvisomant). Surgery to relieve arthritis, nerve compression syndromes, snoring and facial deformity is also sometimes required. It is believed that acromegaly is associated with an increased incidence of bowel tumours, and patients in some centres are offered a routine colonoscopic screening when first diagnosed and at the age of 60 years.

Answers

Clinical case

CASE 2.4 – **A 44-year-old woman presents with excessive sweating and an increase in hat size over a 3-year period.**

A1: What do you think the likely diagnosis is?

Acromegaly is likely. It should be remembered that there can be large discrepancies between circulating GH levels and the phenotypic changes that result. Some patients with very high levels of GH do not seem to develop many of the phenotypic features of acromegaly. Other patients with only modestly elevated GH levels sometimes continue to grow. Growth of the hands and feet is relatively pronounced because of the multiple cartilaginous interfaces between the many small bones. Growth of the skull is minimal and is a feature that is more characteristic of Paget's disease of bone. In acromegaly, increased hat size is the result of facial soft tissue growth rather than bony growth, although on radiograph and CT some skull thickening does occur.

Excessive sweating is also a feature of oestrogen withdrawal and thyrotoxicosis, both of which should be considered because they are much more prevalent problems, even though neither would explain the rest of this patient's symptoms.

A2: What tests could you do to confirm this?

In many cases, the phenotypic changes of acromegaly are so obvious that little needs to be done to confirm the diagnosis. The condition might be 'burnt out', however, and, as persistent disease is an indication for surgery, it is important to measure a few random GH levels (three samples 20–30 min apart) and an IGF-I, and to request an MRI scan of the pituitary. The pulsatile nature of GH release means that a single measure of GH is not useful. If doubt remains about the diagnosis (and usually it does not), failure to suppress GH to <2 mU/L (0.6 mg/L) after 75 g glucose orally confirms the diagnosis.

A3: What tests would help establish the cause?

Rarely, acromegaly is part of the multiple endocrine neoplasia type 1 (MEN-1) syndrome, Carney complex or the isolated familial acromegaly syndrome. Somatotrophic adenomas have been described in association with GH-releasing hormone-secreting gangliocytomas in the region of the pituitary. The cause of acromegaly, however, is *always* a somatotrophic adenoma secreting too much GH.

A4: What is the initial management?

In an elderly patient with comorbidity, in whom somatotroph adenoma is unlikely to cause local space-occupying problems, it is perfectly reasonable to do nothing. In a younger patient, trans-sphenoidal microadenomectomy or debulking of a macroadenoma is still first-line treatment. In terms of GH reduction, drug treatment with somatostatin analogues or the new GH-receptor blockers has a higher chance of success than surgery, but both are prohibitively expensive and, as far as we know at the moment, necessitate long-term treatment.

A5: What are the long-term complications/sequelae?

Complications of acromegaly and its treatment are hypopituitarism, local space-occupying issues (such as visual field changes) and the effects of excessive GH levels on somatic growth and metabolism. Growth hormone is diabetogenic, and acromegaly is associated with hypertension and an enhanced risk of

cardiomyopathy (which might be specific to acromegaly), and respiratory complications related to altered chest shape and movements.

REVISION PANEL

- Thyrotoxicosis is a common endocrine condition resulting from excess thyroid hormone as part of Graves' disease, a multinodular goitre or a solitary toxic nodule.
- Thyrotoxicosis can be treated medically with anti-thyroid medication (e.g. carbimazole), radioactive iodine or surgery.
- Addison's disease results in glucocorticoid and mineralocorticoid deficiency from autoimmune primary adrenal insufficiency, but secondary glucocorticoid deficiency may result from pituitary disease and lack of ACTH.
- Addison's disease requires life-long hormone replacement with glucocorticoids (e.g. hydrocortisone) and mineralocorticoids (e.g. fludrocortisone).
- Hypercortisolaemia (Cushing's syndrome) may result from either excess adrenal glucocorticoid synthesis (adrenal tumour), excessive steroid therapy, or secondary to excess ACTH production from a pituitary adenoma, carcinoid tumour or rarely other ACTH-secreting tumours (e.g. lung).
- The optimal treatment of Cushing's syndrome is surgery to remove the source of excessive ACTH.
- Acromegaly results from excessive GH production from a pituitary tumour. If the tumour is active before sex hormone production, then this will result in gigantism.
- The optimal treatment of acromegaly and gigantism is to remove the tumour responsible for excess growth hormone production.

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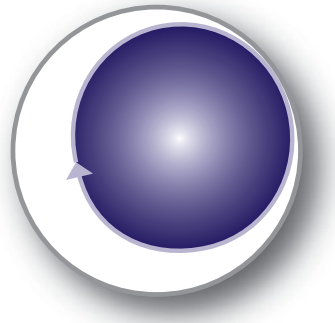

3 Rheumatology

Mark Pugh

POLYARTHRITIS

MONOARTHRITIS

SYSTEMIC RHEUMATOLOGICAL ILLNESSES

BACK PAIN

POLYARTHRITIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: How would you investigate this patient?
Q3: How would you confirm the likely diagnosis?
Q4: How would you initially manage the patient?
Q5: What are the principles of long-term management?
Q6: What is the prognosis?

CASE 3.1 – **A 38-year-old man develops painful and swollen hand joints.**

A 38-year-old man presents with a 4-month history of pain and swelling of the knuckles, wrists, knees, ankles and toes. He has no significant past history and the general practitioner confirms the swelling of the joints and notes a history of more than an hour's stiffness of the joints in the morning. Initial blood tests reveal a microcytic anaemia of 11.8 g/dL and a C-reactive protein (CRP) of 9.6 g/dL.

CASE 3.2 – **Pain in the hands, knees and feet in a 46-year-old woman.**

A recently postmenopausal woman presents with a 6-month history of pain and swelling in her hands, knees, neck and feet. The pain limits her ability to use her hands, and the knee and foot pain limits her mobility. Apart from her joint pain she is otherwise well and there is no contributory past medical history. Examination demonstrates tender double bumps over the ends of her fingers, especially the index and middle finger, tenderness around the base of the thumb, limited neck movement, crunching knees with swelling, and bilateral early bunions.

CASE 3.3 – **Knee pain in a schoolgirl.**

A 16-year-old girl has a 6-year history of intermittent knee pain. She presented previously at the age of 10 years also for knee pain, which was attributed to growing pains. Now she describes pain in the knees worse at the end of the day and especially bad after exercise. Her knees are often sore after sitting, and difficult pain on ascending stairs has adversely affected her school attendance. Knee swelling occurs sometimes. She also has pain in her hands, elbows and tops of her legs. Her joints often click so loudly that other people pass remarks. She seems well in other respects and, apart from the previous assessment for knee pain, there is no past medical history. Her general practitioner detected no obvious joint problem and the full blood count (FBC), erythrocyte sedimentation rate (ESR) and rheumatoid factor (RF) were reported as normal.

OSCE counselling case

OSCE COUNSELLING CASE 3.1 – **'What can be done if I get a flare-up of my rheumatoid arthritis?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Patients generally describe any pain around a joint as 'arthritis'. Arthritis, by definition, means inflammation of the joint and therefore in the absence of confirmatory signs should not be diagnosed. Arthralgia is the name for a painful joint without signs of inflammation. Pain can also be referred as well as originating from ligaments, tendons, muscles, nerves, arteries and skin around the joint.

There are a wide number of causes of arthritis, including:

- degenerative: osteoarthritis
- trauma
- infective: viral, septic, reactive, parasitic, fungal
- endocrine: hypothyroid, hyperthyroid, hyperparathyroid
- malignancy: paraneoplastic, secondary or primary malignancy
- allergic: erythema nodosum, drug-induced
- autoimmune: connective tissue disease, seronegative arthritis, vasculitis
- crystal arthritis: gout, pseudo-gout
- congenital: Stickler's syndrome.

Answers

Clinical cases

CASE 3.1 – **A 38-year-old man develops painful and swollen hand joints.**

A1: What is the likely differential diagnosis?

With a history of multiple, small joint swelling, more than 60 min of morning stiffness and a raised ESR, rheumatoid arthritis is a likely diagnosis. Other causes of arthritis also need to be considered, such as other connective tissue disorders, seronegative arthritis, infection, endocrine disorders, drugs and malignancy.

A2: How would you investigate this patient?

A full history and examination are important. Examination should confirm the presence of inflammation of the joints characterized by pain and swelling. All the joints and other systems should be examined, looking for evidence of systemic involvement and other possible causes of the arthritis apart from rheumatoid arthritis. Ultrasound or magnetic resonance imaging (MRI) could be used where the signs of synovitis are equivocal.

A3: How would you confirm the likely diagnosis?

The diagnosis is clinical, with the presence of inflammation in the characteristic joints being sufficient to indicate arthritis. The American College of Rheumatology diagnostic criteria are often quoted, but the inclusion of erosions and rheumatoid nodules means that these criteria have low sensitivity in early disease. A high CRP or positive RF, although not always present in early disease, suggests a likelihood of progression to early erosions.

A4: How would you initially manage the patient?

The initial management should be clinically to confirm the diagnosis, followed by baseline investigations including FBC, CRP (or similar measurement of inflammation), urea and electrolytes (U&Es), liver function tests (LFTs), and screening for RF and antinuclear factors. These tests should be consistent with rheumatoid arthritis and should not suggest an alternative diagnosis. The tests are also useful because many of the drugs used to treat rheumatoid arthritis are toxic. Radiographs of the hands and feet, any other involved joints and the chest will often not demonstrate change early in the disease course but will be useful to monitor disease progression. If the presentation is sufficiently characteristic, the patient should be referred for specialist assessment immediately to maximize the chances of commencing treatment early in the disease course, which has been shown to improve the prognosis. The use of analgesics and anti-inflammatory drugs may provide some symptom relief while baseline investigations are undertaken. When rheumatoid arthritis is confirmed, the patient should be offered disease-modifying anti-rheumatoid drugs (DMARDs), usually in combinations including methotrexate, without delay to prevent the development of joint damage.

A5: What are the principles of long-term management?

The ongoing management of rheumatoid arthritis involves ensuring complete control of inflammation, monitoring joint damage, checking for other systemic manifestations, and screening for the development of treatment side effects. As with the development of any chronic illness, patient education

about the illness and its treatment is important to allay fears and promote treatment compliance. Patients with autoimmune arthritis are at significant risk of the development of cardiovascular disease and should be screened for this.

A6: What is the prognosis?

Extra-articular manifestations of rheumatoid arthritis include:

- *skin:* ulcers and nodules
- *lung:* fibrosis, effusions and nodules
- *neurological:* myopathies and neuropathies
- *eye:* secondary Sjögren's syndrome and inflammation
- *systemic:* anaemia, weight loss and fevers
- *skeletal:* osteoporosis
- *cardiovascular:* high incidence of cardiovascular disease and rare muscle, valve or pericardial involvement.

The progress for joint damage is as follows: 5–10 per cent of patients do not develop damage; the remainder of patients do develop damage, with 40–70 per cent after a chronic disease course developing significant levels of damage and disability, and 20–40 per cent after a relapsing and remitting course associated with lesser levels of damage. Aggressive early treatment is believed to hold the key to improving the long-term prognosis in rheumatoid arthritis.

CASE 3.2 – **Pain in the hands, knees and feet in a 46-year-old woman.**

A1: What is the likely differential diagnosis?

There is a wide differential, but the presence of Heberden's nodes in the hands, a characteristic pattern of joint involvement and the absence of synovitis point to a diagnosis of osteoarthritis.

A2: How would you investigate this patient?

Blood tests are not essential but will help rule out alternative diagnoses. Radiographs of the symptomatic joints may demonstrate the typical changes of joint space narrowing, subchondral sclerosis, bone cysts and osteophytes.

A3: How would you confirm the likely diagnosis?

A history and examination should be sufficient to rule out alternative diagnoses and confirm the diagnosis. A radiograph is probably the most useful diagnostic test, but early changes can be subtle and it is possible to have osteoarthritis coexisting with gout or an inflammatory arthritis.

A4: How would you initially manage the patient?

Conservative measures should be addressed, including weight control, the use of padded footwear such as trainers, and regular exercise. A walking stick can help knee symptoms, and orthoses will help foot symptoms. Physiotherapy can alleviate local symptoms. Topical non-steroidal anti-inflammatory drugs (NSAIDs) or capsaicin cream provide some relief. Intra-articular steroids are safer than NSAIDs and may be appropriate to relieve joint symptoms. Patients should always be encouraged to use analgesics other than NSAIDs as first-line drugs, e.g. paracetamol. Although scientific data are sparse, there is some evidence that complementary therapies may provide some symptom relief, and they are popular with patients.

A5: What are the principles of long-term management?

The complications of osteoarthritis relate to the development of disability secondary to joint involvement. Patients can be reassured that, although activity may produce increased symptoms, only heavy manual

work or professional-level sports activity will probably accelerate joint damage. Treatment may produce complications that require treatment, of which NSAID-induced gastrointestinal damage is probably the most common. Surgery, especially of the knee and hip, is very successful for patients with significant pain and disability associated with significant radiological damage.

A6: What is the prognosis?

Most patients are concerned about the development of future disability but can be reassured that this is unlikely The key to successful management is to ensure that the patient self-manages the problem because cure is not possible and medical disease modification remains unachievable.

CASE 3.3 – **Knee pain in a schoolgirl.**

A1: What is the likely differential diagnosis?

Benign hypermobility is the most likely diagnosis. An underlying inflammatory arthritis is unlikely because of the length of the history, the normal-looking joints and the absence of inflammatory markers in the blood, but it needs to be ruled out.

A2: How would you investigate this patient?

A history looking for pointers to alternative diagnoses, such as psoriasis, or systemic features of a connective tissue disorder or juvenile idiopathic arthritis, is important. A family history of joint pains in childhood is often present, highlighting a familial link in this disorder. Examination of the joints, looking for the absence of joint deformity or ongoing synovitis, would virtually rule out an underlying inflammatory arthritis. Radiographs and blood tests would be helpful to rule out alternative diagnoses.

A3: How would you confirm the likely diagnosis?

Generalized benign hypermobility is diagnosed by demonstrating hypermobility in classic sites, including bending the little finger to a right angle, bending the thumb back to touch the forearm, hyperextension of the elbow, and bending forwards and placing the palms of the hands flat on the floor. Although normal on initial examination, retropatellar pain can often be elicited by Clarke's test (compression of the patella with restricted knee extension). Flat feet are usually present. More unusual causes of hypermobility, such as Marfan's and Ehlers–Danlos syndromes, should be considered.

A4: How would you initially manage the patient?

Reassurance that this is not the start of a deforming arthritis is usually very important. Anti-inflammatory and analgesic drugs offer some relief and can be important if the pain is severe enough to disrupt sleep or limit activities. Physiotherapy can improve pain by limiting joint movement through muscle development. Orthoses to correct flat feet and raise the heel can improve not only foot and ankle symptoms but also those from the knee, hip and back.

A5: What are the principles of long-term management?

Occasionally these patients can have recurrent dislocations of the shoulder, hip or knee. This may require joint-stabilizing surgery but if possible this should be avoided. On a day-to-day basis, most of the problems relate to maintaining normal functions such as school attendance and physical activity.

A6: What is the prognosis?

Symptoms typically improve with age, but improvement is not universal. Benign hypermobility does not appear to be associated with the development of early osteoarthritis.

OSCE counselling case

OSCE COUNSELLING CASE 3.1 – **'What can be done if I get a flare-up of my rheumatoid arthritis?'**

Patients can find the psychological impact of flare-ups difficult and need to be reassured that, even with a background of good control, flare-ups can occur. Sometimes no identifiable reason can be found to explain the flare-up; otherwise a waning of the effect of current medication, intercurrent infection or stress may be involved. Single joint flare-ups are usually easier to deal with than multiple joint problems. Patients should be advised to maximize their analgesic and anti-inflammatory medication, rest the affected joint and use ice packs. With no more intervention, the flare-up may settle. If it does not, intra-articular steroid for a localized problem, or intramuscular, oral or intravenous steroid for a more generalised flare-up, may be necessary. A change in disease-modifying therapy or stepping up to biological therapy may be indicated if the flare-up signals a loss of effect of the patient's current therapy.

MONOARTHRITIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: How would you investigate this patient?
Q3: How would you confirm the likely diagnosis?
Q4: How would you initially manage the patient?
Q5: What are the principles of long-term management?
Q6: What is the prognosis?

CASE 3.4 – **An elderly man presents with a reddened, very painful and swollen ankle of short duration.**

A 73-year-old man requires an urgent appointment for assessment of a painful left ankle. This started suddenly 2 days ago and is now so painful that he cannot put his foot to the floor. On examination, the ankle is red and significantly swollen, but the rest of his joints are unremarkable. He has a history of two episodes of pain, redness and swelling of his right big toe, which settled over 2–3 weeks with NSAIDs and rest. Currently, he is on bendroflumethiazide for treatment of hypertension but is otherwise fit and well.

CASE 3.5 – **'It all started when my second toe swelled like a red sausage.'**

A 32-year-old woman describes a painful swelling of the second toe. This came on spontaneously 7 weeks ago. Examination of her other joints, including her back, reveals no abnormality of joint shape or function. While examining her joints, you notice scaling patches of skin with underlying erythema over her elbows and knees. She has had these for 3–4 years and has treated it as dermatitis with simple cream. More recently, she has noticed some flaking of her toenail on the end of the painful toe. The rest of the general physical examination is normal.

CASE 3.6 – **A 50-year-old man with a painful knee.**

A 50-year-old travelling salesman presents with difficult pain in his right knee after he has been driving for more than an hour. This has been coming on for the past 3 years. He describes discomfort while walking up stairs and occasional pain in his knee in bed at night. Typically he has few symptoms earlier in the day, but his knee aches by the end of the day. On review of his musculoskeletal system, he has a history of low back pain, and pain in the ends of his fingers, the base of the thumb and big toe. He had a cartilage operation on his right knee at the age of 29 years after a football injury.

OSCE counselling case

OSCE COUNSELLING CASE 3.2 – **'I am not keen on taking medication every day. Is there anything else I can do to help my osteoarthritis?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Monoarthritis is usually caused by a different diagnosis from polyarthritis, although there is some overlap. Septic arthritis is typically monoarticular and therefore joint aspiration is a more important investigation in this group of patients than in patients with polyarthritis. Aspiration can both aid diagnosis and be of therapeutic value.

Septic arthritis requires prolonged antibiotic treatment, and every effort should be made to confirm the diagnosis before treatment is started. Most peripheral joints can be aspirated at the bedside; however, hip joint aspiration is usually best done with ultrasonic guidance.

Other causes of monoarthritis include osteoarthritis, crystal arthritis (e.g. gout), sarcoidosis and seronegative arthritis.

Answers

Clinical cases

CASE 3.4 – **An elderly man presents with a reddened, very painful and swollen ankle of short duration.**

A1: What is the likely differential diagnosis?

With a similar history of self-limiting arthritis in the toe and a risk factor for hyperuricaemia with diuretic therapy, the most likely diagnosis is gout. The diagnosis not to miss is septic arthritis. This could also represent an alternative crystal arthropathy or an intermittent seronegative rheumatoid arthritis.

A2: How would you investigate this patient?

At the time of the attack, there is typically a very high ESR or CRP, with a raised white blood cell (WBC) and platelet count. The serum urate is sometimes decreased during an acute attack, producing a falsely normal-looking serum urate level. Hyperuricaemia is common in gout but not essential, and a normal urate level does not exclude the diagnosis. Factors associated with gout include alcohol, warfarin therapy, low-dose aspirin, myeloproliferative disorders, tumour lysis, psoriasis and renal function. Tophi show up on radiographs, and gout can produce a typical pattern of joint damage, although radiological findings are not always present.

A3: How would you confirm the likely diagnosis?

The definitive diagnostic test would be joint aspiration of the affected joint, with demonstration of urate crystals under a polarizing microscope; appropriate microbiological assessment should also rule out sepsis. Identification of urate crystals from another larger and possibly easier to aspirate joint, tophus or bursa would be virtually diagnostic. A raised serum urate level is usual but not inevitable.

A4: How would you initially manage the patient?

The initial management of gout attempts to control pain and promote resolution of the acute attack. Rest is advised and patients should be well hydrated. If gout is secondary to an underlying medical problem such as renal failure, this may need addressing. Provided that there are no contraindications, medical options include NSAIDs, colchicine, and intramuscular or intra-articular steroids. If nothing else, the attack should settle spontaneously in 4 weeks.

A5: What are the principles of long-term management?

Prophylactic treatment should not be started until 2–3 weeks after the acute event (due to the risk of exacerbation). Once the patient has recovered from the acute attack it, may be necessary to start prophylactic treatment. The most commonly used drug is allopurinol, which is started at a low dose and titrated upwards, balanced against normalization of the hyperuricaemia. The drug is usually well tolerated but, in the event of problems such as rash and occasional leucopenia, alternatives include the uricosurics probenecid and sulfinpyrazone, febuxostat or low-dose daily colchicine. Sometimes it is necessary to use combination therapy to ensure the treatment goal of a low normal serum urate level.

A6: What is the prognosis?

Repeated attacks of gout can damage the underlying joint. The associated hyperuricaemia may produce a nephropathy or renal stones. Provided the hyperuricaemia can be controlled by correcting the cause or using specific therapy, however, the outlook for this condition is very good.

CASE 3.5 – 'It all started when my second toe swelled like a red sausage.'

A1: What is the likely differential diagnosis?

The rash is likely to be psoriasis and the dactylitis is most probably associated psoriatic arthritis. Infection and gout can also produce dactylitis.

A2: How would you investigate this patient?

Examination of the flexures and scalp may reveal additional psoriasis. Further examination of the fingernails may reveal characteristic nail pitting. A radiograph of the toe will most probably reveal little of diagnostic value but, as psoriatic arthritis is typically a chronic problem, a radiograph should be done for baseline assessment to allow future mapping of possible damage. Routine blood testing will usually reveal a raised inflammatory response.

A3: How would you confirm the likely diagnosis?

The diagnosis is clinical, based on a picture of a distal small joint and predominantly lower limb large joint arthritis in association with, or with a history of, psoriasis. Routine testing should not point to another diagnosis. Family history is often helpful, revealing arthritis, psoriasis or inflammatory bowel disease.

A4: How would you initially manage the patient?

The first aim should be to control the patient's pain. Anti-inflammatory medication may settle the attack; intra-articular steroid injection may also help. Some patients need to start taking DMARDs to control the problem. Anti-tumour necrosis factor (TNF) therapy can be used in patients with resistant disease.

A5: What are the principles of long-term management?

This may represent the start of a chronic and possibly more widespread problem requiring long-term therapy. It should always be borne in mind that in the future the patient may develop associated ankylosing spondylitis, iritis, inflammatory bowel disease and genitourinary tract inflammation.

A6: What is the prognosis?

The prognosis depends on the number of joints involved. Limited joint involvement has an excellent long-term outlook, whereas multiple joint involvement has a prognosis similar to that of chronic progressive rheumatoid arthritis.

CASE 3.6 – A 50-year-old man with a painful knee.

A1: What is the likely differential diagnosis?

Based on the history of previous cartilage surgery and pain on exercise at the end of the day, as well as pain in typical sites, osteoarthritis is the most likely diagnosis.

A2: How would you investigate this patient?

The most useful single investigation would be a weight-bearing radiograph of the knee. Radiographs of the other sites may also reveal degenerative changes. Blood tests looking for alternative diagnoses may be helpful.

A3: How would you confirm the likely diagnosis?

The absence of any other cause of arthritis and the presence of the typical radiological changes of osteoarthritis, including joint space narrowing, subchondral sclerosis, subchondral bone cysts and osteophytes, should be sufficient. Examination of the knee may demonstrate a joint effusion, decreased joint movement with discomfort, and possible crepitus.

A4: How would you initially manage the patient?

Aspiration of the knee may ease symptoms, especially when combined with intra-articular steroid injection. Physiotherapy may relieve symptoms. Simple analgesics or NSAIDs may provide additional relief.

A5: What are the principles of long-term management?

Osteoarthritis is not associated primarily with systemic complications but drug treatment is and therefore should be used in the lowest dose and for the shortest period possible.

A6: What is the prognosis?

Full recovery is unlikely, and the chronic nature of the problem may threaten this man's livelihood. Consideration should be given to advice about an automatic car or possibly a change in position in his company if his symptoms cannot be helped. Surgical treatment may be necessary in the longer term but is not inevitable.

OSCE counselling case

OSCE COUNSELLING CASE 3.2 – **'I am not keen on taking medication every day. Is there anything else I can do to help my osteoarthritis?'**

The patient's concerns about medication can sometimes be allayed by discussion about the risks and benefits of medication. Education about the nature of the condition will promote independence. Reducing obesity, minimizing traumatic activity and using padded footwear will improve the prognosis. Orthoses can improve the symptoms of foot osteoarthritis, and a walking stick can help mobility in patients with knee and hip osteoarthritis. Regular exercise aimed at improving aerobic fitness, muscle strength and proprioception will also improve mobility. Other forms of physiotherapy can be used to treat local symptoms. Many patients who dislike the idea of taking oral medication are happy to consider topical treatment in the form of NSAIDs or capsaicin. Intra-articular steroids or hyaluronic acid derivatives can also help symptoms.

SYSTEMIC RHEUMATOLOGICAL ILLNESSES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: How would you investigate this patient?
Q3: How would you confirm the likely diagnosis?
Q4: How would you initially manage the patient?
Q5: What are the principles of long-term management?
Q6: What is the prognosis?

CASE 3.7 – **A young woman with joint pains and feeling unwell.**

A 29-year-old woman presents with a 6-month history of pain and swelling, which started in the fingers and wrists and then spread to her shoulders, knees and ankles. She was treated for pleurisy twice 4 and 3 months ago, and since then says she has felt unwell. Most recently, she says that she has developed a rash on her cheeks and forehead.

CASE 3.8 – **'You've seen me before with sinusitis. Now I feel terrible, my eye is sore and I think I coughed up blood today.'**

A 49-year-old man feels unwell with temperatures, myalgia, and pain in his wrists, knees and ankles. He is losing weight and cannot work. His left eye has become increasingly sore and red. For some time he has had a cough productive of yellow/white sputum, but today he coughed up red blood. Investigations reveal a haemoglobin (Hb) of 10.8 g/dL, white cell count (WCC) of 14.8×10^9/L and ESR of 98 mm/h. Urinalysis demonstrated blood +++ and protein ++. Apart from a 3-year history of sinusitis requiring antibiotics and nasal spray, there is no significant past medical history.

CASE 3.9 – **An elderly woman with aching shoulders and thighs, a painful temporal headache and a sudden onset of sight loss in her right eye.**

A 73-year-old woman describes a 3-week history of stiffness in her proximal arms and thighs, which have become increasingly painful. The pain is especially bad at night and first thing in the morning. In the past 2 days she has noticed tenderness in the scalp when combing her hair and headache over the same site. Today she awoke to realize that she had no sight in her right eye.

OSCE counselling case

OSCE COUNSELLING CASE 3.3 – **'Will having lupus give me problems if I want to become pregnant?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

The multisystem involvement of this group of conditions, although rare in routine practice, requires all clinicians to maintain awareness of them. Involvement of systems such as the kidneys and lungs can often be silent in the early stages, requiring active screening. Many of the differential diagnoses in this group will have similar investigation findings such as a high CRP and a positive antinuclear antibody (ANA), which can be found in infection and malignancy.

The connective tissue disorders are a group of conditions including rheumatoid arthritis, systemic lupus erythematosus (SLE), Sjögren's syndrome, myositis/dermatomyositis, scleroderma and undifferentiated connective tissue disease. Although recognizably different, they share many features and should be screened for as a group.

The vasculitides are a diverse group of conditions that can be primary or secondary in nature. The primary, or systemic, vasculitides are usually classified on the basis of the size of the arteries involved:

- *large vessel:* temporal and Takayasu's vasculitis
- *medium-sized:* polyarteritis nodosa, Kawasaki's disease
- *small vessel:* Wegener's granulomatosis, Churg–Strauss syndrome, microscopic polyarteritis, Henoch–Schönlein purpura, essential cryoglobulinaemic vasculitis, leucocytoclastic vasculitis.

Secondary causes include the connective tissue diseases, infection, malignancy and allergy, e.g. drug induced.

Answers

Clinical cases

CASE 3.7 – **A young woman with joint pains and feeling unwell.**

A1: What is the likely differential diagnosis?

With a symmetrical small and large joint arthritis, a systemic illness including pleurisy and a facial rash in a woman, SLE (lupus) is a possible diagnosis. Consider infection, sarcoid, vasculitis and malignancy.

A2: How would you investigate this patient?

A routine blood screen including FBC, ESR, U&Es and LFTs should be ordered, as well as ANA, double-stranded DNA (dsDNA) and antibodies to extractable nuclear antigen (ENA). Urinalysis looking for blood or protein should be checked. In view of the previous chest symptoms, a chest radiograph should be ordered.

A3: How would you confirm the likely diagnosis?

Finding a positive ANA rarely leads to a diagnosis of lupus. The diagnosis, like much of rheumatology, is clinical, and a specialist opinion usually needs to be sought to confirm it. Often the American College of Rheumatology revised diagnostic criteria are used as a basis to establish the diagnosis, which requires having four of a list of 11 typical features of the condition. Lupus is also diagnosed by demonstrating typical histological features, especially when patients do not fulfil the College diagnostic criteria.

A4: How would you initially manage the patient?

Once the diagnosis has been confirmed, the management depends on the extent of systemic involvement – e.g. a patient with active lupus nephritis will require more aggressive management initially than a patient who has mild arthritis and a rash. Isolated rash and arthritis can be managed with NSAIDs, hydroxychloroquine and sunblock. Systemically ill patients often require prednisolone, usually combined with immunosuppressive drugs to control their disease.

A5: What are the principles of long-term management?

The management of lupus requires a broad range of clinical skills and may require input from several disciplines. Patients with complex disease are best managed by clinicians with experience of the condition. Lupus can affect any system in the body, and any new symptoms should be investigated to check for possible lupus involvement. Renal, lung and cardiovascular involvement need to be screened for regularly. The use of toxic therapies can complicate matters with side effects. There is also an increased risk of infection as a result of the immunosuppressing nature of SLE and its treatments. In a young woman, future pregnancies may well need careful planning because the disease and drugs may adversely affect fertility. Pregnancy can impose additional strains on already damaged organs such as the lungs or kidneys.

A6: What is the prognosis?

Spontaneous remission or cure is unlikely. The prognosis of lupus depends on the severity of the condition and is particularly influenced by the presence or absence of renal disease, with only 70 per cent of patients with renal disease being alive after 15 years.

CASE 3.8 – 'You've seen me before with sinusitis. Now I feel terrible, my eye is sore and I think I coughed up blood today.'

A1: What is the likely differential diagnosis?

With renal and upper and lower respiratory symptoms, eye inflammation, myalgia and arthralgia, and blood evidence of inflammation, systemic vasculitis is probable, and in this case Wegener's granulomatosis is the most likely subtype. Alternative diagnoses such as malignancy need to be positively ruled out.

A2: How would you investigate this patient?

Tests should aim to assess the cause, extent and severity of the involvement. Full blood count, ESR, U&Es and LFTs may all demonstrate abnormal results. A sinus radiograph, possibly including CT, chest radiograph, 24-h urine protein loss and urine microscopy should also be performed. Testing for ANA, complements C3 and C4 and anti-neutrophil cytoplasmic antigen (ANCA) will help establish the diagnosis. Specialist ophthalmological and ear, nose and throat (ENT) assessment and treatment may be helpful. Renal or lung investigation may require specialist input.

A3: How would you confirm the likely diagnosis?

Treatment of vasculitis is long term and typically requires long-term toxic therapy; therefore biopsy is regarded as the gold standard for diagnosis. The nasal mucosa, lung and kidney are possible sites for biopsy. A positive cytoplasmic ANCA/PR3 result is highly specific and sensitive for Wegener's granulomatosis.

A4: How would you initially manage the patient?

Having assessed the extent of involvement, treatment typically involves an induction phase designed to arrest inflammation and a longer-term treatment phase aimed at maintaining disease suppression. Drugs commonly used are steroids, immunosuppressants and cytotoxics. Co-trimoxazole is prescribed for patients with *Staphylococcus aureus* in the nose because it is believed to reduce relapses of the condition when used in combination with other immunosuppressants.

A5: What are the principles of long-term management?

In this patient with renal involvement, potential renal failure needs to be assessed. The lung involvement can progress to fibrosis. Involvement of the upper airways can produce aggressive local damage, even eroding through the floor of the anterior skull. Untreated eye involvement can lead to blindness. Secondary infection is a constant threat as a result of the condition or treatment. Flare-ups are not uncommon, often requiring temporary increases in treatment.

A6: What is the prognosis?

A medical cure is not possible. Long-term follow-up with careful multisystem assessment is essential to maximize the success of treatment. The prognosis is adversely affected by renal involvement; overall, the 10-year survival rate is about 80 per cent.

CASE 3.9 – **An elderly woman with aching shoulders and thighs, a painful temporal headache and a sudden onset of sight loss in her right eye.**

A1: What is the likely differential diagnosis?

The history of polymyalgic symptoms, temporal headache and sudden onset of blindness strongly suggests a diagnosis of temporal arteritis.

A2: How would you investigate this patient?

This is a rare example of a rheumatological emergency. Consideration should be given to whether ordering tests will delay the introduction of prednisolone. After just 48 h of prednisolone therapy, the typical blood findings of a highly raised ESR and the characteristic biopsy evidence will disappear. Prompt initiation of steroids, however, may promote return of vision in the affected eye and should preserve vision in the non-affected eye.

A3: How would you confirm the likely diagnosis?

The definitive test is biopsy of an affected temporal artery. As a result of the irregular pattern of vessel involvement, single biopsy may be falsely negative in up to 30 per cent of patients.

A4: How would you initially manage the patient?

The initial management involves high-dose prednisolone, typically 40 mg/day or more. As treatment will last for more than 3 months, the patient should be commenced on bone protection therapy with a bisphosphonate and calcium and vitamin D3.

A5: What are the principles of long-term management?

The longer-term management involves reducing the steroids, balancing them against the recurrence of symptoms such as headache and proximal myalgia and a raised ESR. Most patients will eventually be able to come off steroids. If it is not possible to reduce the maintenance steroid dose, it may be necessary to commence steroid-sparing drugs such as azathioprine or methotrexate.

A6: What is the prognosis?

Blindness occurs in up to 15 per cent of patients with this condition. The mortality is not raised compared with a matched population, even though aortic aneurysm and cerebral and myocardial infarction are rare complications of the condition.

OSCE counselling case

OSCE COUNSELLING CASE 3.3 – **'Will having lupus give me problems if I want to become pregnant?'**

Having lupus can affect pregnancy in a number of ways. Overall, lupus increases the risk of a conception not progressing to term from the normal 10 per cent to 25 per cent. Antiphospholipid antibody syndrome increases the risk of miscarriage. Women who have Ro and La antibody-associated lupus have an approximately 5 per cent chance of transplacental spread of antibodies, producing neonatal lupus, which can include neonatal heart block. Renal and pulmonary disease can be complicated by pregnancy. Finally, many of the drugs used to treat lupus may adversely affect fertility.

BACK PAIN

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: How would you investigate this patient?
Q3: How would you confirm the likely diagnosis?
Q4: How would you initially manage the patient?
Q5: What are the principles of long-term management?
Q6: What is the prognosis?

CASE 3.10 – **A sudden onset of back pain in an elderly woman.**

A 72-year-old woman describes an acute onset of mid-back pain. She has not had anything like this before and presents to the accident and emergency (A&E) department. There was no obvious precipitant for her back problem. A radiograph reveals a wedge fracture of T8.

CASE 3.11 – **A stiff painful back and a red eye.**

An ophthalmologist recommends a 26-year-old man to seek an opinion about his long history of back pain and stiffness after developing a red and painful left eye.

OSCE counselling case

OSCE COUNSELLING CASE 3.4 – **'What can I do to prevent osteoporotic fractures in the future?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Most adults will suffer back pain at some stage, but for many people it is a chronic problem. For this group of patients, reassurance, active support and advice to mobilize early and not expect a complete cure are important if disability is to be avoided. Patients under the age of 25 years or over the age of 55 years who present with constant back pain of longer than 6 weeks' duration usually require radiological assessment. A history of malignancy, pain that wakes the patient, demonstrable motor weakness, bowel or bladder involvement and associated systemic involvement suggest significant pathology that may require more than just a simple radiograph.

Answers

Clinical cases

CASE 3.10 – **A sudden onset of back pain in an elderly woman.**

A1: What is the likely differential diagnosis?

A spontaneous osteoporotic fracture of the spine is the probable diagnosis. Other causes of a fracture include trauma, infection and malignancy. Women generally have a lower bone stock than men and with increasing age are prone to develop osteoporosis. The condition can be secondary to a number of medical conditions, including chronic obstructive pulmonary disease (COPD), malabsorption, inflammatory arthritis, steroid use, premature menopause, hyperparathyroidism, hyperthyroidism, chronic renal failure, immobility and autoimmune arthritis.

A2: How would you investigate this patient?

A history should be taken to look for the above risk factors, and for a past history of other low trauma fractures. Blood testing should be normal in primary osteoporosis, but it is important to rule out secondary causes of osteoporosis and alternative diagnoses. Family history is a very important risk factor for osteoporosis.

A3: How would you confirm the likely diagnosis?

The gold standard for diagnosis is a dual-energy X-ray absorptiometry (DEXA) scan of the lumbar spine and hip. Other techniques exist, including qualitative computed tomography (QCT), peripheral DEXA scan and ultrasonography of the heel. A DEXA scan of the spine and hip is best at predicting hip fracture and is sensitive and specific enough to allow monitoring of therapy. In this case, provided that no alternative diagnoses are present, it is not necessary to scan the woman to justify starting medication.

A4: How would you initially manage the patient?

Pain control is the first goal of management. Typically this will require opiate-based treatment and advice about rest. The pain normally settles progressively over 12 weeks. Calcitonin injections or nasal spray can be used in the first week after a fracture to augment pain control. The use of transcutaneous electronerve stimulation can augment pain control. Surgery, although still at an early stage of development, can be used to reform the vertebrae and reduce pain.

A5: What are the principles of long-term management?

The fracture, although painful, rarely produces neurological deficit. The principal risk is that having one osteoporotic fracture is a strong risk for future fractures. Further vertebral fracture can produce a fixed kyphosis. Fracture of the hip is the most serious of the osteoporosis-associated fractures; up to one-third of patients may die and only one-third of patients will return to an independent existence after the fracture. Treatment involves bisphosphonates and usually calcium and vitamin D3. Further fractures despite appropriate treatment with bisphosphonates may require treatment with a parathyroid hormone (PTH) analogue or denosumab, a monoclonal antibody treatment.

A6: What is the prognosis?

Treatment of osteoporosis needs to be linked to a fall-prevention strategy to maximize the longer-term outlook. Successful treatment reduces the risk of future fracture by half.

CASE 3.11 – **A stiff painful back and a red eye.**

A1: What is the likely differential diagnosis?

The connection to make is iritis and ankylosing spondylitis. It is possible that no connection exists, in which case in a young person the cause of the back pain could be mechanical, post-traumatic, associated with disc disease or developmental.

A2: How would you investigate this patient?

A blood screen may demonstrate raised inflammatory markers. A radiograph may demonstrate sclerosis and erosion of the sacroiliac joint and squaring of the vertebrae, with calcification of the intervertebral ligaments. Magnetic resonance imaging can demonstrate changes not visible on a radiograph. An isotope bone scan can detect inflammation in the sacroiliac joint or lower back.

A3: How would you confirm the likely diagnosis?

Demonstration of the typical radiological changes, although not present in every case, is diagnostic. The presence of the human leucocyte antigen HLA-B27 gene is not diagnostic because it is found in at least 7 per cent of the general population. Its absence, however, virtually rules out ankylosing spondylitis.

A4: How would you initially manage the patient?

The principal mode of treatment of mild to moderate forms of the disease is physiotherapy. This can be augmented by NSAIDs; phenylbutazone, banned from general use, still has a place for pain relief in this condition. Methotrexate and sulfasalazine, although helpful for peripheral disease, do not influence axial disease significantly. More aggressive ankylosing spondylitis not responding to the above measures can be treated with anti-TNF therapies.

A5: What are the principles of long-term management?

The more the spine is involved in ankylosis, the more complications can occur, including the mechanical effects of kyphosis or ankylosis of the ribs producing respiratory restriction, and a risk of fracture as a result of associated osteoporosis and the altered mechanics of the stiff spine. It is possible to develop an associated peripheral arthritis, psoriasis, iritis, colitis and inflammation of the genitourinary tract. Rarely, associated cardiac and pulmonary complications can occur.

A6: What is the prognosis?

Long-term surveillance aims to detect the complications of this chronic illness early. An essential part of follow-up also involves the monitoring of compliance with physiotherapy. The prognosis is adversely affected by age of onset before 16 years, early hip involvement, raised CRP and peripheral joint involvement.

OSCE counselling case

OSCE COUNSELLING CASE 3.4 – **'What can I do to prevent osteoporotic fractures in the future?'**

About 70 per cent of the risk of developing osteoporosis is genetic, but a number of factors are important. Lifestyle measures such as refraining from smoking, keeping alcohol consumption within recommended limits and maintaining a healthy body mass index (BMI) are beneficial. Calcium intake equivalent to 800 mg/day is important throughout adult life. The use of vitamin D3 supplementation in frail elderly people is associated with a reduced incidence of hip fractures. Levels of exercise in childhood and adolescence are one of the determining factors of peak bone mass. In later life, regular exercise reduces bone loss and decreases the incidence of falls. In elderly people who are at risk, the use of hip protectors may reduce the incidence of hip fractures. Premature menopause is a risk factor for osteoporosis, and the use of hormone replacement therapy (HRT) delays the onset of menopausal bone loss until therapy is stopped. This translates into a lifetime fracture reduction risk of about 3 per cent. In people with risk factors, a DEXA scan can be used to assess bone density, and appropriate therapy can reduce the risk of future fracture.

REVISION PANEL

- Rapid diagnosis and early commencement of combination therapy and possibly biological drugs improve the prognosis in rheumatoid arthritis.
- Blood tests and X-rays are typically normal in early osteoarthritis.
- Hypermobility is a common cause of recurrent intermittent joint pain in young teenagers.
- Flare-ups of underlying autoimmune arthritis often signal the need to increase treatment.
- Gout presents with intermittent severe arthritis, often affecting the big toe joint, and is usually associated with a raised serum urate level.
- Dactylitis, a swollen digit, is classically associated with psoriatic arthritis or gout, but rarely it may be a sign of infection.
- An isolated positive ANA result is rarely associated with lupus (SLE). The diagnosis is based on characteristic clinical and investigational results.
- Systemic vasculitis is rare, but recognition and appropriate treatment are important to reduce mortality. Most patients are systemically unwell and have signs that can be confused with infection. Early major organ involvement can be silent and needs active screening to detect.
- Giant cell arteritis requires urgent diagnosis and commencement of high-dose steroids to reduce the risk of blindness.
- Osteoporosis is generally asymptomatic until a patient fractures something. Pre-fracture diagnosis is most frequently made with a DEXA scan. Treatment can significantly reduce the future risk of fracture.
- Ankylosing spondylitis usually develops in young males who nearly always possess the HLA-B27 gene. Be aware, however, that this gene is relatively common and having it only rarely leads to ankylosing spondylitis.

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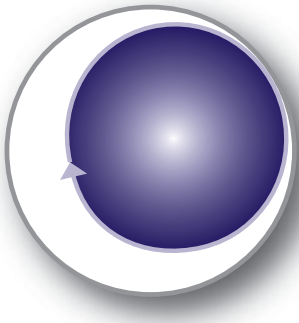


4 Renal medicine

Indranil Dasgupta

RENAL EMERGENCIES

RENAL CASE STUDIES

CHRONIC KIDNEY DISEASE

RENAL EMERGENCIES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely diagnosis?
Q2: What investigations would be performed?
Q3: What would be the initial management?
Q4: What would be the long-term management?

CASE 4.1 – A 60-year-old man presenting with diarrhoea, vomiting and renal impairment.

A 60-year-old man, previously fit and well, presents to the accident and emergency (A&E) department with a 1-week history of diarrhoea and vomiting. He is unwell, clammy, his skin turgor is poor, his pulse is 120/min and his blood pressure is 80/60 mmHg. Initial investigations show serum sodium of 126 mmol/L, potassium of 3.0 mmol/L, urea of 28 mmol/L and creatinine of 306 μmol/L (estimated glomerular filtration rate [eGFR] 19 mL/min/1.73 m^2).

CASE 4.2 – A 72-year-old man presenting with hyperkalaemia.

A 72-year-old man has been referred by his general practitioner (GP) to the emergency assessment unit with a history of being non-specifically unwell for 2 days. He has a past history of ischaemic heart disease, atrial fibrillation, congestive cardiac failure and stable chronic kidney disease (CKD). His regular medications include isosorbide mononitrate, digoxin, furosemide, spironolactone and an angiotensin-converting enzyme (ACE) inhibitor. On examination, the patient is mildly confused, dehydrated, peripherally cold, bradycardic and hypotensive (blood pressure 96/60 mmHg). His initial blood tests show a sodium of 130 mmol/L, potassium of 7.2 mmol/L, urea of 42 mmol/L and creatinine of 412 μmol/L (eGFR 14 mL/min/1.73 m^2).

CASE 4.3 – A 68-year-old woman with chronic kidney disease (CKD) presenting with shortness of breath.

A 68-year-old woman, known to have CKD, has presented to the A&E department with acute shortness of breath. Computer records suggest that her most recent serum creatinine from about a month earlier was 256 μmol/L (eGFR 21 mL/min) and her regular medication includes furosemide 80 mg daily. She has recently been commenced on a non-steroidal anti-inflammatory drug (NSAID) for arthritis. On examination, she has oedema up to the mid-thighs, jugular venous pressure (JVP) is raised at 6 cm, and there are crackles in both lung bases up to the mid-zones. Her admission electrocardiogram (ECG) does not show any ischaemic changes. Her urea and electrolytes (U&Es) results show: sodium 138 mmol/L, potassium 5.6 mmol/L, urea 38 mmol/L and creatinine 446 μmol/L (eGFR 12 mL/min/1.73 m^2).

CASE 4.4 – **A 34-year-old man presenting with severe hypertension and renal impairment.**

A 34-year-old man of African Caribbean origin has been referred by his GP for severe hypertension. On examination, his blood pressure is 240/140 mmHg, he is slightly confused, there is mild pedal oedema, there are a few basal crackles, and neurological examination is normal except for bilateral papilloedema. Urine analysis shows blood ++ and protein ++. His haemoglobin is 10.2 g/dL and U&Es show sodium 136 mmol/L, potassium 3.0 mmol/L, urea 14 mmol/L and creatinine 206 μmol/L (eGFR 54 mL/min/1.73 m^2).

Key concepts

COMMON CAUSES OF ACUTE KIDNEY INJURY (AKI)

- *Pre-renal* – due to ineffective perfusion of kidneys that are structurally normal:
  - hypovolaemia – blood loss, gastrointestinal loss, burns
  - low cardiac output states
  - shock
  - certain drugs – NSAIDs, ACE inhibitors.
- *Renal* – structural damage to glomeruli and tubules:
  - acute tubular necrosis (ATN) – most common cause (45 per cent), results from prolonged hypoperfusion (as above)
  - acute glomerulonephritis and vasculitis
  - acute interstitial nephritis – idiopathic, drugs, infection
  - vascular disease.
- *Post-renal* – due to urinary tract obstruction:
  - prostatic hypertrophy
  - bladder tumour
  - gynaecological malignancy
  - neuropathic bladder.

INVESTIGATIONS TO ORGANIZE IN AKI

- *Urine:*
  - dipstick (blood and protein suggest acute glomerulonephritis)
  - microscopy (red blood cell [RBC] casts diagnostic of acute glomerulonephritis)
  - urine electrolytes (to distinguish pre-renal failure from ATN).
- *Blood:*
  - FBC, clotting (for disseminated intravascular coagulation [DIC], rarely haemolytic uraemic syndrome/thrombotic thrombocytopenic purpura [TTP])
  - U&Es, calcium and PO_4, glucose, creatine kinase (for rhabdomyolysis), CRP (for vasculitis, sepsis)
  - immunology – autoantibodies (for systemic lupus erythematosus, [SLE]), anti-neutrophil cytoplasmic antigen (ANCA; for vasculitis), anti-glomerular basement membrane (GBM) antibodies (for Goodpasture's disease), complements (low in SLE and infective endocarditis), immunoglobulins (for immunoglobulin A [IgA] nephropathy, myeloma)
  - blood cultures (sepsis, infective endocarditis), hepatitis B and C (in preparation for dialysis).
- *ECG* – for hyperkalaemic changes.
- *Chest X-ray* – for pulmonary oedema, pneumonia.
- *Abdominal ultrasound* – to exclude urinary obstruction.

INDICATIONS FOR URGENT DIALYSIS IN AKI

- severe hyperkalaemia (>6.5 mmol/L or less with ECG changes, despite medical treatment)
- pulmonary oedema
- severe acidosis (pH <7.1)
- severe uraemia (vomiting, encephalopathy)
- uraemic pericarditis.

Overall mortality in AKI is about 50 per cent (up to 80 per cent in patients who require dialysis).

Answers

Clinical cases

CASE 4.1 – **A 60-year-old man presenting with diarrhoea, vomiting and renal impairment.**

A1: What is the likely diagnosis?

The likely diagnosis is pre-renal failure or ATN due to reduced circulatory blood volume secondary to diarrhoea and vomiting. Loss of circulatory volume, due to either salt and water depletion or haemorrhage, leads to reduced renal blood supply. This results in selective cortical vasoconstriction and oliguria (urine output <400 mL/day). Initially this is reversible, but when prolonged it leads to ATN (ischaemic injury to the proximal tubular epithelial cells) and rarely to acute cortical necrosis.

A2: What investigations would be performed?

Urinalysis (dipstick test for blood and protein), urine microscopy, urine electrolytes, FBC, and serum bicarbonate, calcium and phosphate levels need to be done. The presence of a significant amount of blood and protein (++ or more) would raise a suspicion of acute glomerulonephritis. Urine sodium below 20 mmol/L would suggest reversible pre-renal failure, while urine sodium above 40 mmol/L would suggest ATN has set in. Low haemoglobin or a raised serum phosphate may indicate the presence of pre-existing CKD.

A3: What would be the initial management?

Intravenous (IV) access and an IV infusion should be set up immediately. The ideal fluid replacement in this setting would be normal saline with potassium supplementation. In the presence of severe metabolic acidosis, sodium bicarbonate (1.26%) infusion should be considered. It is preferable to transfer the patient to a high-dependency unit with a view to establishing central venous access to monitor central venous pressure (CVP). Pulse, blood pressure and urine output should be monitored hourly. In the absence of CVP monitoring, lung bases should be auscultated frequently to prevent overhydration leading to pulmonary oedema. Urea and electrolytes should be repeated in 4–6 h to review progress.

A4: What would be the long-term management?

Pre-renal failure is a rapidly reversible condition. In established AKI (formerly known as acute renal failure [ARF]) due to ATN, it may take as long as 6 weeks for renal function to return to normal; the patient will require dialysis treatment for this period (1 per cent of patients require long-term dialysis). If the patient is haemodynamically compromised, an initial period of continuous veno-venous haemofiltration (CVVH) may be necessary (generally in the intensive care unit). If renal function does not improve within 24 h, an ultrasound scan should be requested to exclude urinary tract obstruction. Small shrunken kidneys on ultrasound scan would suggest that the patient suffers from CKD.

CASE 4.2 – **A 72-year-old man presenting with hyperkalaemia.**

A1: What is the likely diagnosis?

The likely diagnosis is severe hyperkalaemia due to a combination of a potassium-sparing diuretic and an ACE inhibitor in the setting of chronic renal impairment. There is also a possible acute-on-chronic renal impairment due to over-diuresis, as evidenced by a disproportionately high blood urea level and low sodium.

A2: What investigations would be performed?

A 12-lead ECG should be done to see if there are any changes of hyperkalaemia – tall-peaked T-waves, widening of QRS, reduction in height of P- (may disappear) and R-waves, and sine wave pattern (pre-cardiac arrest).

A3: What would be the initial management?

Severe hyperkalaemia (>6.5 mmol/L) and the presence of ECG changes in this scenario warrant urgent treatment of hyperkalaemia, as follows:

- calcium gluconate – 10 mL of 10% IV over 5 min to counteract the adverse effect of hyperkalaemia on the cardiac conduction system (through central line or large cannula in a big vein to avoid delay)
- infusion of 10 u insulin in 50 mL of 50% glucose IV through a pump over 30 min to drive K^+ into intracellular space
- nebulized salbutamol – 5 mg to help K^+ enter intracellular space
- sodium bicarbonate – 50 mL of 8.4% IV over 30 min should be considered, especially if acidotic (*caution:* may precipitate tetany if the serum calcium is low)
- Calcium Resonium® – 30 g by rectum or 15 g orally to help exchange K^+ for Ca^{2+} in the gut
- check U&Es in 2 h and repeat glucose and insulin infusion and nebulized salbutamol if serum potassium remains dangerously high (>6.5 mmol/L) or ECG changes persist
- if serum potassium remains above 6.5 mmol/mL or ECG changes persist despite treatment, haemodialysis may be required
- IV infusion of normal saline to correct dehydration.

A4: What would be the long-term management?

The ACE inhibitor and spironolactone must be stopped. Refer the patient to a nephrologist for long-term management. If renal function returns to near baseline, the ACE inhibitor may be restarted cautiously in the future if clinically indicated, i.e. poor left ventricular function on echocardiography. The patient should be followed up closely, preferably in the renal clinic.

CASE 4.3 – A 68-year-old woman with chronic kidney disease (CKD) presenting with shortness of breath.

A1: What is the likely diagnosis?

This patient's severe shortness of breath is likely to be due to pulmonary oedema secondary to severe fluid retention. Acute deterioration in renal function has probably been precipitated by the recent introduction of an NSAID. Non-steroidal anti-inflammatory drugs reduce renal blood flow in patients with pre-existing renal disease and thereby cause deterioration of renal function. They can also cause acute interstitial nephritis, leading to acute renal impairment.

A2: What investigations would be performed?

A chest X-ray should be done to confirm the diagnosis of pulmonary oedema (Figure 4.1). Arterial blood gas analysis should be done to assess the degree of hypoxia, to ascertain whether there is any evidence of CO_2 retention, and to assess the degree of metabolic acidosis associated with renal failure.

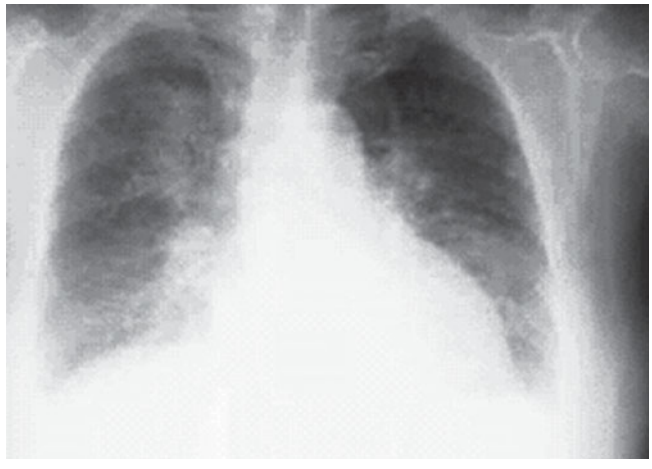


Figure 4.1 Chest radiograph for Case 4.3.

A3: What would be the initial management?

The initial management is furosemide 80 mg IV. If there is no significant diuresis, furosemide should be repeated using a higher dose (up to 250 mg IV). High-concentration oxygen should be given with a facemask. It may be necessary to use continuous positive airway pressure (CPAP) or even to ventilate the patient in intensive care if she is severely hypoxic or gets tired. If the patient remains severely short of breath and oligoanuric despite high-dose IV furosemide, she will need to be referred for urgent haemodialysis or haemofiltration.

A4: What would be the long-term management?

Long-term management will depend on whether the patient's renal function returns to or near baseline after stopping the NSAID. If her renal function improves, long-term management will consist of salt and fluid restriction, high-dose oral diuretic therapy, and avoidance of nephrotoxic agents. The patient will need to be prepared for dialysis treatment. If her renal function fails to improve, she will require acute dialysis, leading to long-term dialysis treatment.

CASE 4.4 – **A 34-year-old man presenting with severe hypertension and renal impairment.**

A1: What is the likely diagnosis?

The likely diagnosis is malignant hypertension. Malignant hypertension is defined as severe hypertension, often above 200/140 mmHg, which is associated with papilloedema, usually accompanied by retinal haemorrhage and exudates, with or without renal impairment or neurological symptoms. It most commonly occurs in patients with long-standing uncontrolled hypertension. Differential diagnosis of this patient would be acute glomerulonephritis with severe hypertension.

A2: What investigations would be performed?

A chest X-ray must be done to confirm or exclude pulmonary oedema. If confusion persists or deteriorates (deteriorating Glasgow coma score, [GCS]), an urgent computed tomography (CT) scan of the brain should be done to exclude infarction or haemorrhage.

A3: What would be the initial management?

Controlled lowering of blood pressure should be attempted with IV infusion of labetalol (a combined alpha- and beta-adrenergic blocker) or sodium nitroprusside (a combined arteriolar and venous dilator). The goal is to lower blood pressure by 10 per cent in the first hour and by 10–15 per cent in the next 2–6 hours (to around 160/100 mmHg at 6 h). Rapid lowering of blood pressure may lead to cerebral vasospasm, resulting in cerebral infarction. The patient should, ideally, be treated in a high-dependency unit. If parenteral antihypertensive agents are not available, oral agents may be used, but their use (especially sublingual nifedipine) is associated with the risk of rapid lowering of blood pressure, leading to stroke or myocardial infarction.

A4: What would be the long-term management?

Once the blood pressure is controlled, the patient should be switched to oral antihypertensive therapy after 6–12 h, with gradual reduction of diastolic blood pressure to 85–90 mmHg over a few weeks. The patient should be investigated for a secondary cause of hypertension. Renal biopsy is indicated if renal function fails to stabilize with blood pressure control. Long-term follow-up is needed for careful monitoring of renal function and strict control of blood pressure, as renal function may deteriorate progressively to end-stage renal failure (ESRF).

RENAL CASE STUDIES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely diagnosis?
Q2: How would you investigate this patient?
Q3: How would you manage this patient?
Q4: What is the prognosis?

CASE 4.5 – A 22-year-old woman presenting with progressive swelling of the legs.

A 22-year-old white European woman presents to her GP with progressive swelling of her legs of 2 weeks' duration. She is otherwise asymptomatic. On examination, she has oedema up to both knees and her blood pressure is 120/70 mmHg. Urinalysis reveals +++ proteins but no blood, serum creatinine is 92 μmol/L and serum albumin is 18 g/L.

CASE 4.6 – A 34-year-old man presenting with microscopic haematuria.

A 34-year-old man is found to have microscopic haematuria on an insurance medical examination. He is asymptomatic. His blood pressure is 124/80 mmHg and his serum creatinine is 102 μmol/L.

CASE 4.7 – A 62-year-old woman presenting with raised serum creatinine, microscopic haematuria and proteinuria.

A 62-year-old woman presents to her GP with symptoms of tiredness, lethargy, aching joints, poor appetite and nausea of 4–6 weeks' duration. Physical examination is unremarkable, except for pallor and a blood pressure of 160/100 mmHg. Routine blood tests reveal a haemoglobin of 10 g/dL, blood urea of 26 mmol/L and serum creatinine of 386 μmol/L (eGFR 14 mL/min/1.73 m^2). The patient is referred to the local hospital. Further examination reveals purpuric spots on both legs and +++ blood and +++ protein on urinalysis.

CASE 4.8 – A 76-year-old man presenting with dysuria and nocturia.

A 76-year-old man presents to his GP with a history of difficulty in passing urine in the form of hesitancy, poor stream and occasional pain of 3 months' duration. He also has nocturia. Physical examination is unremarkable. Urinalysis shows the presence of + blood and + protein. Blood testing shows a raised serum creatinine of 560 μmol/L (eGFR 11 mL/min/1.73 m^2). The patient is urgently referred to the nearby district general hospital. Further examination in the hospital reveals a palpable bladder and a smoothly enlarged prostate on rectal examination.

CASE 4.9 – **A 58-year-old man with raised serum creatinine.**

A 58-year-old South Asian man is found to have a raised serum creatinine of 156 μmol/L (reference range 60–120 μmol/L). He has been on antihypertensive treatment for 10 years and a smoker for 40 years. He is on nifedipine, atenolol and simvastatin. His serum creatinine was 121 μmol/L a year ago.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following.

RELATIONSHIP BETWEEN SERUM CREATININE AND GLOMERULAR FILTRATION RATE

See Figure 4.2.

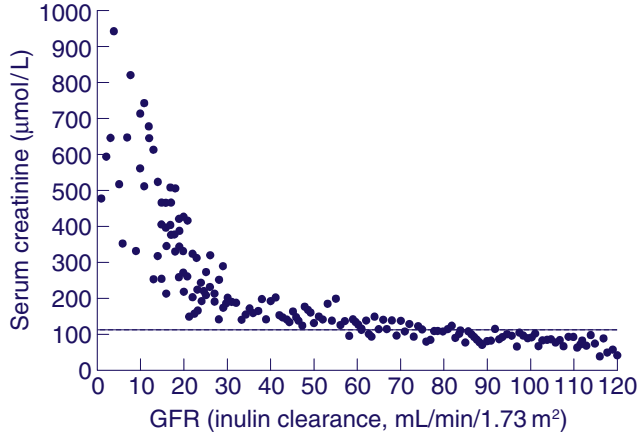


Figure 4.2 Relationship between serum creatinine and glomerular filtration rate (GFR). Serum creatinine remains normal until GFR is about 60 mL/min.

FORMULAE FOR CALCULATING CREATININE CLEARANCE AND GFR

Cockroft–Gault formula – creatinine clearance (mL/min)

Males: creatinine clearance = [1.23 × (140 − age) × weight]/[creatinine]
Females: creatinine clearance = [1.04 × (140 − age) × weight]/[creatinine]

MDRD formula – GFR (mL/min/1.73 m²)

Males: $GFR = 186 \times ([creatinine]/88.4)^{-1.154} \times age^{-0.203}$
Females: $GFR = 138 \times ([creatinine]/88.4)^{-1.154} \times age^{-0.203}$
Multiply by 1.21 if the patient is African Caribbean.

STAGES OF CHRONIC KIDNEY DISEASE

See Table 4.1.

Table 4.1 Stages of chronic kidney disease – updated classification

Stage*	GFR (mL/min/1.73 m^2)	Description
1	≥90	Kidney damage with normal or high GFR
2	60–89	Mild
3A	59–45	Moderate
3B	44–30	Moderate
4	29–15	Severe
5	<15	End-stage kidney failure or on dialysis

*Add the suffix p to denote significant proteinuria.
Adapted from the National Institute for Health and Clinical Excellence CKD Guidelines (2008).

COMMON CAUSES OF END-STAGE RENAL FAILURE

Diabetes is the most common cause of ESRF, accounting for about 24 per cent of cases in England and Wales (nearly 50 per cent in the USA). The other main causes are glomerulonephritis (12 per cent), pyelonephritis (8 per cent), renovascular disease (7 per cent), hypertension (6 per cent) and adult polycystic kidney disease (7 per cent) (UK Renal Registry, 2009). In a fifth of patients in England and Wales, the aetiology is uncertain because these patients present late, when it is difficult to establish a primary renal diagnosis.

Answers

Clinical cases

CASE 4.5 – **A 22-year-old woman presenting with progressive swelling of the legs.**

A1: What is the diagnosis?

The diagnosis is nephrotic syndrome, defined as the presence of oedema, heavy proteinuria (>3 g/day) and hypoalbuminaemia with or without hypercholesterolaemia and hypertension.

The most common cause of nephrotic syndrome is minimal-change nephropathy, especially in children. In adults, membranous nephropathy and focal segmental glomerulosclerosis (FSGS) are also common causes of nephrotic syndrome. In as many as 30 per cent of patients, nephrotic syndrome is due to a systemic disease such as diabetes mellitus, SLE, amyloidosis or multiple myeloma.

A2: What further investigations would you do?

The patient should be referred to a nephrologist for a renal biopsy. Blood sugar and lipids should be checked. Blood should be sent off for immunological tests such as antinuclear antibodies (ANA), complements, serum immunoglobulins and cryoglobulins.

A3: How would you manage this patient?

Management depends on the findings of the renal biopsy. Minimal-change disease is treated with high-dose prednisolone (1 mg/kg, maximum 80 mg/day). This is continued until 1 week after remission (which may take up to 16 weeks). The dose is then reduced gradually, with a view to stopping between 8 and 12 weeks. Sometimes FSGS responds to a prolonged course of corticosteroids. Patients with resistant and relapsing disease are treated with ciclosporin. Membranous nephropathy with deteriorating kidney function is often treated with ciclosporin or a chemotherapeutic agent such as cyclophosphamide or chlorambucil. Oedema is treated with salt restriction and loop diuretics. Severely nephrotic patients are treated with heparin and admitted to hospital to prevent venous thromboembolism. An ACE inhibitor is often used to treat hypertension and reduce proteinuria. Hypercholesterolaemia should be treated with a statin.

A4: What is the prognosis?

Minimal-change nephrotic syndrome in children responds promptly to high-dose corticosteroid therapy. In adults, it does not always respond to corticosteroids as quickly and often relapses. Membranous nephropathy spontaneously remits in up to 25 per cent of patients but progresses to ESRF in about 40 per cent of patients at 15 years. In about 50 per cent of patients, FSGS leads to ESRF and often recurs in transplanted kidney.

CASE 4.6 – **A 34-year-old man presenting with microscopic haematuria.**

A1: What is the diagnosis?

The diagnosis is isolated microscopic haematuria. The most common causes of this in young people are IgA nephropathy and thin basement membrane disease. IgA nephropathy is the most common form of glomerulonephritis and is characterized by deposition of IgA in the mesangium. Thin basement membrane disease is a familial condition characterized by uniform thinning of the glomerular basement

membrane. The other causes of microscopic haematuria are stones, cystic diseases of the kidney, tumour and inflammatory diseases of the urinary tract. Urological causes predominate in older patients.

A2: What further investigations would you do?

Urinalysis needs to be repeated, as transient microscopic haematuria may not be significant. The presence of significant proteinuria (++ or more) may signify a more aggressive from of glomerulonephritis. Ideally, urine should be sent for microscopy to ensure there are two or more RBCs per high-power field. Dipsticks are very sensitive and often detect less significant haematuria, haemoglobin and myoglobin. An ultrasound scan of the kidneys and urinary tracts should be done to exclude a macroscopic pathology. Serum immunoglobulins, complements, autoantibodies and ANCA should be checked. A raised serum IgA level will support a diagnosis of IgA nephropathy. Normal autoantibody, complement and ANCA tests suggest that an underlying autoimmune disease or vasculitis is unlikely. If there is significant proteinuria (>1 g/day), renal biopsy is indicated to exclude acute glomerulonephritis. In older patients with microscopic haematuria, a flexible cystoscopy should be carried out to exclude bladder pathology.

A3: How would you manage this patient?

No specific treatment is indicated. The patient should be followed up on a regular basis – perhaps annually – for measurement of blood pressure, urinalysis and serum creatinine. Should the patient develop significant proteinuria or there is a rise in serum creatinine, renal biopsy should be considered. If the patient develops hypertension, it should be treated, preferably with an ACE inhibitor.

A4: What is the prognosis?

Prognosis is usually good. IgA nephropathy rarely progresses to advanced renal failure in the absence of significant proteinuria, hypertension or raised serum creatinine at presentation. Thin basement membrane disease rarely causes proteinuria, renal impairment or hypertension.

CASE 4.7 – **A 62-year-old woman presenting with raised serum creatinine, microscopic haematuria and proteinuria.**

A1: What is the diagnosis?

The diagnosis is acute glomerulonephritis possibly associated with systemic vasculitis.

A2: What further investigations would you do?

Urine microscopy should be done – the presence of RBC casts will support the diagnosis of acute glomerulonephritis. Blood should be sent off for immunological tests including ANCA, anti-GBM antibodies, ANA, immunoglobulins and complements. A positive ANCA test will support a diagnosis of systemic vasculitis (cytoplasmic ANCA [cANCA] is associated with Wagener's granulomatosis; perinuclear ANCA [pANCA] is associated with microscopic polyangiitis). A positive ANA (especially anti-double-stranded DNA [dsDNA]) with low complements supports a diagnosis of lupus nephritis. Raised ant-GBM antibody titre suggests Goodpasture's disease. Chest X-ray should be requested to look for consolidation, cavitation or pulmonary haemorrhage, supporting a diagnosis of either systemic vasculitis or anti-GBM disease. An ultrasound scan of the kidneys should be done. Renal biopsy will confirm the diagnosis of acute glomerulonephritis.

[This 'real' patient had a positive cANCA test, and renal biopsy showed the presence of acute necrotizing crescentic glomerulonephritis.]

A3: How would you manage this patient?

Immunosuppressive treatment is initiated after confirmation of diagnosis by a renal biopsy. If the patient is too ill to biopsy, a presumptive diagnosis is made based on clinical features and a positive ANCA test. The standard immunosuppressive regime consists of oral prednisolone (1 mg/kg/day, maximum 80 mg/day) and cyclophosphamide (2 mg/kg/day). Intravenous pulsed methyl prednisolone or plasma exchange is used for induction of remission in patients with aggressive (life- or organ-threatening) disease. After 2 weeks, the dose of prednisolone is reduced gradually to 15 mg at 3 months and 10 mg at 6 months. To minimize the side effects with prolonged use, cyclophosphamide is changed after 3 months to azathioprine for maintenance treatment. Because of the risk of relapse (30–50 per cent at 3–5 years), long-term maintenance treatment using small doses of prednisolone and azathioprine is often continued.

A4: What is the prognosis?

Untreated systemic vasculitis is associated with high mortality (90 per cent at 2 years). Immunosuppressive treatment, as described above, leads to control of the disease in 80–90 per cent of patients. Pulmonary haemorrhage and dialysis dependence at presentation are poor prognostic features. As a rule, patients who require dialysis treatment at presentation are less likely to have significant improvement in their kidney function.

CASE 4.8 – **A 76-year-old man presenting with dysuria and nocturia.**

A1: What is the diagnosis?

The diagnosis is acute or acute-on-chronic renal impairment due to bladder neck obstruction by an enlarged prostate.

A2: What investigations would you do?

Urinary catheterization should be done – a large residual volume of urine confirms the diagnosis of urinary retention due to bladder neck obstruction. Ultrasound scan of the abdomen and pelvis reveals bilateral hydronephrosis, hydroureter and an enlarged prostate. Bilateral small kidneys or cortical thinning would suggest that the obstruction is long-standing (chronic retention). Serum prostate-specific antigen (PSA) assay should be done – a high serum concentration suggests possible prostatic malignancy (*caution:* a sample taken after rectal examination or catheterization may show a spuriously high serum level).

A3: How would you manage this patient?

Immediate bladder catheterization should be done to relieve obstruction. If catheterization is difficult, the urology team should be informed, as suprapubic catheterization may be required. Fluid balance (intake and output) should be monitored, as the patient is likely to have a large diuresis. Urea and electrolytes should be monitored daily. If the patient is unable to drink a large amount of fluid to keep up with the urine output, IV fluid (normal saline with or without potassium chloride, depending on the serum potassium level) should be infused. When renal function stabilizes, the urology team should be involved for long-term management of prostatic enlargement. Occasionally, bilateral nephrostomy drainage is required if there is no significant diuresis after bladder catheterization or no significant improvement in hydronephrosis on repeat ultrasound scanning.

A4: What is the prognosis?

The prognosis depends on the chronicity of urinary obstruction. In most cases, renal function improves significantly and remains stable for many years. In patients with long-standing chronic obstruction,

especially those who have very thin renal cortex on ultrasound scan, renal function may not improve at all. These patients go on to need dialysis treatment.

CASE 4.9 – **A 58-year-old man with raised serum creatinine.**

A1: What is the diagnosis?

The likely diagnosis is CKD. Although this patient's serum creatinine was just outside the normal range a year ago, his eGFR using the Modification in Diet in Renal Disease Study (MDRD) formula was 57 mL/min/1.73 m^2 and his current eGFR is 40 mL/min/1.73 m^2. Serum creatinine is not a reliable test to assess renal function, as it is influenced by a number of factors, including age, muscle mass, renal tubular secretion and extra-renal loss of creatinine. A number of regression equations that can predict GFR and creatinine clearance are available, of which the MDRD and Cockroft–Gault are most commonly used.

The cause of chronic renal failure in this case is uncertain pending further investigations, although hypertensive nephrosclerosis is a possibility.

A2: How would you investigate this patient?

Urinalysis, FBC, serum calcium and phosphate, immunology and renal ultrasound would be the initial investigations. A low haemoglobin, high serum phosphate and bilateral small kidneys on ultrasound scan will support the diagnosis. Normal-sized kidneys with significant microscopic haematuria and proteinuria, with or without a positive immunological test, will indicate the need for a renal biopsy to establish an underlying cause of CKD.

A3: How would you manage this patient?

This patient has moderate CKD (stage 3). Hypertension and proteinuria are the two most important progression promoters. Aggressive blood pressure control is the most important measure to prevent or slow down progression of renal disease to ESRF. The target blood pressure should be 130/80 mmHg. The ACE inhibitors and angiotensin receptor blockers reduce proteinuria and have been shown to retard progression of renal disease. These patients also have very high cardiovascular risk and should be urged to stop smoking, lose weight if obese and be treated for hyperlipidaemia. The patient should be advised to avoid NSAIDs and other nephrotoxic drugs.

A4: What is the prognosis?

Chronic kidney disease in this patient is likely to progress to ESRF requiring dialysis or renal transplantation. Patients with CKD stage 3 have a significantly increased risk of cardiovascular morbidity and mortality.

CHRONIC KIDNEY DISEASE

Questions

OSCE counselling cases

OSCE COUNSELLING CASE 4.1 – **'I have recently been diagnosed with chronic kidney disease. What problems can I expect to have?'**

OSCE COUNSELLING CASE 4.2 – **'As a patient with chronic kidney disease, do I have a higher risk of heart disease?'**

OSCE COUNSELLING CASE 4.3 – **'As a patient with kidney failure, do I need to stick to a special diet?'**

OSCE COUNSELLING CASE 4.4 – **'As a patient with chronic kidney disease, do I need to avoid any drugs?'**

OSCE COUNSELLING CASE 4.5 – **'I have chronic kidney disease. When will I need to go on dialysis treatment, and what are the treatment options?'**

Answers

OSCE counselling cases

OSCE COUNSELLING CASE 4.1 – 'I have recently been diagnosed with chronic kidney disease. What problems can I expect to have?'

Mild or moderate chronic kidney disease (GFR >30 mL/min/1.73 m^2) does not generally cause any symptoms. In severe CKD (GFR <30 mL/min/1.73 m^2), common symptoms are tiredness and generalized itching. As dialysis approaches, patients develop anorexia, nausea and vomiting. These 'uraemic symptoms' are due to progressive accumulation of waste products (uraemic toxins) and anaemia.

The common complications of CKD are as follows.

- *Anaemia:* this results mainly from a low concentration of erythropoietin. The other factors that contribute to anaemia in CKD are functional iron deficiency, anaemia of chronic disease, upper gastrointestinal blood loss, and direct suppression of bone marrow by the waste products. Anaemia is investigated and erythropoietin treatment considered when haemoglobin drops below 11 g/dL.
- *Salt and fluid retention:* this leads to oedema, hypertension and, in severe cases, pulmonary oedema. The patient is advised to restrict salt and fluid intake and is treated with loop diuretics.
- *Hypertension:* this is common, and strict blood pressure control is needed to slow down or prevent deterioration of kidney function. The target blood pressure is 130/80 mmHg. The ACE inhibitors and angiotensin receptor blockers are particularly beneficial in terms of protection of renal function.
- *Renal bone disease or osteodystrophy:* this is not a single entity but comprises secondary hyperparathyroidism, adynamic bone disease (due to low bone turnover), osteomalacia or a combination of these. Phosphate retention and diminished production of active vitamin D (due to impaired 1-alpha hydroxylation) are the initiating events. The patient is advised to follow a low phosphate diet from an early stage and is put on phosphate binders such as calcium carbonate and acetate. The patient is also treated with alpha-hydroxylated vitamin D (alphacalcidol) or calcitriol if the serum parathyroid hormone (PTH) concentration is high.
- *Cardiovascular disease:* patients with chronic kidney disease have a very high risk of heart disease and strokes.
- *Malnutrition:* this occurs due to a combination of anorexia with nausea and vomiting in the later stages of CKD, and dietary restrictions imposed to tackle high serum phosphate and potassium. Most renal units employ dietitians who advise these patients regularly.
- *Infections:* these are common because of reduced immunity due to a combination of impaired T-cell and neutrophil functions. The patient is immunized with hepatitis B vaccination at an early stage. It is also recommended that the patient has influenza vaccination annually and pneumococcal vaccination every 5 years.

OSCE COUNSELLING CASE 4.2 – 'As a patient with chronic kidney disease, do I have a higher risk of heart disease?'

Chronic kidney disease is associated with high cardiovascular risk. There is a graded relationship between reduced eGFR and the risk of death, cardiovascular events and hospitalization – the lower the eGFR, the higher the risk. One study showed that the hazard ratios for cardiovascular events were 1.4, 2, 2.8 and 3.4, and those for death were 1.2, 1.8, 3.2 and 5.9, in patients with CKD stages 3a, 3b, 4 and 5, respectively, compared with patients with stage 2 CKD.

Patients with ESRF who are on dialysis have an even higher cardiovascular risk. Death due to cardiovascular disease is 10–20 times higher in patients on dialysis compared with the general population.

Apart from the classic risk factors such as hypertension, hyperlipidaemia and smoking, these patients also have left ventricular hypertrophy, chronic anaemia, abnormal apolipoproteins, raised serum phosphate (with or without a high Ca×P product), arterial calcification, elevated plasma homocysteine level, enhanced coagulability, chronic inflammation and abnormal endothelial function. All of these probably contribute towards the extremely high cardiovascular morbidity and mortality in these patients. It is, therefore, important to treat blood pressure aggressively, urge the patient to stop smoking, and put the patient on statin. Serum phosphate level is generally controlled with dietary restriction and the use of phosphate binders. Anaemia should be treated early and effectively with erythropoietin.

OSCE COUNSELLING CASE 4.3 – **'As a patient with kidney failure, do I need to stick to a special diet?'**

Most renal units have specialist renal dietitians who advise patients regularly regarding their dietary and fluid restrictions. Patients with chronic renal failure need to restrict their phosphate intake at an early stage; recent guidelines suggest phosphate restriction should be instigated when GFR drops below 60 mL/min. Phosphate is found in almost all foods but is especially high in milk and milk products, liver, dried beans and nuts. Dialysis does not clear phosphate very effectively, and therefore the patient needs to continue on a low phosphate diet even when on dialysis. Patients are also asked to restrict their potassium intake. Major sources of potassium are fruits (especially citrus fruits and banana), vegetables, chocolate, coffee and salt substitutes. Salt restriction is recommended to help blood pressure control and fluid retention, even when the patient is on dialysis. Patients are advised to restrict their total fluid intake to about a litre a day unless they have a significant urine output.

OSCE COUNSELLING CASE 4.4 – **'As a patient with chronic kidney disease, do I need to avoid any drugs?'**

A variety of insults that would have little impact on healthy kidneys may cause significant loss of renal function in patients with pre-existing kidney damage. When more than one nephrotoxic factor is present, the risk of worsening renal function is much increased. Apart from renal disease itself, important predisposing factors include the following:

- old age – GFR falls by 50 per cent by 80 years of age due to normal ageing processes
- diabetes
- atherosclerosis – peripheral vascular disease often involves the renal arteries
- cardiac failure – low cardiac output leads to 'pre-renal' uraemia
- hypovolaemia
- hepatic failure – associated with renal vasoconstriction and 'pre-renal' uraemia
- myeloma – with or without hypercalcaemia or hyperuricaemia
- transplant kidney – vulnerable even with a normal creatinine.

Common nephrotoxic agents include the following:

- ACE inhibitors and angiotensin receptor blockers – reduce GFR in renal arterial stenosis (RAS) and sometimes in chronic renal failure; do not use if RAS is likely. Captopril is shorter-acting and so more quickly reversible. Beware a major drop in blood pressure in volume-depleted patients. Check creatinine before and 7 days after starting treatment. Watch potassium levels
- NSAIDs – reduce the vasodilatory effect of prostaglandins and lead to unopposed vasoconstriction
- aminoglycosides – trough and peak levels should be measured. The nephrotoxic effect may also be related to the total cumulative dose received
- ciclosporin – has a dose-related NSAID-like effect
- X-ray contrast – protection of GFR with adequate hydration pre-study is essential

- tetracyclines – doxycycline is metabolized in the liver and is the only safe tetracycline for use in renal disease.

OSCE COUNSELLING CASE 4.5 – ‘ I have chronic kidney disease. When will I need to go on dialysis treatment, and what are the treatment options?’

Renal replacement therapy (RRT) is generally required when the GFR is around 10–15 mL/min/1.73m^2 (end-stage kidney failure). Most patients with CKD are symptomatic (with anorexia, nausea and vomiting) at this stage. Some people advocate starting RRT earlier, but there is no convincing evidence to suggest a survival benefit of early commencement of dialysis. Patients with diabetes often become symptomatic at an earlier stage and start dialysis with a higher GFR compared with patients without diabetes. Some patients with CKD start dialysis as an emergency because of intractable hyperkalaemia or severe pulmonary oedema.

There are three modalities of RRT:

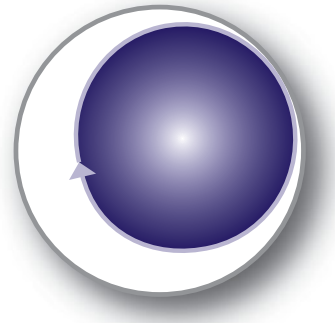
- haemodialysis
- peritoneal dialysis – either continuous ambulatory or automated
- renal transplantation.

The optimal choice of modality of RRT depends on the patient’s age, functional capacity, comorbidities, family support and choice. Some patients receive all three modalities of RRT at various stages of their illness. Some patients, who choose not to have dialysis treatment or are deemed unlikely to benefit from dialysis, are treated conservatively with full supportive treatment, including erythropoietin therapy.

The annual acceptance rate and prevalence of RRT in the UK are, respectively, 108 and 774 per 1 million population. Forty seven per cent of prevalent patients have a functioning transplant, and 43 per cent of patients are on haemodialysis.

REVISION PANEL

- Acute kidney injury may be: (i) *pre-renal*, due to ineffective perfusion of kidneys that are structurally normal, (ii) *renal*, due to structural damage to the glomeruli and tubules, or (iii) *post-renal*, due to urinary tract obstruction.
- Indications for urgent renal dialysis include severe hyperkalaemia (>6.5 mmol/L or less with ECG changes, despite medical treatment), pulmonary oedema, severe acidosis (pH <7.1), severe uraemia (vomiting, encephalopathy) and uraemic pericarditis.
- ECG findings of hyperkalaemia include tall-peaked T-waves, widening of QRS, reduction in the height of P- (may disappear) and R-waves, and a sine wave pattern (pre-cardiac arrest).
- Nephrotic syndrome is defined as the presence of oedema, heavy proteinuria (>3 g/day) and hypoalbuminaemia, with or without hypercholesterolaemia and hypertension.
- The most common causes of microscopic haematuria in young people are IgA nephropathy and thin basement membrane disease. Other causes are stones, cystic diseases of the kidney, tumour and inflammatory diseases of the urinary tract. Urological causes predominate in older patients.
- Systemic vasculitis (such as Wagener’s granulomatosis) may present with raised serum creatinine, microscopic haematuria and proteinuria and requires urgent immunosuppressive therapy.
- The common complications of CKD are anaemia, salt and fluid retention, hypertension, renal bone disease or osteodystrophy, cardiovascular disease, malnutrition and infections.
- Patients with CKD require long-term dietary phosphate and potassium restriction.



5 Cardiology

Morgan Cadman-Davies, Nevianna Tomson and Neeraj Prasad

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What specific questions would you ask the patient?
Q2: What is the likely diagnosis?
Q3: What examination would you perform?
Q4: What would be the initial management?
Q5: What investigations would you request to confirm a diagnosis?
Q6: What other issues should be addressed?

CASE 5.1 – **A 34-year-old woman with palpitations.**

A 34-year-old woman presents with a 3-h history of palpitations. She is mildly dyspnoeic and has some chest pain. She has been feeling anxious and had insomnia for the past few weeks. On direct questioning, she admits to a 10-day history of diarrhoea. On examination, she has a tachycardia and her pulse is irregular.

CASE 5.2 – **A 53-year-old man with sudden onset of chest pain.**

A 53-year-old man is brought into the accident and emergency (A&E) department by ambulance complaining of sudden onset of severe central chest pain. He is cold and clammy and appears breathless.

CASE 5.3 – **An 80-year-old woman collapses, requiring cardiopulmonary resuscitation (CPR).**

A 80-year-old woman collapsed at home and has been brought into A&E unconscious. She was given basic life support at home by her daughter, who works as a ward sister on coronary care. The paramedics are performing CPR as the patient is wheeled into A&E accompanied by her tearful daughter.

CASE 5.4 – **A 65-year-old man with tearing chest pain.**

A 65-year-old man is brought into A&E complaining of severe tearing pain between the shoulder blades. Initially the pain was extremely severe, but it has now mildly subsided to a dull ache in the chest. He is normally fit and well, apart from hypertension, for which he has been seeing his general practitioner (GP).

CASE 5.5 – **A 25-year-old man with a heart murmur.**

A 25-year-old man recently attended a medical in the process of joining the police force. He has been told that he has a heart murmur.

OSCE counselling cases

OSCE COUNSELLING CASE 5.1 – **'Can I stop my warfarin?'**

A 24-year-old woman had a metal prosthetic heart valve inserted 4 years ago after a severe episode of bacterial endocarditis that degenerated her mitral valve. She has done very well since the surgery and has been on warfarin, regularly attending an anticoagulation clinic. She has come to see you today because she wants to have a family but has read on the Internet that warfarin can damage the baby. Can she stop her warfarin?

OSCE COUNSELLING CASE 5.2 – **'I'm on various medicines for my angina. How should I take them and what side effects do they have?'**

A 73-year-old man has recently been diagnosed with angina. He is able to walk 300 m before experiencing chest tightness but considerably less distance when there is an incline. His recent exercise stress test has indicated ischaemic heart disease (IHD) and he has been prescribed sublingual glyceryl trinitrate (GTN) tablets and a beta-blocker. Advise him on how to use the medication and explain any side effects of which he should be aware.

OSCE COUNSELLING CASE 5.3 – **'I have heart failure. Do I need to take my medications for life?'**

A 65-year-old man with known IHD, hypertension and diabetes mellitus has recently been complaining of shortness of breath. An echocardiogram has confirmed left ventricular (LV) systolic dysfunction, which is moderately severe, and he has been started on ramipril 10 mg once a day, bisoprolol 2.5 mg once a day and spironolactone 25 mg once a day. He is very concerned about the number of medications that he is now on because these are additional to his other therapies. Explain the importance of his diagnosis and treatments to him.

Key concepts

To work through the core clinical cases in this chapter, you will need to understand the following key concepts.

BENEFITS OF DRUG MANAGEMENT IN CHRONIC HEART FAILURE

- *Diuretics:* loop diuretics and thiazide diuretics improve symptoms of congestion.
- *Spironolactone 25–50 mg once a day:* improves survival in severe (New York Heart Association [NYHA] stage III/IV) heart failure.
- *Angiotensin-converting enzyme (ACE) inhibitors:* improve symptoms, exercise capacity and survival in patients with asymptomatic and symptomatic systolic dysfunction:
  - lisinopril 2.5 mg initial dose, 20 mg once a day target dose, sometimes up to 30 mg once a day
  - ramipril 1.25–2.5 mg initial dose, 10 mg once a day target dose
  - captopril* 6.25 mg initial dose, 50 mg three times a day target dose (now used infrequently).
- *Angiotensin II antagonists:* treatment of symptomatic heart failure in patients intolerant to ACE inhibitors*:
  - losartan and valsartan.
- *Beta-blockers:* improve symptoms and survival in stable patients who are already receiving an ACE inhibitor with LV systolic dysfunction:
  - bisoprolol 1.25 mg once a day titrated with close monitoring to 10 mg once a day
  - carvedilol 3.125 mg twice a day, increasing with close monitoring to 25–50 mg twice a day.
- *Digoxin:* improves symptoms and exercise capacity and reduces admissions to hospital.
- *Nitrates and hydralazine:* improve survival in symptomatic patients who are intolerant to ACE inhibitors or angiotensin II receptor antagonists*.
- *Amiodarone:* prevents arrhythmias in patients with symptomatic ventricular arrhythmias.
- *Ivabradine:* can be used to reduce heart rate if rate <60 bpm on beta blockers or if intolerant to beta blockers.

*Prefer long-acting drugs such as ramipril, which can be used in a twice a day dosing regime if the blood pressure is low.

BENEFITS OF INTERVENTIONS IN CHRONIC HEART FAILURE

Some patients fail to respond to maximal pharmacological therapy and remain symptomatic.

If there is poor contractile function with prolongation of QRS duration (i.e. reduced cardiac output measured by left ventricular ejection fraction [LVEF] on echocardiography), the patient may get symptomatic benefit from a biventricular pacing system designed to improve contractility ± correction of life-threatening arrhythmias if also fitted with an internal defibrillator. Indications for insertion of a biventricular pacemaker ± a defibrillator are:

- stage III/IV NYHA heart failure
- either QRS >150 ms or QRS 120–149 ms with mechanical dyssynchrony on echocardiography
- LVEF <35 per cent, non-sustained ventricular tachycardia (VT) on Holter monitoring and inducible VT on electrophysiology studies
- already on optimal pharmacological therapy.

CARDIAC ARRHYTHMIAS

See Table 5.1 and Figures 5.1 and 5.2.

Table 5.1 Arrhythmias

Arrhythmia	Basic pathology	Medical management	Intervention or surgical management
Non-myocardial infarction (MI)-related			
AF or atrial flutter	Increasing prevalence with age Look for possible underlying causes: *cardiac* – mitral valve disease, IHD, pericarditis, cardiomyopathy, endo-/myocarditis, post-cardiac surgery; *atrial myxoma*; *lung pathology* – pneumonia, pulmonary embolic malignancy, trauma/surgery; *metabolic* – thyrotoxicosis, excessive alcohol, electrolyte imbalance/acidosis	Control rate with digoxin/beta-blocker/amiodarone and restore to sinus rhythm by chemical (flecainide/amiodarone)/electrical cardioversion Heparin or warfarin should be considered If hypotensive, consider immediate DC cardioversion Acute AF/flutter often reverts spontaneously within 24 h Correct underlying cause if possible	Persistent AF/flutter needs anticoagulation with warfarin and consideration for DC cardioversion, depending on underlying pathology Electrophysiological ablation should be considered Occasionally AV node ablation and permanent pacemaker are needed to control heart rate in patients not responsive to other medical therapy
SVT	Accessory pathway between atria and ventricles causing re-entrant circuit, e.g. Wolff–Parkinson–White syndrome, AV node re-entrant tachycardia, ectopic atrial focus or AF/atrial flutter	DC cardioversion if hypotensive Vagal manoeuvres, e.g. carotid massage/Valsalva manoeuvre IV adenosine (3–12 mg) Consider intravenous or oral verapamil or beta-blocker (but not in Wolff–Parkinson–White syndrome, where flecainide can be considered)	Rarely atrial overdrive pacing Electrophysiology studies and ablation if medical treatment not adequate
VT	Associated with IHD, hypertensive heart disease, cardiomyopathy Can be precipitated by bradycardia, hypokalaemia, hypomagnesaemia, MI or long QT interval	Synchronized DC cardioversion if hypotensive; if stable give IV lidocaine Correct metabolic abnormalities Amiodarone may be necessary to stabilize patient	Consider electrophysiological studies/ablation or implantable defibrillator

Continued

Arrhythmia	Basic pathology	Medical management	Intervention or surgical management
Ventricular premature beats	Ectopic focus within ventricle	Treatment offers no benefit to survival Give antiarrhythmic if symptomatic (beta-blocker)	Rarely electrophysiological ablation for very frequent unifocal ventricular ectopic beats
Torsades de pointes	Associated with inherited or acquired prolongation of QT interval, e.g. drugs, hypokalaemia, hypomagnesaemia, hypocalcaemia, IHD	Correct electrolyte imbalance Stop drugs prolonging QT interval Intravenous magnesium Consider beta-blocker in hereditary QT interval	Consider temporary pacing Discuss with EP team
VF	See Case 5.4		
Post-MI arrhythmias			
AF/atrial flutter	AF often transient post-MI	Rate control; usually reverts spontaneously; treat as above if present	
VF	Acute MI is common cause of VF	As non-MI treatment Note that antiarrhythmic drug treatment is not necessary after VF within first 24 h of acute MI	Recurrent or late VF (>48 h) indicates risk of subsequent sudden death; these patients should be considered for coronary angiography for possible revascularization and ICD
VT	Associated with IHD, especially acutely post-MI	Treatment as above Note that antiarrhythmic drug treatment is not necessary after VF within first 24 h of acute MI	Recurrent or late VT (>48 h) indicates risk of subsequent sudden death; these patients should be considered for coronary angiography for possible revascularization and ICD
Ventricular premature beats	Common acutely post-MI/post-thrombolysis	Often no treatment required	
Sinus bradycardia	Commonly complicates RV infarction/ inferior infarction	If heart rate <60 beats/min with hypotension or cardiac failure, give IV atropine 0.6 mg	Temporary or permanent pacing may be needed

Continued

AV block	Commonly complicates RV infarction/ inferior infarction	First-degree heart block requires no treatment	Temporary or permanent pacing may be needed
		Second-/third-degree heart block with inferior infarction requires treatment only if associated with hypotension, syncope, cardiac failure or 'escape' ventricular arrhythmias. Atropine 0.6 mg IV bolus up to 3 mg IV can be given	Second-/third-degree heart block associated with anterior infarction should always be considered for temporary pacing because may lead to ventricular standstill

AF, atrial fibrillation; AV, atrioventricular; DC, direct current; ICD, implantable cardioverter defibrillation; IHD, ischaemic heart disease; IV, intravenous; MI, myocardial infarction; RV, right ventricular; SVT, supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.

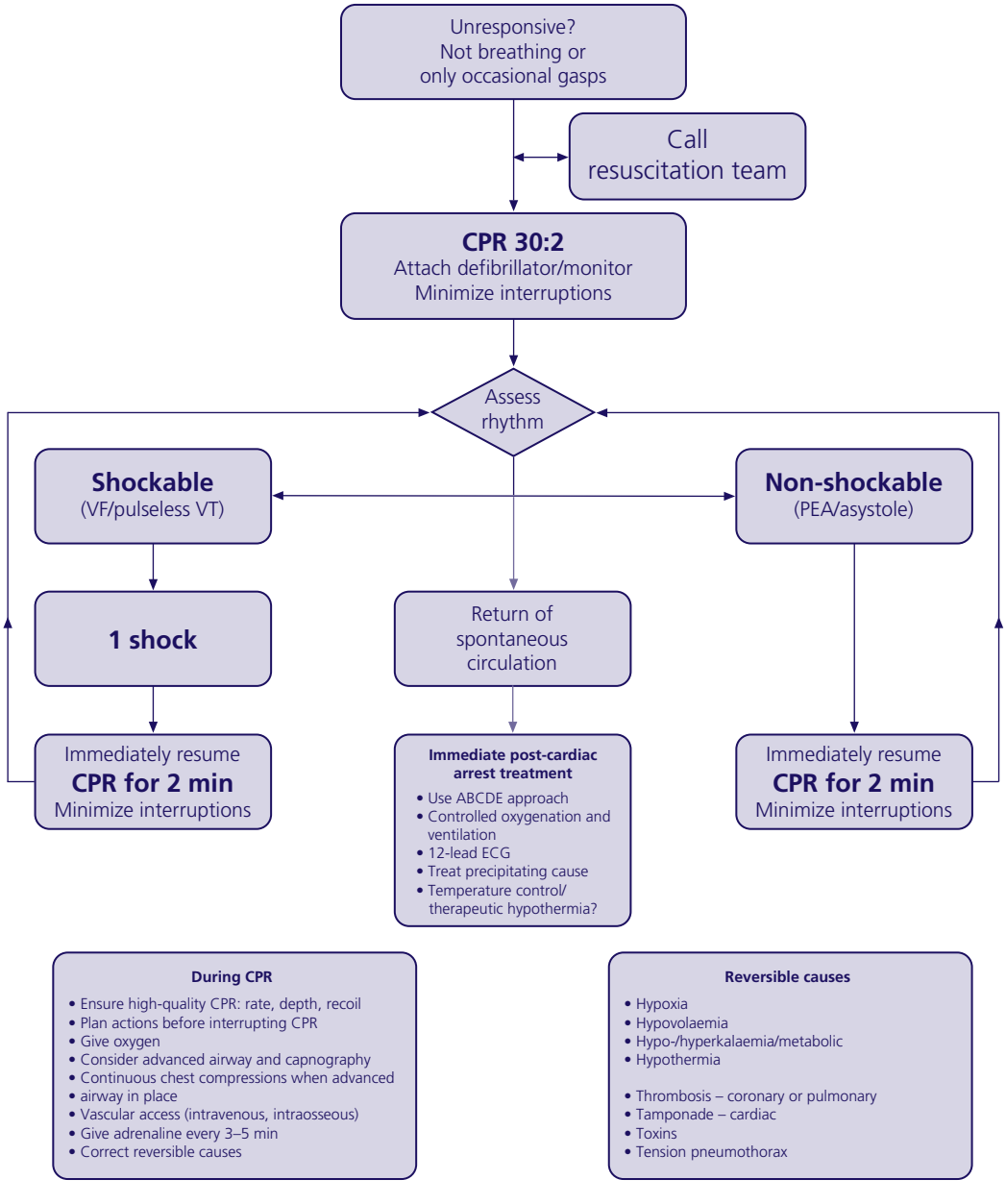


Figure 5.1 Adult advanced life support.

CPR, cardiopulmonary resuscitation; ECG, electrocardiogram; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia.

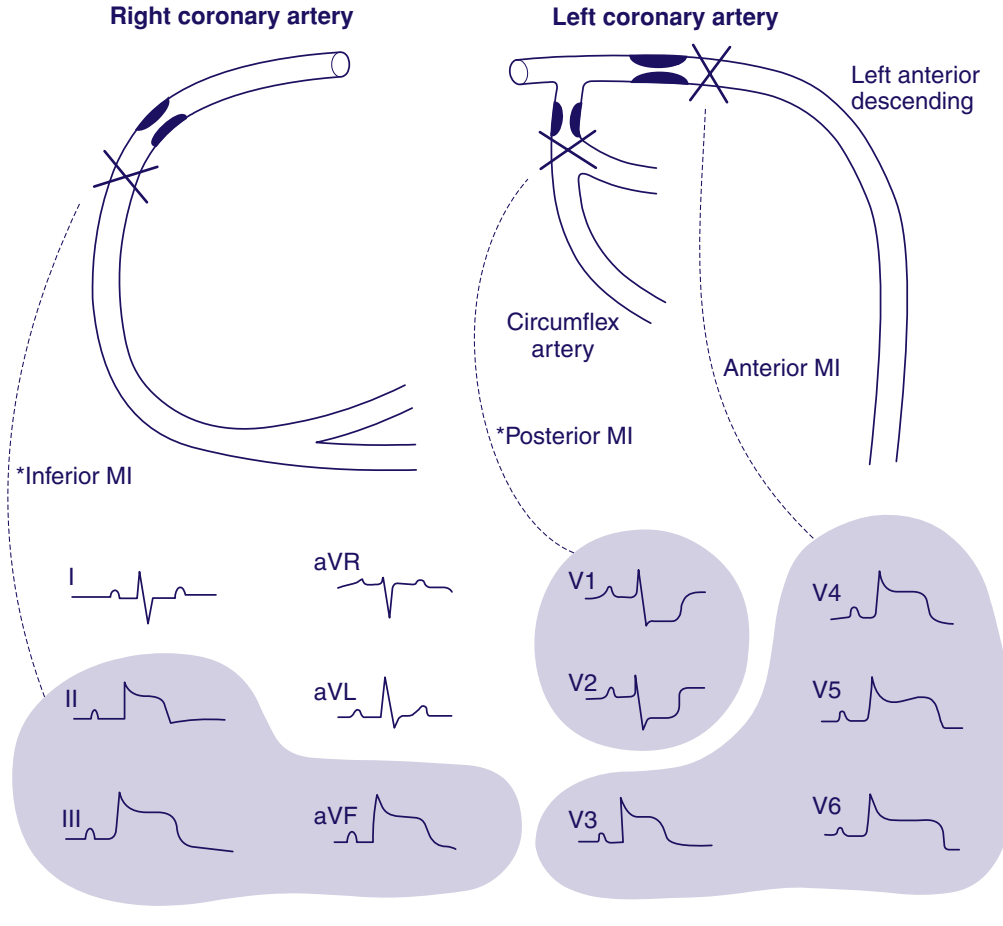


Figure 5.2 Chest pain.

*There is an overlap between inferior and posterior, depending on the patient's anatomy, i.e. where the right coronary artery or circumflex artery is dominant.
MI, myocardial infarction.

VALVULAR HEART DISEASE

See Table 5.2.

Table 5.2 Valvular heart disease

	Cause	Symptoms	Signs	Management
Aortic stenosis	Degenerative (± calcification), calcification of congenital bicuspid valve, occasionally rheumatic fever	Symptoms usually occur only when aortic orifice is reduced to a third of its normal size: angina, dyspnoea and exercise-induced syncope	Slow-rising pulse and narrow pulse pressure; thrusting non-displaced or displaced apex; an ejection click may precede harsh ejection systolic murmur, which is loudest over right upper sternal edge and radiates to carotids	Valve replacement if symptomatic and high valve gradient on echocardiogram Valvuloplasty in young patients (rarely) Transcatheter aortic valve insertion for patients with high surgical risk; decision taken by multidisciplinary team, with interventional cardiologists, cardiac surgeons and cardiac anaesthetist
Aortic regurgitation	Damage of aortic valve cusps: bicuspid aortic valve (congenital), infective endocarditis, rheumatic fever; dilation of aortic root/valve ring: arthritides, e.g. Reiter's syndrome, ankylosing spondylitis, severe hypertension, aortic dissection, rare causes e.g. Marfan's syndrome, syphilis	Usually asymptomatic unless severe; exertional dyspnoea and fatigue	Collapsing pulse and wide pulse pressure; nail-bed capillary pulsations (Quinke's sign), head nodding (de Musset's sign), and pistol shot sounding femoral arteries are sometimes seen; apex is laterally displaced and thrusting; early diastolic murmur at lower left sternal edge heard best with the patient sitting forward in full expiration	Regular dental visits and good dental hygiene Diuretics and vasodilators for mild symptoms Valve replacement after patient is symptomatic or left ventricle or aortic root is dilating

Mitral stenosis	Rheumatic fever	Exertional dyspnoea, cough ± haemoptysis, palpitations	AF, malar flush, palpable first heart sound ('tapping' apex); loud first heart sound, opening snap in early diastole, followed by rumbling mid-diastolic murmur at apex with presystolic accentuation; pulmonary hypertension, RVH and eventually right heart failure	Valvuloplasty if valve not calcified and no significant mitral regurgitation Valve replacement
Mitral regurgitation	MVP, rheumatic fever, papillary muscle dysfunction/rupture post-MI, LV dilation, endocarditis; rare causes – SLE, Marfan's syndrome	Exertional dyspnoea and lethargy; pulmonary oedema if acute regurgitation	Laterally displaced apex; soft first heart sound; pansystolic murmur loudest at apex and radiating to axilla and throughout precordium; third heart sound often present	Regular dental visits and good dental hygiene Diuretics and ACE inhibitors Valve repair or replacement if symptomatic or progressive LV dilation or dysfunction (i.e. reducing LVEF)
Mitral valve prolapse	Unknown cause (more common in women); associated with Marfan's syndrome/IHD	Usually asymptomatic; can present with atypical chest pain or palpitations	Midsystolic click ± murmur; mitral regurgitation may occur	Beta-blockers if symptomatic If severe MR, as above
Tricuspid stenosis	Rheumatic fever, carcinoid	Usually associated with mitral and aortic valve disease, which dominate symptoms and signs		Valvuloplasty or valve replacement

Continued

	Cause	Symptoms	Signs	Management
Tricuspid regurgitation	Raised pulmonary pressure (look for causes, e.g. pulmonary embolism, lung disease, left heart causes [mitral valve disease, LV dysfunction]); can be physiological; rare causes – rheumatic heart disease, infective endocarditis, carcinoid	Symptoms and signs of underlying lung pathology and right heart failure may be present	Raised JVP and giant 'v' waves, pulsatile liver and pansystolic murmur at left lower sternal edge, accentuated with inspiration; peripheral oedema and ascites may be present	If functional, signs usually improve with diuretic therapy Annuloplasty or replacement very rarely required
Pulmonary stenosis	Congenital (usually with other defects, e.g. Fallot's tetralogy)	Fatigue, syncope, RV failure	Systolic murmur at left sternal edge; signs of right heart failure	Valvuloplasty, valve replacement
Pulmonary regurgitation	Pulmonary hypertension, endocarditis (in people who misuse IV drugs)	Usually asymptomatic	Early diastolic murmur at upper left sternal edge	Treatment rarely needed
Ventricular septal defect	Congenital, post-MI (ventricular septal rupture)	May be asymptomatic; Eisenmenger's syndrome occurs later in life when pulmonary vascular disease develops	Pansystolic murmur loudest at third or fourth intercostal space; pulmonary hypertension signs may be present	Repair defect surgically or consider percutaneous approach
Atrial septal defect	Congenital	Arrhythmias and heart failure	Wide fixed splitting of S2; pulmonary ejection systolic murmur as result of increased flow; pulmonary hypertension with tricuspid or pulmonary regurgitation may occur	Surgical or percutaneous closure if symptomatic or developing Eisenmenger's syndrome

ACE, angiotensin-converting enzyme; AF, atrial fibrillation; IHD, ischaemic heart disease; JVP, jugular venous pressure; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; MVP, mitral valve prolapse; RVH, right ventricular hypertrophy; SLE, systemic lupus erythematosus

Answers

Clinical cases

CASE 5.1 – **A 34-year-old woman with palpitations.**

A1: What specific questions would you ask the patient?

Elicit from the history the onset of symptoms and any associated features (e.g. chest pain, dyspnoea, nausea, tremor). The patient's symptoms may be related to the arrhythmia, or an ischaemic event might have caused it. The patient may be able to identify whether the rhythm is regular or irregular or to tap out the arrhythmia. Determine whether the palpitations have occurred in the past. Ask specifically for precipitating or relieving factors and for any medical conditions that the patient has that predispose to arrhythmias, e.g. thyrotoxicosis or valvular heart disease. A drug history is very important because some drugs may precipitate arrhythmias or influence the management of the arrhythmia (e.g. verapamil must not be given to patients who are on beta-blockers because it may result in circulatory collapse).

A2: What is the likely diagnosis?

The likely diagnosis is atrial fibrillation (AF) secondary to thyrotoxicosis as a result of the history of diarrhoea and insomnia that are features in this condition. Other causes of arrhythmia to consider are described in the key concepts.

A3: What examination would you perform?

A full physical examination is necessary. Determine the rate, character and volume of the pulse. Note if the patient is haemodynamically stable: record the blood pressure and examine for signs of heart failure. Auscultate for heart murmurs. Examine for thyroid status if appropriate.

A4: What would be the initial management?

This depends on the cause of the palpitations. If the patient has a tachycardia and is haemodynamically unstable (systolic blood pressure <80 mmHg, reduced level of consciousness, severe pulmonary oedema), consider immediate direct current (DC) cardioversion. If the patient has a bradycardia and is haemodynamically compromised, give atropine 0.6–1.2 mg IV. If there is persistent bradycardia, consider external pacing while organizing transvenous pacing wire insertion. See Key concepts.

A5: What investigations would you request to confirm a diagnosis?

Record a 12-lead electrocardiogram (ECG) to determine the nature of the arrhythmia (regular versus irregular, narrow versus broad QRS complex). Take blood for routine haematology, biochemistry, calcium, magnesium, cardiac enzymes, thyroid function tests and glucose. A chest radiograph is useful to estimate heart size and look for signs of pulmonary oedema.

A6: What other issues should be addressed?

This depends on the arrhythmia and its underlying cause (see Key concepts).

CASE 5.2 – **A 53-year-old man with sudden onset of chest pain.**

A1: What specific questions would you ask the patient?

There is a wide range of differential diagnoses for chest pain and it is thus very important to establish the exact nature of the pain. A constricting central chest pain that occurs on exertion and is relieved by rest or GTN suggests angina. A similar crushing central chest pain when more prolonged and of greater severity indicates myocardial infarction (MI); unlike angina, the pain of MI is not relieved by rest or GTN and is typically associated with extreme distress, sweating, nausea/vomiting and dyspnoea. Cardiac pain can radiate to one or both arms and up the neck to the jaw. Risk factors for IHD to seek are diabetes mellitus, hypertension, hyperlipidaemia, smoking and any family history of IHD. Male sex, increasing age and obesity are also risk factors. Other causes of chest pain to consider include pericarditis, dissecting aortic aneurysm, pulmonary embolus, pleurisy, gastro-oesophageal reflux, perforated peptic ulcer, pancreatitis and cholecystitis.

A2: What is the likely diagnosis?

The most likely diagnosis is MI. This is usually caused by rupture of an atherosclerotic plaque with formation of thrombus and complete occlusion of a coronary artery.

A3: What examination would you perform?

A full physical examination is needed. The patient is usually very distressed and appears pale, grey and sweating. The pulse must be noted because arrhythmias are common, particularly if the MI is of the right coronary artery, which supplies the sinoatrial node. Hypotension may also occur; blood pressure is often measured in both arms to look for any significant difference (>15 mmHg) that may indicate aortic dissection. The jugular venous pressure (JVP), if raised, indicates right heart failure and right ventricular (RV) infarction must be considered. Listen for any murmurs and then examine for pulmonary oedema. Cardiogenic shock can be recognized from the following: systolic blood pressure <90 mmHg, heart rate >100 beats/min or <40 beats/min, pulmonary oedema (oxygen saturation <90 per cent), cold peripheries, agitation/confusion and oliguria.

A4: What would be the initial management?

Immediate treatment is aimed at relief of pain, limitation of infarct size and management of complications if they arise. Oxygen is administered via a facemask (28% if history of chronic bronchitis/emphysema) and the patient is attached to an ECG monitor. Intravenous access is obtained and 5 mg diamorphine is given with 10 mg metoclopramide as an antiemetic. Further 2.5 mg boluses of diamorphine should be given until the patient is pain-free. Soluble aspirin 300 mg and sublingual GTN (provided that the patient is not hypotensive) must also be given if not already administered by the ambulance paramedics. A 12-lead ECG is done as a priority to decide whether primary percutaneous coronary angioplasty (PCI) or thrombolysis is appropriate. Patients who have a ST elevation MI should have primary PCI with or without stenting of vessel occlusion as early as possible, which improves the clinical outcome. If the time to primary PCI is over 2 h (or 90 min for patients under 75 years of age), immediate thrombolysis should be administered (streptokinase or recombinant tissue plasminogen activator [rTPA] and intravenous heparin) and the patient should be transferred for rescue PCI within 3–24 h. Patients with a non-ST elevation MI should also have PCI. High-risk patients should have PCI within 24 h and lower-risk patients within 72 h. G2b3a inhibitors can be considered with dynamic ECG changes or ongoing ischaemia if an interventional option is delayed. See Key concepts.

A5: What investigations would you request to confirm a diagnosis?

The diagnosis is usually made on the basis of a history and 12-lead ECG, and confirmed later with a rise in cardiac enzymes. ST-segment elevation on the ECG occurs within minutes and is followed by T-wave inversion that persists after the ST segment returns to baseline. The indication of transmural infarction

is the development of Q-waves, usually hours or days later. The infarct site may be determined by the location of ECG changes. Other ischaemic changes on the ECG that may occur are new left bundle-branch block, right bundle-branch block, tachy- or bradyarrhythmias, left or right axis deviation or atrioventricular (AV) block. Troponin-T myofibrillar protein and high-resolution troponin-T are routinely measured, rising within 4 h and remaining elevated for 2 weeks. This is a specific marker of myocardial disease and important diagnostically. Creatine phosphokinase (CPK) (and more specifically the isoenzyme CK-MB) and lactate dehydrogenase (LDH) can be used as markers of disease severity or to indicate reinfarction. CK-MB rises at 4–8 h, peaks at 24 h and returns to normal in 3–4 days. A chest radiograph to determine cardiac size and look for pulmonary oedema must be performed. Blood must be taken for routine haematology and biochemistry investigations, and for random glucose and cholesterol measurement.

A6: What other issues should be addressed?

The patient should be admitted to the coronary care unit if possible and have bedrest for 24–36 h. Subcutaneous heparin is used as prophylaxis against deep venous thrombosis. Patients with uncomplicated MI can be discharged home after 5 days. Complications that may occur include cardiogenic shock, reinfarction, dysrhythmias, pericarditis, acute mitral regurgitation, ventricular septal defect and myocardial rupture. If pain persists or there is no resolution of ST elevation, the patient is considered for repeat thrombolysis or referred for urgent angiography, with the aim of revascularization, usually by coronary angioplasty. Secondary prevention post-MI is important; each patient is prescribed aspirin, a beta-blocker, an ACE inhibitor and a lipid-lowering statin (atorvastatin 80 mg daily if tolerated), unless specific contraindications are present. The patient should be on clopidogrel or prasugrel for 1 year if a coronary stent is implanted. On discharge, patients should be advised to inform the Driver and Vehicle Licensing Authority (DVLA) of their admission; they can usually resume driving in 6 weeks and return to work in 3 months. Every patient should be entered into a cardiac rehabilitation programme and have active follow-up.

CASE 5.3 – **An 80-year-old woman collapses, requiring CPR.**

A1: What specific questions would you ask the patient?

Obtain as much history as possible from the daughter and paramedics. Events immediately preceding the arrest are particularly important because they may indicate the cause. Enquire specifically about any illness that the patient may have had and obtain a past medical history, such as IHD, diabetes mellitus (consider hypoglycaemia) and depression (consider drug overdose). Establish the medication that the patient is on and enquire about illicit drug use if appropriate (especially in a young patient, where examination may yield evidence of IV drug misuse). It is also important to identify the length of time before resuscitation and the duration of resuscitation before admission. Without CPR, permanent cerebral dysfunction occurs after 3–4 min of cardiopulmonary arrest. The longer the period of arrest, the less likely it is that resuscitation will be successful and the patient restored to a healthy life.

A2: What is the likely diagnosis?

The most common cause of a cardiac arrest is ventricular fibrillation (VF). Other causes include other dysrhythmias (pulseless VT, bradydysrhythmia), sudden pump failure (MI), circulatory obstruction (pulmonary embolus) and cardiovascular rupture (myocardial rupture/dissecting aortic aneurysm).

A3: What examination would you perform?

The initial assessment of the airway, breathing and circulation would have already been performed by the paramedics. Examine the patient briefly to check that CPR is effective: palpate for a pulse and check that both lungs are ventilated. Look for any signs of bleeding such as haematemesis or melaena that

may suggest hypovolaemia as the cause of the arrest. If the abdomen is distended, an intra-abdominal catastrophe such as a ruptured abdominal aortic aneurysm may be suspected.

A4: What would be the initial management?

Effective basic life support and early defibrillation are the most vital elements of successful resuscitation. The patient is already being resuscitated by the paramedics, and IV access has usually been established. The patient should be attached to a defibrillator via ECG leads to determine whether the cardiac rhythm is 'shockable' (VF/pulseless VT) or not shockable (asystole/electromechanical dissociation). If the patient is in a shockable rhythm, DC cardioversion should be given without delay. Advanced CPR should be continued according to the algorithm determined by the patient's cardiac rhythm each time it is assessed (see Key concepts). The patient should be intubated if this has not already been done. Adrenaline (1 mg IV) should be given every 3 min; if the patient is in asystole, 3 mg atropine should be given once only. In refractory VF/VT (after four cycles of advanced life support [ALS]), amiodarone is recommended. An arterial blood gas (ABG) is taken during ALS; if hyperkalaemia is present, calcium chloride is administered. Bicarbonate can be given in severe acidosis (pH < 7.0) and in hyperkalaemia. Treatable causes must be considered (see Figure 5.1) and where possible an attempt made to correct them.

A5: What investigations would you request to confirm a diagnosis?

In the event of successful resuscitation, a 12-lead ECG must be done to look for evidence of MI that may have precipitated the arrest. A chest radiograph may show pulmonary oedema or identify rib fractures secondary to vigorous CPR and is useful to check the position of the endotracheal tube. Routine blood biochemistry, haematology, cardiac enzymes, glucose and group and save are taken, and blood is cross-matched if a bleed is suspected. An ABG will indicate whether ventilation is adequate.

A6: What other issues should be addressed?

Most patients need admission to intensive care post-arrest and may require ventilation and support with inotropes such as adrenaline. The patient may require a central line and therapeutic hypothermia. A member of the medical team must speak with the family and inform them of the future management and likely prognosis.

CASE 5.4 – **A 65-year-old man with tearing chest pain.**

A1: What specific questions would you ask the patient?

Establish the nature of the pain. Aortic dissection pain can mimic MI, and caution must be taken to distinguish the two because treatment is different. Abrupt onset of tearing chest pain that radiates to the back and abdomen indicates dissection. Patients may present with symptoms and signs of occlusion of one or more of the branches of the aorta as the dissection progresses: stroke, limb ischaemia, paraplegia, MI. Risk factors to enquire about include hypertension, arteriosclerosis (IHD/peripheral vascular disease), pregnancy, history of trauma and rarely Marfan's syndrome.

A2: What is the likely diagnosis?

The most likely diagnosis is aortic dissection. This may be proximal (type I starts in the ascending aorta but progresses down the aorta; type II is localized to the ascending aorta) or distal (type III starts in the descending aorta after the arch), involving the descending aorta only.

A3: What examination would you perform?

A full examination is necessary. A blood pressure difference between the right and left arms (> 15 mmHg) occurs in 10 per cent of patients with a dissection. There may be a difference in pulse between the

right and left arms or radial and femoral pulses. An elevated JVP and pulsus paradox indicate cardiac tamponade caused by rupture of the aortic wall into the pericardium. Aortic regurgitation may be heard when the aortic root is involved. The patient should be examined for any neurological deficit.

A4: What would be the initial management?

Resuscitation is the initial management. Oxygen must be given via a facemask. Intravenous access is established and pain relief with diamorphine given. Systolic blood pressure must be reduced to 100–120 mmHg using drugs that decrease the inotropic force of the heart, e.g. labetalol infusion.

A5: What investigation would you request to confirm a diagnosis?

The diagnosis of aortic dissection can be made in several ways. The diagnosis is often suspected from the chest radiograph, which may demonstrate a widened mediastinum. This is an unreliable sign, however, and chest computed tomography (CT) with contrast or magnetic resonance imaging (MRI) is usually preferred to make the diagnosis non-invasively. An echocardiogram is also useful to look at the aortic root in detail in type I or II dissection, but a transoesophageal echocardiogram is preferred if possible to obtain detailed views of the descending thoracic aorta. Cardiac catheterization will aid planning of surgical repair.

A6: What other issues should be addressed?

Over 50 per cent of patients die in the first 24 h of presentation. Urgent surgical repair is needed in type I or II dissection, and frequently in type III dissection, if the patient is to have a chance of survival.

CASE 5.5 – **A 25-year-old man with a heart murmur.**

A1: What specific questions would you ask the patient?

Elicit from the history whether the patient has any symptoms suggestive of valvular stenosis or regurgitation: dyspnoea, oedema, dizziness, syncope, palpitations or chest pain. Haemoptysis or recurrent bronchitis may indicate pulmonary hypertension. A past medical history may suggest a cause, such as rheumatic heart disease or MI causing papillary muscle rupture. Consider underlying conditions and family history that may predispose to valvular abnormalities, such as dilated or hypertrophic cardiomyopathy, Marfan's syndrome or ankylosing spondylitis. Ask about any symptoms that may suggest endocarditis (rash, fevers) or predisposing factors such as IV drug misuse.

A2: What is the likely diagnosis?

A heart murmur is heard when there is turbulent blood flow, the cause usually being an abnormal heart valve that may be incompetent (regurgitant), stenotic or both. An 'innocent murmur' produced by a normal heart valve tends to occur in the setting of a hyperdynamic circulation, such as anaemia, thyrotoxicosis or pregnancy. See Key concepts for causes of each murmur.

A3: What examination would you perform?

A full physical examination is necessary. Determine the characteristics of the pulse and blood pressure. Look for signs of right heart failure (raised JVP, ankle oedema, enlarged liver) and for pulmonary oedema indicating LV failure. Determine whether the murmur is systolic or diastolic. The character of the murmur (e.g. pansystolic in mitral regurgitation) and the location and radiation of the murmur will give further clues to the diagnosis (see Key concepts). Bear in mind that a soft midsystolic murmur that varies with posture and is not associated with signs of heart disease is usually benign.

A4: What would be the initial management?

Medical therapy is aimed mainly at treatment of complications (AF, heart failure). Surgical treatment may be valve repair, valve replacement or valvotomy (see Key concepts). Surgery must be performed before irreversible LV dysfunction and pulmonary oedema become established.

A5: What investigations would you request to confirm a diagnosis?

Valve dysfunction is confirmed with trans-thoracic echocardiography, trans-oesophageal echocardiogram or cardiac MRI. An ECG may show LV hypertrophy and confirm AF or, if the patient is in sinus rhythm, show the bifid P-wave ('P mitrale') of left atrial hypertrophy in mitral stenosis or the tall P-wave ('P pulmonale') of pulmonary hypertension. A chest radiograph may indicate cardiomegaly.

A6: What other issues should be addressed?

Prosthetic valves are either mechanical (e.g. Starr–Edwards ball-and-cage valve (old type of valve), Björk–Shiley tilting disc valve) or bioprosthetic valves (porcine xenograft). Bioprosthetic pig valves typically degenerate after about 10 years and hence are preferably used in elderly people. Mechanical valves last longer but need life-long anticoagulation. All prosthetic valves and native abnormal valves are susceptible to infection. Patients should always be advised that antibiotic prophylaxis is no longer required for routine surgical or dental procedures under new guidance, but good dental hygiene is important.

OSCE counselling cases

OSCE COUNSELLING CASE 5.1 – **'Can I stop my warfarin?'**

The answer is *definitely not!* Anticoagulation must never be stopped in a patient with a metal heart valve without a specialist cardiology consultation and a robust alternative plan.

If the patient stops anticoagulation, there is a significant risk of thrombosis, especially in the hypercoagulable state of pregnancy. A clot may obstruct the valve, causing sudden stenosis, or embolize and cause a stroke.

Her worries are genuine, however. Warfarin does indeed have teratogenic effects, particularly if the patient requires high doses, and it can also cause intracerebral haemorrhage in the fetus. Women who continue warfarin throughout pregnancy have approximately a 7 per cent chance of having a baby with a congenital abnormality and a further 16 per cent risk of stillbirth or spontaneous abortion. There are also increased complications after delivery.

The answer is to advise the patient to change to heparin (subcutaneous) for the first 3 months of the pregnancy, restart warfarin at 3 months and change again to heparin 2–4 weeks before the expected delivery date. Heparin is not teratogenic, but it is associated with a higher risk of abortion and a higher incidence of bleeding. This can be monitored and the dose adjusted. This requires a tertiary cardiology review/plan; some centres will use subcutaneous heparin throughout pregnancy.

Another point of note is that warfarin is excreted in breast milk (in small amounts), and it is advisable that mothers on warfarin should not breastfeed.

OSCE COUNSELLING CASE 5.2 – **'I'm on various medicines for my angina. How should I take them and what side effects do they have?'**

GTN

Nitrates are potent vasodilators, but the main benefit in angina is by causing a reduction in venous return, which reduces LV work. Sublingual GTN is used to treat symptoms in angina on an as-required basis. It comes in spray or tablet form, with the advantage of the spray having a longer storage life once opened. The onset of action is 1–2 min and effects last for up to 20 min. Sublingual GTN can be taken repeatedly, but the patient should be advised to seek medical attention if they do not get any relief after repeated use.

Headaches are common, especially in the first few days after starting treatment. The patient should be advised that if the headache is severe, they can spit out or swallow the tablet to deactivate it. Flushing and postural hypotension causing syncopal attacks are also reported and may limit therapy.

Beta-blockers

Beta-blockers decrease myocardial oxygen demand by causing a fall in heart rate and blood pressure and decreasing myocardial contractility. They are contraindicated in asthma and chronic obstructive pulmonary disease, however, and are relatively contraindicated in diabetes mellitus, peripheral vascular disease and severe LV dysfunction.

Lethargy is a common side effect of beta-blockers; interference with exercise capacity may cause patients to discontinue their medication. Coldness of extremities and sleep disturbances may also lead to non-compliance. Bradycardia and other conduction disorders may also occur.

OSCE COUNSELLING CASE 5.3 – **'I have heart failure. Do I need to take my medications for life?'**

Unfortunately, a diagnosis of heart failure (in this case, moderate to severe on echocardiogram assessment) is associated with a worse prognosis than most cancers (50 per cent 5-year mortality rate if untreated). With correct therapeutic management, the patient's symptoms will improve and his annual risk of death will be cut by half.

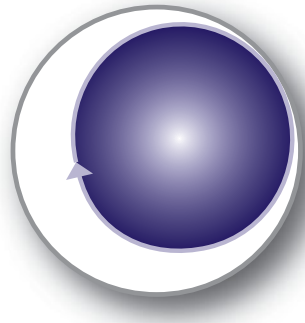
It is very important to use medications that have been shown in large randomized trials to be effective (see Key concepts).

Ask the patient whether he is having any particular problem with the drugs prescribed, particularly symptoms of hypotension. Advise the patient that, if possible, the dose of bisoprolol may be increased to try to reach the target dose of 10 mg once a day. Advise the patient that he will require regular blood checks (initially every 1–2 weeks and then every 3 months, watching for hyperkalaemia and rising creatinine) because of the potential interaction between ACE inhibitors and spironolactone.

The patient should be advised to monitor his weight regularly and to seek advice if his weight rises, because this may be a sign of fluid overload.

REVISION PANEL

- Cardiac arrhythmias may occur due to IHD, valvular heart disease and thyrotoxicosis. In a young person, thyrotoxicosis should be excluded.
- If the patient has a tachycardia and is haemodynamically unstable (systolic blood pressure <80 mmHg, reduced level of consciousness, severe pulmonary oedema), consider immediate DC cardioversion.
- If the patient has a bradycardia and is haemodynamically compromised, give atropine 0.6–1.2 mg IV. If there is persistent bradycardia, consider external pacing while organizing transvenous pacing wire insertion.
- Risk factors for IHD include diabetes mellitus, hypertension, hyperlipidaemia, smoking, family history, male sex, increasing age and obesity.
- Apart from coronary ischaemia, other causes of chest pain to consider include pericarditis, dissecting aortic aneurysm, pulmonary embolus, pleurisy, gastro-oesophageal reflux, perforated peptic ulcer, pancreatitis and cholecystitis.
- A heart murmur is heard when there is turbulent blood flow, the cause usually being an abnormal heart valve that may be incompetent (regurgitant), stenotic or both.
- An 'innocent murmur' produced by a normal heart valve tends to occur in the setting of a hyperdynamic circulation, such as anaemia, thyrotoxicosis or pregnancy.
- Always exclude bacterial endocarditis if a patient is acutely unwell with a cardiac murmur.
- Anticoagulation should never be stopped in a patient with a prosthetic metal heart valve without careful consideration.



6 Care of elderly people

Peter Wallis

FALLS

IMMOBILITY

ACUTE CONFUSIONAL STATES

INCONTINENCE

IATROGENIC ILLNESS IN FRAIL OLDER PATIENTS

FALLS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the differential diagnosis?
Q2: What features in the history support the diagnosis?
Q3: What additional features in the history would you seek to support the potential diagnoses?
Q4: What other features would you look for on clinical examination?
Q5: What investigations would you perform?
Q6: What treatment options are available?

CASE 6.1 – A 71-year-old man has been brought to the accident and emergency (A&E) department after a fall while shopping.

He lost consciousness momentarily and has little recollection of the event. He describes previous episodes of dizziness, sometimes on exertion and often associated with shortness of breath. His past history includes a hiatus hernia, diverticular disease, and osteoarthritis of his neck and knees. He is taking regular omeprazole, a dietary fibre supplement and a compound analgesic containing paracetamol and codeine (co-codamol). Examination discloses a regular pulse and blood pressure of 114/76 mmHg. There is an ejection systolic cardiac murmur radiating to the neck. The lung fields are clear. Neurological examination is normal.

CASE 6.2 – An 82-year-old woman presents with recurrent falls.

The patient is housebound. Her most recent fall occurred while getting up to go to the toilet at night. She has arthritis, heart failure and poor vision as a result of macular degeneration, and she has had a previous hip replacement. She receives treatment with furosemide, ramipril, co-codamol, amitriptyline and temazepam. She is very frail. The main findings on examination are: abbreviated mental test 6/10, vision – large print only, kyphotic spine, brisk reflexes bilaterally, peripheral oedema, clear lung fields and normal jugular venous pressure (JVP), heart rate 112/min, atrial fibrillation (AF), blood pressure sitting 114/62 mmHg, mitral regurgitation.

CASE 6.3 – A 78-year-old man who lives alone is brought to A&E after being found on the floor at home by his neighbour.

The patient is confused and disoriented. His head is bruised and he appears unkempt. He is immobile and there is cog-wheel rigidity in all his limbs. There are no focal neurological signs. Reflexes are hard to elicit as a result of the muscle stiffness. Plantar responses are down-going. There are signs of a lower

respiratory tract infection. Temperature is 38.2 °C, blood pressure is 102/60 mmHg and heart rate is 94/min.

The investigation discloses: normal plasma glucose and electrolytes; urea 24 mmol/L; creatinine 142 μmol/L; haemoglobin (Hb) 15.5 g/dL; white cell count (WCC) 14.3×10^9/L; platelets 342×10^9/L; chest radiograph – consolidation right lower lobe; electrocardiogram (ECG) – sinus tachycardia.

OSCE counselling cases

OSCE COUNSELLING CASE 6.1 – What advice would you give the following patient?

An elderly housebound woman has fallen at home on several occasions and has recently attended A&E with a Colles' (wrist) fracture. Her daughter is concerned about the presence of osteoporosis and seeks your advice at the surgery about the need for calcium tablets to prevent further fractures.

OSCE COUNSELLING CASE 6.2 – 'What is the underlying condition, and how has it come about?'

A housebound 94-year-old woman who has epilepsy (controlled with phenytoin) presents with falls, weakness and generalized aches and pains. Biochemical tests reveal calcium (corrected) 1.85 mmol/L (normal range 2.05–2.60 mmol/L); phosphate 0.68 mmol/L (normal range 0.8–1.45 mmol/L); albumin 32 g/L (normal range 35–48 g/L); alkaline phosphatase (ALP) 458 U/L (normal range 30–200 U/L).

What is the likely diagnosis? What factors might have precipitated this condition? What signs would you look for on examination? How would you treat the condition?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Older people are at much greater risk of falling compared with younger people. Most falls occur at home. The risk of falling is much higher in older people who reside in an institutional environment such as a residential or nursing home or hospital, as a result of the increased frailty of this group of patients. One-third of people aged over 65 years will fall in a year, often repeatedly. Falls resulting in injury are a leading cause of death in older people, accounting for two-thirds of injury-related deaths in people aged 85 years and over. Most falls do not result in death, but they can give rise to substantial morbidity. The fear of falling often leads to loss of confidence, increased dependence on others and restriction of activity.

Most patients fall because of age-related or disease-associated damage to one or more systems essential for the maintenance of balance and posture. Vision, vestibular, sensory, locomotor, cardiovascular and central processing mechanisms are all important in this regard. A careful history detailing the circumstances surrounding the fall is essential. Often there is little recollection of the prodromal events, and so corroborative information from a witness is invaluable. Patients will often provide their own explanation – 'I must have tripped, doctor' – but be cautious about accepting such well-meaning accounts of events without further enquiry. Accurate diagnosis, treatment of predisposing illness, and amelioration of risk factors such as impaired vision, polypharmacy, inadequate footwear and environmental hazards are all important. Multidisciplinary falls clinics (with physiotherapy and occupational therapy support) and exercise programmes (including activities that promote balance and strength) can reduce the risk of falling.

Many falls result in bone fractures such as wrist, pelvis, neck of humerus or, most feared of all, hip. Such fragility fractures should prompt an assessment for osteoporosis, which can be assumed to be present in patients over 75 years old. Treatments for osteoporosis include bisphosphonates, calcium and vitamin D supplements. The latter are particularly indicated for older people who are housebound or cared for in a residential or nursing home setting. Hip protectors can reduce the risk of femoral neck fractures in selected frail older people when worn.

Answers

Clinical cases

CASE 6.1 – **A 71-year-old man has been brought to A&E after a fall while shopping.**

A1: What is the differential diagnosis?

- aortic stenosis
- cardiac arrhythmia
- silent myocardial infarction (MI)
- postural hypotension
- vasovagal episode
- hindbrain transient ischaemic attack (TIA).

A2: What features in the history support the diagnosis?

The syncopal event occurred on exertion, and this is consistent with significant aortic stenosis. In this situation, syncope can be precipitated by impaired cardiac output or a transient arrhythmia such as ventricular tachycardia. The history of previous exertional dizziness and breathlessness lends support to this diagnosis.

Silent MI or cardiac arrhythmia must be considered too. Myocardial infarction can present without chest pain, particularly in older patients.

Postural hypotension – postural dizziness when standing (e.g. arising from bed at night) – might be volunteered. Enquire about medications with hypotensive properties (e.g. diuretics, antihypertensives, antidepressants). Co-codamol is not usually a cause of postural hypotension, but the opiate component (codeine) can reduce alertness and impair balance.

Vasovagal episodes are a common cause of syncopal events, particularly in younger patients. In this case, the lack of any precipitating event (e.g. prolonged standing) or prodromal symptoms (e.g. faintness, nausea) and the presence of other cardiac symptoms and signs make the diagnosis unlikely.

Finally, the patient has an arthritic neck. When severe, this can compromise the vertebrobasilar circulation, especially if there is significant atheroma affecting the vertebrobasilar system and circle of Willis. The apparent absence of sudden neck movement before syncope and the lack of other features such as dizziness, vertigo, nausea or sudden loss of tone in the legs ('drop attack') make this diagnosis less likely.

A3: What additional features in the history would you seek to support the potential diagnoses?

The presence of exertional chest pain (angina) and dyspnoea supports the diagnosis of aortic stenosis (syncope, angina, dyspnoea = SAD).

A4: What other features would you look for on clinical examination?

In aortic stenosis, the following might be present:

- ejection systolic murmur radiating to the neck
- slow rising pulse
- low pulse pressure

- ejection click sometimes heard
- early diastolic murmur if there is also aortic regurgitation
- quiet second heart sound.

In silent MI, the following might be present:

- signs of heart failure
- cool, clammy peripheries resulting from low cardiac output.

In postural hypotension, there is a fall in standing blood pressure <20 mmHg associated with symptoms of dizziness or faintness. In hindbrain ischaemia, symptoms are sometimes precipitated by head movement.

A5: What investigations would you perform?

ECG, chest radiograph, cardiac enzymes or troponin testing, echocardiography and ECG (Holter) monitoring should be done.

A6: What treatment options are available?

A precise diagnosis is essential first. If aortic stenosis is severe, the patient should be referred to a cardiologist for consideration of valve replacement. Transaortic valve implantation has extended the option of valvular repair to include patients not previously considered robust enough for open heart surgery. The patient should be advised to avoid sudden strenuous exertion in the meantime.

Admission is necessary if MI or arrhythmia is suspected. If there is postural hypotension, consider discontinuing or reducing the dose of any offending medication. The patient should be educated regarding avoidance of precipitating events. Compression hosiery should be used.

Aspirin and statin should be given for hindbrain TIA.

CASE 6.2 – **An 82-year-old woman presents with recurrent falls.**

A1: What is the differential diagnosis?

There are multiple causes, including:

- poor vision
- postural hypotension
- polypharmacy
- neurological dysfunction – previous stroke, cervical myelopathy, vitamin B12 deficiency
- arthritis/osteomalacia
- arrhythmia – AF.

A2: What features in the history support the diagnosis?

- *Poor vision:* the fall occurred at night when environmental hazards are more difficult to see and avoid.
- *Postural hypotension:* the fall occurred as the patient was getting out of bed to go to the toilet. She is on a lot of medications that can impair postural blood pressure control – a diuretic, an angiotensin-converting enzyme (ACE) inhibitor and amitriptyline (a tricyclic antidepressant with anticholinergic properties).
- *Polypharmacy:* postural hypotension:
  - impaired balance and cognition caused by temazepam, opiate analgesic and tricyclic antidepressant
  - muscle weakness; diuretic-induced hypokalaemia.
- *Neurological dysfunction:* brisk reflexes are suggestive of upper motor neuron dysfunction. Common causes at this age include stroke disease, cervical myelopathy and occasionally vitamin B12 deficiency.

As a result of the history of falls and the finding of cognitive impairment, a chronic subdural haematoma should also be considered.
- *Atrial fibrillation:* poorly controlled (rapid) ventricular rate on exertion causing syncope. AF might also be a manifestation of sick sinus syndrome, predisposing to supraventricular tachycardia or bradycardia.

A3: What additional features in the history would you seek to support the potential diagnoses?

- *Poor vision:* access to spectacles, ability to read or identify objects, adequacy of lighting in the home.
- *Postural hypotension:* dizziness or falls when upright, with associated symptoms of faintness or syncope, and rapid recovery when recumbent.
- *Polypharmacy:* concordance with medication regimen and any potential to exceed the intended dosing schedule.
- *Neurological dysfunction:* history suggestive of previous stroke or TIA.
- *Neck arthritis:* giddiness on head movement and pain radiating to shoulders and upper limbs (cervical spondylitic radiculopathy) suggest cervical myelopathy as a potential cause of falling.
- *Enquire about* diet, previous gastric surgery, bowel (terminal ileal) disease or resection, anaemia and symptoms of sensory neuropathy in suspected vitamin B12 deficiency.
- *Fluctuating alertness:* confusion or consciousness with a history of falls and head injuries (even trivial) should highlight the possibility of subdural intracranial bleeding.
- *Bone pains and muscle weakness:* in a housebound patient with poor diet, these point to osteomalacia.
- *Cardiac arrhythmia:* recurrent episodes of dizziness or syncope unrelated to posture or activity with prompt recovery suggest an intermittent cardiac rhythm disturbance.

A4: What other features would you look for on clinical examination?

- *Poor vision:* Snellen chart to assess visual acuity, examination of eyes for common causes of visual loss in older people (i.e. refractive disorder), cataracts, glaucoma, macular degeneration, diabetic retinopathy.
- *Postural hypotension:* lying and standing blood pressure.
- *Neurological disorders:* thorough central nervous system (CNS) examination essential. Focal upper motor neuron signs suggestive of stroke or subdural haematoma. Up-going plantar responses, consistent with cervical myelopathy; peripheral neuropathy and posterior column dysfunction (joint position/vibration sense) suggest vitamin B12 deficiency.
- *Arthritis/osteomalacia:* joint examination, back pain, muscle weakness.

A5: What investigations would you perform?

The following tests are necessary:

- lying and standing blood pressure
- ECG
- plasma urea, creatinine and electrolytes (U&Es) and glucose
- full blood count (FBC) (and vitamin B12/folate levels if macrocytic anaemia present)
- radiograph of painful bones and significantly arthritic joints
- vitamin D, calcium, albumin and alkaline phosphatase (ALP; for osteomalacia).

Other tests might be indicated after preliminary assessment and investigation, including:

- cervical spine radiograph with option to proceed to magnetic resonance imaging (MRI) cervical spine if cervical myelopathy is probable and surgery is a realistic option

- computed tomography (CT) of the brain
- thyroid function.

A6: What treatment options are available?

- *Vision:* occupational therapist home visit to remove environmental hazards and improve lighting. Assess for spectacles and ophthalmic referral as needed.
- *Postural hypotension and polypharmacy:* review the need for and doses of all medications.
- *Neurological dysfunction:* beyond the scope of this case scenario.
- *Osteomalacia:* calcium and vitamin D supplements.
- *Atrial fibrillation:* discuss the need for rhythm or rate control – options include cardioversion, digoxin, beta-blockers and amiodarone. If the patient has a bradyarrhythmia, they will require assessment for cardiac pacemaker. Owing to the risk of further falls, anticoagulation with warfarin is often not appropriate without very careful assessment of the ongoing risks. Always involve the patient, family and general practitioner (GP) in such discussions.

CASE 6.3 – **A 78-year-old man who lives alone is brought to A&E after being found on the floor at home by his neighbour.**

A1: What is the differential diagnosis?

- pneumonia
- dehydration
- parkinsonism
- head injury with intracranial bleed or contusion.

A2: What features in the history support the diagnosis?

Hypostatic pneumonia and dehydration often complicate a long period of immobility after a fall. Aspiration pneumonia should also be considered.

The generalized muscle cog-wheel rigidity is suggestive of parkinsonism. Reflexes can be difficult to elicit in this situation. Spasticity caused by cerebrovascular disease would more usually be associated with hyperreflexia and up-going plantar responses. Parkinsonism might be a result of idiopathic Parkinson's disease or secondary to other causes such as medication (e.g. neuroleptics such as haloperidol or risperidone) or vascular (arteriosclerotic). The patient's unkempt state suggests a chronic insidious decline before this acute presentation. Parkinson's disease and parkinsonism can present in this way.

Head injury is obvious on examination, but the severity is difficult to assess. A subdural haematoma (acute or chronic) must be considered in this setting.

A3: What additional features in the history would you seek to support the potential diagnoses?

Further history from family, neighbours and so on is essential to establish the time course and pattern of the patient's decline and any history of previous falls. An accurate medication history is required, from the GP's records if necessary. Any suggestion of alcohol abuse is important. As always, details of past medical history are essential, such as a history of stroke disease, vascular dementia, and previous psychiatric history requiring neuroleptic medication.

A4: What other features would you look for on clinical examination?

Assessment of conscious level and airway is essential because the patient is at risk of airway obstruction and aspiration.

Signs of weight loss or lymphadenopathy (tuberculosis [TB]) and clubbing (bronchial carcinoma) should be looked for. The rigidity of parkinsonism is usually of lead-pipe or cog-wheel type. A pill-rolling resting tremor may also be present, but not invariably so.

Evidence should be sought of urinary outflow obstruction (enlarged bladder), faecal impaction (rectal examination), bony injuries (hip, skull) and pressure sores, which can be overlooked in this setting.

A5: What investigations would you perform?

Additional investigations include:

- arterial oxygen saturation/blood gases
- blood and sputum cultures (for pneumonia)
- calcium (confusion caused by hypercalcaemia)
- urea, creatinine, electrolytes and creatinine kinase (for dehydration, kidney failure, rhabdomyolysis)
- ECG (for arrhythmias)
- radiographs of skull and sites of other apparent bony injuries
- CT of head (for acute or chronic subdural haematoma).

A6: What treatment options are available?

The following treatment options are available:

- rehydration with monitoring of urine output
- oxygen therapy as directed by O_2 saturation or arterial blood gas (ABG) measurements
- broad-spectrum antibiotics for hypostatic/aspiration pneumonia (e.g. benzylpenicillin, levofloxacin and metronidazole – but consult local antibiotic guidelines)
- discontinuation of any drugs likely to cause parkinsonism
- if idiopathic Parkinson's disease is suspected, gradual introduction of L-dopa-based medication (e.g. co-careldopa) once resuscitation completed.

OSCE counselling cases

OSCE COUNSELLING CASE 6.1 – What advice would you give the following patient?

The daughter has a valid point, but you will need to explain that to prevent further fractures measures are needed to reduce the risk of falling in addition to a consideration of treatment for osteoporosis.

The patient would benefit from a multidisciplinary assessment to identify remediable medical illnesses that might precipitate falls (e.g. cardiovascular disease, medications, poor eyesight, Parkinson's disease). Advice from a physiotherapist or occupational therapist on measures to enhance fitness and safety at home, and to secure help if further falls supervene, is also essential.

If the patient is aged 75 years or older, osteoporosis can be assumed in the setting of a low trauma fracture. Having excluded secondary causes of osteoporosis (e.g. thyrotoxicosis, steroid therapy, multiple myeloma, hyperparathyroidism), treatment for age-associated osteoporosis should be considered. In this setting, calcium and vitamin D supplements are helpful and relatively safe, although it is prudent to measure the plasma calcium level before and 6–8 weeks after initiating treatment. A regular bisphosphonate is also indicated, providing the requirements for safe and effective oral dosing can be followed. Oesophageal and peptic ulcer disease and renal impairment will require caution with respect to bisphosphonate therapy. Thorough discussion with the patient is essential before initiating treatment.

OSCE COUNSELLING CASE 6.2 – 'What is the underlying condition, and how has it come about?'

The likely diagnosis is osteomalacia. Lack of exposure to sunlight, poor diet if socially isolated, poor health, and enhanced metabolism of vitamin D as a result of treatment with phenytoin (a liver enzyme inducer) may have precipitated the condition. Diseases causing malabsorption and chronic renal failure can also predispose to osteomalacia.

You need to look for proximal muscle weakness, bony tenderness (pseudo-fractures or Looser's zones on radiograph), and skeletal deformities such as kyphosis and bowing of the limbs. Significant hypocalcaemia can precipitate tetany with a positive Chvostek sign (spasm of the facial muscles on tapping over the branches of the facial nerve in front of the ear) and Trousseau's sign (spasm of the hand and forearm muscles after compression of the forearm).

The blood level should be checked for 25-hydroxy-vitamin D, and vitamin D supplements should be given either orally or intramuscularly. An adequate calcium intake should be provided, if necessary with oral calcium supplements (1 g/day). There should be a thorough discussion with the patient about the risks and benefits of changing to an alternative anticonvulsant such as sodium valproate.

IMMOBILITY

Questions

Clinical cases

For each of the case scenarios given, consider the following:

CASE 6.4

Q1: What is the differential diagnosis?
Q2: What features in the history support the diagnosis?
Q3: What additional features in the history would you seek to support the potential diagnoses?
Q4: What other features would you look for on clinical examination?
Q5: What investigations would you perform?
Q6: What treatment options are available?

CASE 6.5

Q7: What investigations would you perform?
Q8: What treatment options are available?
Q9: What are the likely causes of his immobility?
Q10: What can be done to improve the situation at home?

CASE 6.6

Q11: What treatment options are available?
Q12: In addition to regular medical and nursing attention, which members of the multidisciplinary team ought to be involved with care?
Q13: What medical complications might supervene during the next 4–6 weeks?

CASE 6.4 – **A 74-year-old man who has difficulty walking is referred to the elderly medicine day hospital.**

The patient is confined to his chair unless assisted to stand. He cannot get into bed at night. His past history includes neck surgery for cervical spondylosis. He has hypertension treated with nifedipine. He is obese, his legs are oedematous and he is incontinent of urine. He has ulceration and cellulitis affecting his lower legs. A CNS examination reveals normal cognition and cranial nerves, but weak arms and legs (power 4/5), brisk reflexes bilaterally and up-going plantar responses. His feet are warm but foot pulses are impossible to assess owing to oedema.

CASE 6.5 – **You have been called to see a 72-year-old man who lives alone at home.**

The district nurse has become increasingly concerned about his health. The patient has been housebound for some time but is now unable to rise from his chair. He is a large man and his left hip is very painful. There is no history of a fall. He is unkempt and his clothes smell of urine. He is a heavy smoker, and he is breathless and wheezy with a chronic cough. His legs are swollen and blistered. Detailed examination is difficult but reveals signs of airflow obstruction, cyanosis, elevated JVP and peripheral oedema. Movement at the left hip is restricted and painful. He is very reluctant to leave his home.

CASE 6.6 – **A 68-year-old previously active woman is unable to walk or stand having sustained a stroke (left middle cerebral artery territory infarction) 3 weeks previously.**

The patient has a dense right hemiparesis, homonymous hemianopia and sensory disturbance. She is also dysphasic and has difficulty swallowing. Recovery has been complicated by aspiration pneumonia. She has a urinary catheter and needs regular toileting. She is in AF, and her blood pressure is 142/78 mmHg. She is reluctant to engage with her programme of rehabilitation.

OSCE counselling cases

OSCE COUNSELLING CASE 6.3 – **A 75-year-old man who lives in a nursing home is confined to his bed or chair as a result of a previous left-sided stroke.**

The patient is a large man and his care is made even more challenging as a result of the presence of dysphasia, dysphagia and mild cognitive impairment. The patient's GP visits the nursing home periodically to review his care and general condition. Give five important areas that the GP should enquire about or assess when visiting the patient. Give a brief explanation of why each of these areas needs review.

OSCE COUNSELLING CASE 6.4 – **A 65-year-old woman is reviewed in clinic following recent colonic surgery.**

Shortly after surgery the patient developed a hot swollen leg from a deep vein thrombosis (DVT), confirmed on duplex scanning. She has been started on anticoagulation therapy. She is upset that this developed and wants you to explain why it occurred and what was done to prevent it. How would you approach answering this patient?

OSCE COUNSELLING CASE 6.5 – **The wife of an elderly man is distressed because her husband's attendance at the local elderly care day hospital for physiotherapy has been discontinued. He had a severe stroke 3 months ago and is now confined to a wheelchair. He has difficulty speaking as a result of dysphasia. What advice would you give?**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Many chronic diseases in older people present with difficulty walking or transferring from chair to bed. Immobility itself is not a diagnosis but a symptom for which there are any number of causes. Common illnesses in older people that impair walking include:

- stroke disease
- osteoarthritis
- parkinsonism
- dementia
- visual impairment
- chronic cardiorespiratory disease
- injuries and complications of falling
- problems with feet and footwear.

Careful and accurate assessment is essential, with the aim of identifying treatable causes in order to focus the efforts of the multidisciplinary team. Remember that being immobile can lead to further disabling and potentially fatal complications such as pressure sores, hypostatic pneumonia, DVT, osteoporosis, limb contractures, urinary retention and faecal impaction. Depression often occurs in such situations.

Answers

Clinical cases

CASE 6.4 – **A 74-year-old man who has difficulty walking is referred to the elderly medicine day hospital.**

A1: What is the differential diagnosis?

- cervical myelopathy
- gravitational and calcium antagonist-induced lower limb oedema
- infected leg ulcers
- possible DVT.

A2: What features in the history support the diagnosis?

The history of neck surgery for arthritis and the finding of upper motor neuron signs in the arms and legs (with no evidence of neurological dysfunction above the neck) is highly suggestive of cervical myelopathy consequent to degenerative disease of the cervical spine.

Impaired mobility, obesity and dependency of the lower legs predispose to venous stasis, oedema and ulceration (and in due course infection). This is a potent setting for venous thrombosis. Calcium antagonists can exacerbate peripheral oedema.

Urinary incontinence is inevitable in this setting owing to immobility and impaired bladder control caused by compression of the cervical spinal cord.

A3: What additional features in the history would you seek to support the potential diagnoses?

- history of neck trauma or injury or arthritic symptoms – acute-on-chronic deterioration will require urgent neurosurgical opinion and possible intervention
- constipation – common in this setting and exacerbated by calcium antagonists
- history of previous venous thrombosis or peripheral vascular disease
- symptoms of breathlessness or chest pain (pulmonary embolism).

A4: What other features would you look for on clinical examination?

- signs of pulmonary embolism or heart failure
- pressure sores (buttocks, sacrum, heels)
- faecal impaction and urinary retention.

A5: What investigations would you perform?

- FBC (infection)
- renal function and plasma glucose (renal failure and diabetes mellitus)
- urinalysis:
  - heavy proteinuria if oedema caused by nephrotic syndrome
  - glycosuria
  - protein and blood consistent with urinary infection

- midstream urine specimen (MSU; infection)
- leg ulcer swab and blood cultures (to guide antibiotic therapy)
- venous and arterial Doppler studies of legs (detection of venous thrombosis and exclusion of ischaemic leg ulceration)
- cervical spine radiograph (cervical spondylosis/osteoarthritis)
- MRI cervical spine (to detect spinal cord compression)
- chest radiograph and ECG (heart failure and pulmonary embolism).

A6: What treatment options are available?

Neck surgery for cervical myelopathy is unlikely to be successful in this setting as a result of chronicity of symptoms. Surgery could also be very hazardous as a result of significant comorbidity.

The following treatment options are available:

- elevation of legs to diminish oedema
- antibiotics for cellulitis
- compression bandaging or hosiery to control peripheral oedema once cellulitis has resolved and arterial ischaemia has been excluded
- pressure-relief mattress/cushion for areas at high risk of pressure sores
- anticoagulant therapy if venous thrombosis is confirmed (consider DVT prophylaxis if absent)
- discontinuation of calcium antagonist – consider an alternative antihypertensive agent such as a diuretic (might exacerbate incontinence), an ACE inhibitor (might impair renal function) or a beta-blocker (care if uncontrolled heart failure/diabetes present), or an alpha-blocker (watch for postural hypotension)
- treatment for heart failure if confirmed
- attention to bowel and bladder function
- referral to multidisciplinary team for rehabilitation and resettlement at home in due course.

CASE 6.5 – **You have been called to see a 72-year-old man who lives alone at home.**

A7: What investigations would you perform?

Basic investigations should include:

- hip radiograph (essential for osteoarthritis or avascular necrosis of femoral head or fractured neck of femur)
- FBC (secondary polycythaemia and infection)
- renal function tests (uraemia and electrolyte imbalance)
- measurement of ABGs should be considered because of the signs of respiratory failure and possible hypercapnia
- chest radiograph and ECG (to support the diagnosis of chronic obstructive pulmonary disease [COPD] and cor pulmonale)
- peak expiratory flow rate or spirometry before and after inhaled bronchodilator will confirm COPD and determine the degree of reversibility.

A8: What treatment options are available?

Management will be difficult at home as a result of the need for radiographs and specialist tests, and the presence of respiratory failure. Brief hospital assessment (a rapid-access day hospital clinic or short-stay elderly care ward) is advisable to confirm the diagnoses and assess the degree of respiratory failure. Time will be needed for rehabilitation and adaptations to the home environment.

Treatment will be along the following lines:

- analgesia for osteoarthritis (avoiding opiates and non-steroidal anti-inflammatory drugs [NSAIDs] if possible – potential respiratory depression and fluid retention, respectively)
- bronchodilators, controlled oxygen and cautious use of diuretics for COPD and cor pulmonale
- laxatives and enemas for faecal impaction or constipation
- in due course, consideration of hip replacement if the patient is agreeable and cardiorespiratory status permits.

A9: What are the likely causes of his immobility?

The likely causes are:

- osteoarthritic hip – a hip fracture is less likely as a result of the chronicity of the symptoms and absence of trauma
- COPD (chronic bronchitis and emphysema) and cor pulmonale
- urinary incontinence caused by immobility – almost inevitable in this situation, perhaps exacerbated by coexisting prostatism or faecal impaction.

A10: What can be done to improve the situation at home?

Much depends on the patient's potential to improve and the feasibility of hip surgery. Adaptations to the home with appropriate seating and bedding, and a review of toilet and washing arrangements, will be necessary. The patient's ability to climb stairs safely will need to be assessed. He will need assistance with shopping and other household tasks. A multidisciplinary team approach is required to resolve these various issues, including physiotherapy, occupational therapy and social worker involvement. Early discharge from hospital can be achieved with forward planning and use of domiciliary rehabilitation services.

CASE 6.6 – **A 68-year-old previously active woman is unable to walk or stand, having sustained a stroke (right middle cerebral artery territory infarction) 3 weeks previously.**

A11: What treatment options are available?

Depression is common at this stage and can seriously interfere with rehabilitation. An antidepressant in conjunction with psychological support and a positive approach by the multidisciplinary team can help alleviate this.

- *Anticoagulants* – due to AF, there is a risk of further stroke (12–15 per cent per annum), which can be reduced by two-thirds after anticoagulation with warfarin (international normalized ratio [INR] 2.0–3.0).
- *Antiembolic stockings* – reduce the risk of DVT and lower limb oedema.
- *Laxative* – to prevent constipation.
- *Analgesia* – pain and stiffness are common in this situation.
- *ACE inhibitor* – if blood pressure persistently >140/80 mmHg (but be vigilant about the risk of precipitating symptomatic postural hypotension).

A12: In addition to regular medical and nursing attention, which members of the multidisciplinary team ought to be involved with care?

- *physiotherapist* – to prevent contractures, maintain posture, avoid shoulder injury and improve function
- *occupational therapist* – to promote independence and overcome functional impairments caused by motor, sensory and visual impairments
- *speech and language therapist* – including assessment and therapy to improve swallowing
- *dietitian* – modification of diet to enhance safe swallowing and maintain adequate hydration and nutrition
- *stroke nurse specialist/psychologist* – specialist advice, support and counselling to patient and family
- *social worker* to explore any social issues relevant to a timely, safe and supported discharge from hospital.

A13: What medical complications might supervene during the next 4–6 weeks?

- painful shoulder caused by joint subluxation or capsular/rotator cuff injury (correct manual handling essential to minimize this complication)
- DVT/pulmonary embolism
- pneumonia (aspiration or hypostatic)
- urinary tract infection (UTI)
- faecal impaction
- pressure sores
- limb contractures
- depression
- post-stroke epilepsy
- recurrent stroke (haemorrhage transformation or reinfarction).

OSCE counselling cases

OSCE COUNSELLING CASE 6.3 – **A 75-year-old man who lives in a nursing home is confined to his bed or chair owing to a previous left-sided stroke.**

The GP should enquire about or assess the following.

- *Skin care and pressure areas:*
  - pressure sores (especially the sacrum, hips and heels)
  - intertrigo in skin folds such as the groins, axillae and perineum
  - leg ulcers complicating dependent oedema of the lower limbs
  - soft tissue infections.
- *Bladder and bowels:* urinary incontinence is inevitable in this situation and will necessitate regular toileting or containment by pads, sheath drainage or (as a last resort) urinary catheterization. Urinary catheter care will include regular catheter changes (every 3–4 months) to prevent encrustation, blockage and leakage. Bowel function will need review. Faecal incontinence, constipation and faecal impaction with overflow diarrhoea may all need appropriate management.
- *Nutrition:* obesity will exacerbate nursing difficulties. On the other hand, difficulty swallowing, resulting in poor nutrition, might cause weight loss. Provision of food and drink of the appropriate consistency and manoeuvres to improve swallowing will need discussion. Nutritional and vitamin supplementation may prove necessary. Liaison with the dietitian and speech and language therapist may be helpful.
- *Limb contractures/oedema:*
  - Flexion contractures of the limbs can develop over time and can be ameliorated to some extent by appropriate positioning of the hemiplegic limb, physiotherapy, and antispasticity drugs such as baclofen or botulinum toxin injections.
  - Dependent oedema and DVT can develop in an immobile lower limb. Elastic hosiery can help to prevent this.
  - Shoulder pain can develop as a result of incorrect handling/lifting techniques.
- *Respiratory complications:* aspiration or hypostatic pneumonia.
- *Medication review:* the need for laxatives, analgesics and hypnotics and the appropriateness of medication for secondary stroke prevention (aspirin, a statin, antihypertensives) will need periodic review.
- *Social and psychological wellbeing:* good-quality care should encompass this important area. Apathy and depression are common after a disabling stroke. Boredom and isolation can lead to difficult behaviour. Regular visits from friends and family should be facilitated. Interest in former hobbies and pursuits should be encouraged as far as is possible. Social activities and access to radio and television are important, being mindful of the patient's preferences and interests. Advice from a speech and language therapist will be helpful to maximize communication. Anticipatory care discussions should be broached so that the patient's wishes concerning potential future treatment interventions can be recorded. This will require assessment of his mental capacity and, if he is willing, discussion about advance care directives, lasting power of attorney and so on.

OSCE COUNSELLING CASE 6.4 – **A 65-year-old woman is reviewed in clinic after recent colonic surgery.**

The essence of this case is to discuss risk reduction and distinguish this from prevention. Deep vein thrombosis is a well-recognized problem post-surgery. The risk is higher in people with prothrombotic states such as malignancy or a hypercoagulable syndrome (e.g. factor V Lieden mutation) and where

venous return may be compromised (pelvic surgery, lower limbs raised intraoperatively, e.g. lithotomy position or with a pneumoperitoneum – laparoscopic surgery).

To reduce the risk, the patient is given a low-molecular-weight (LMW) heparin, is preoperatively well hydrated with intravenous (IV) fluids (especially if they have had preoperative bowel preparation), will be wearing thromboembolic deterrent stockings and may have been asked to stop any prothrombotic medication before surgery (e.g. tamoxifen). (LMW heparin works by activating anti-thrombin III; it inhibits platelet aggregation and decreases the availability of thrombin. It has a longer half-life than heparin and therefore requires only a single daily administration. The fact that its response is much easier to predict removes the need for monitoring.) During surgery the legs are slightly elevated to aid venous return and intermittent calf compression can be used. Post-surgery, early mobilization is encouraged.

Even with these precautions there is still a risk of a DVT developing. The importance of making the diagnosis and treating appropriately should be emphasized.

If there has been an aberration to the normal protocols, increasing the patient's risk, the aberration should be admitted and a reason sought. There is often a reason that can be explained (e.g. not giving heparin preoperatively if an epidural is to be inserted). Did the preoperative consent discuss the risk of DVT?

OSCE COUNSELLING CASE 6.5 – **The wife of an elderly man is distressed because her husband's attendance at the local elderly care day hospital for physiotherapy has been discontinued.**

This is a difficult situation and the decision has probably been made because the patient is not making progress with rehabilitation. A feeling of abandonment heightens the wife's sense of distress at the withdrawal of therapy by the multidisciplinary team. This situation can be avoided or ameliorated in a number of ways:

- setting clear goals for rehabilitation with realistic timescales that are understood by the patient's family and carers and whenever possible the patient
- use of a graded reduction in therapy, transferring the emphasis of care into more socially oriented activities such as former hobbies and interests
- ongoing support from a stroke nurse or another member of the multidisciplinary team such as a social worker or home-care assistant
- recognition of the needs of the carer – attendance at the day hospital may have been a lifeline for the patient's wife in terms of providing regular respite from caring. Alternative arrangements such as a carer to sit with the patient at home or attendance at a local day centre or stroke club may be helpful.

ACUTE CONFUSIONAL STATES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: Give the most likely causes of the patient's confusional state.
Q2: What initial investigations should you perform?
Q3: What treatment would you consider appropriate?
Q4: [Case 6.9 only] The patient's niece is worried about her aunt returning home alone at the conclusion of the hospital admission. How would you address this concern?

CASE 6.7 – **An 83-year-old man who has been brought to A&E.**

The patient lives in a residential home. For the past 2 days he has become confused. He is not eating or drinking and his walking has deteriorated. He has Parkinson's disease, a history of angina and type 2 diabetes mellitus. His medication includes co-beneldopa, selegiline, gliclazide, a nitrate preparation and aspirin.

On examination the significant findings are as follows:

- abbreviated mental test 4/10; he is agitated and restless
- dry tongue and superficial veins are empty
- blood pressure 108/62 mmHg
- heart rate 104/min, regular
- clear chest
- marked signs of parkinsonism (rigidity, tremor and bradykinesia)
- urinalysis: protein ++, blood +, glucose ++ and ketones negative.

CASE 6.8 – **A 74-year-old man with a history of alcohol abuse admitted to hospital 24 h ago after two witnessed epileptic seizures.**

The patient recovered fully and was initially lucid, but he is now very restless and agitated. He seems to be hallucinating. Examination is difficult. He has a low-grade fever and is tremulous and sweating. There are no obvious focal neurological signs. He is not jaundiced or anaemic. His blood pressure is 178/84 mmHg and his heart rate is 106/min, with AF.

CASE 6.9 – **An 84-year-old woman brought to hospital after being found wandering in the street at night by the neighbours.**

The patient is very disoriented and confused. She is alert but restless and agitated. She is convinced that she is late for work. A telephone call to her niece confirms that the patient has been somewhat confused and forgetful for the past 9 months or so. Further enquiry reveals that the patient needs help with her household and financial affairs. She has never wandered before.

Examination discloses AF (heart rate 126/min), cardiomegaly, mitral incompetence and peripheral oedema. Her feet are in a state of neglect and there is an infected bunion. Abbreviated mental test is 4/10. There are no focal neurological signs. The remainder of the examination is unremarkable.

OSCE counselling cases

OSCE COUNSELLING CASE 6.6 – What advice should be given to the matron of a local nursing home who telephones the local GP to report that one of her elderly residents, who has Alzheimer's disease, has become uncharacteristically agitated and restless?

OSCE COUNSELLING CASE 6.7 – An 84-year-old woman has been brought to A&E, having been found wandering at night.

The patient is alert but confused (Mini-Mental State Examination [MMSE] 12/30 (normal 27+/30)). There are no focal neurological signs, but she is cold (core temperature 35.5 °C). She is unable to give a coherent history. You telephone the patient's daughter to gain more historical information. Give five key aspects of the history that you need to establish in discussion with the daughter.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Acute confusion or delirium is a syndrome rather than a diagnosis and can be the mode of presentation of almost any illness, especially in older people. The most important question is 'why?'. There is great danger (for lack of collateral history) in assuming that the patient has 'always been like this' or that only one factor is involved. Always search for multiple pathology.

Common precipitating factors include:

- infections
- metabolic disturbances (e.g. hypo-/hyperglycaemia, dehydration, electrolyte imbalance, uraemia, hypothermia)
- hypoxia or heart failure
- pain or injury
- surgery or anaesthesia
- drugs (especially anticholinergic, dopaminergic or opiate therapy and alcohol/tranquillizer withdrawal states)
- sensory overload (e.g. unfamiliar surroundings or situations)
- pre-existing cognitive impairment (often mild and previously unnoticed) or sensory impairment (deafness or poor vision), chronic diseases and polypharmacy are all common predisposing factors in older people. Pre-existing dementia will present an acute-on-chronic confusional state
- Delirium can present as a hyperactive (agitated) or hypoactive (drowsy) state. Delirium has a short period of onset (hours or a few days), fluctuates in severity and can alternate between hyper- and hypoactive states.

The cornerstone of management is to detect and correct the underlying causes and use general measures to reorientate and reassure the patient and prevent complications. Sedation should be considered only when agitation or confusion is preventing essential tests or treatment, the patient's behaviour poses a danger to him- or herself or others, or it is necessary to relieve severe distress in an agitated patient. The maxim 'start low and go slow' when prescribing for older patients is particularly germane in this setting.

Answers

Clinical cases

CASE 6.7 – **An 83-year-old man who has been brought to A&E.**

A1: Give the most likely causes of the patient's confusional state.

His confusional state is multifactorial. Precipitating factors may include a UTI, dehydration and hyperglycaemia. Drugs prescribed for Parkinson's disease such as selegiline (a monoamine oxidase type B [MAOI-B] inhibitor) and levodopa can precipitate confusion, particularly in susceptible patients, e.g. those with pre-existing cognitive impairment. Other potential factors might include silent MI (hypotension and history of coronary artery disease) or stroke (symptoms and signs difficult to elicit owing to confusion and agitation). Enquiry about falls and head injury (even trivial) is important because of the potential for subdural haematoma. Hypoglycaemia must be quickly excluded by capillary blood glucose testing. Long-acting hypoglycaemic drugs carry particular risk in this setting (e.g. modified-release gliclazide, glibenclamide).

A2: What initial investigations should you perform?

- FBC – infection
- sepsis screen – urine and blood cultures and chest radiograph
- renal function tests – electrolyte imbalance and uraemia
- capillary/plasma glucose and glycated haemoglobin (HbA1c) – to assess diabetic control
- C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) – non-specific markers of an inflammatory process
- ECG – MI
- arterial oxygen saturation – to identify hypoxaemia caused by cardiopulmonary disease.

A3: What treatment would you consider appropriate?

- rehydration (IV) and correction of electrolyte disturbance
- sliding-scale insulin infusion for control of diabetes
- broad-spectrum antibiotic to cover UTI (after obtaining appropriate cultures)
- discontinue selegiline – this drug is more likely to precipitate confusion than L-dopa-based medications
- maintain co-beneldopa at minimum dose required to control parkinsonian symptoms
- general measures to reassure and reorient the patient
- prevention of falls and pressure sores
- avoid major tranquillizers (e.g. haloperidol), which, in the presence of Parkinson's disease, may precipitate a severe neuroleptic sensitivity reaction. Low-dose short-term quetiapine can be used in Parkinson's disease when necessary, but only after specialist advice and if other measures have failed to ameliorate the patient's agitation and distress.

CASE 6.8 – **A 74-year-old man with a history of alcohol abuse admitted to hospital 24 h ago after two witnessed epileptic seizures.**

A1: Give the most likely causes of the patient's confusional state.

Alcohol withdrawal causing delirium tremens is very likely, given the time course of the patient's confusional state. Hypoglycaemia may also be present, given the history of alcohol abuse and the potential for liver disease.

Occult head injury should also be considered. Patients who are inebriated or fitting are at great risk of injury and will have little, if any, recollection of the event. Older patients who misuse alcohol are particularly susceptible to subdural intracranial bleeding as a result of the combined effects of trauma, cerebral atrophy and coagulopathy.

The history of seizures raises the possibility of an intracranial space-occupying lesion (e.g. subdural haematoma, tumour), although alcohol excess and alcohol withdrawal can also precipitate seizures. Electrolyte imbalance, particularly hyponatraemia (syndrome of inappropriate antidiuretic hormone secretion, [SIADH]), must be considered in the setting of head injury or intracranial space-occupying lesion.

Pneumonia, meningitis and UTI are all possibilities in this setting. Liver encephalopathy is unlikely in the absence of jaundice.

A check for gastrointestinal bleeding (per rectal examination) is important (note sweating and tachycardia), although the elevated blood pressure militates against this.

A2: What initial investigations should you perform?

- capillary glucose – hypoglycaemia
- plasma U&Es – SIADH
- liver function tests (LFTs) and INR – liver damage and synthetic liver function
- FBC – bleeding and infection
- blood cultures – urine dipstick and culture should be sent as soon as a sample can be obtained
- chest radiograph when feasible – pneumonia
- arterial oxygen saturation – hypoxia
- CT of head – space-occupying lesion/bleeding.

Lumbar puncture should be considered (meningitis?) if the above tests fail to identify a cause and there is no evidence of a space-occupying lesion, bleeding or raised intracranial pressure on CT of the brain and no coagulopathy.

A3: What treatment would you consider appropriate?

Delirium tremens is very likely and should be treated with a benzodiazepine (e.g. IV diazepam followed by oral chlordiazepoxide) tapered over 3–4 days. IV thiamine is also advisable because malnourished individuals with alcohol problems are at risk of developing Wernicke's encephalopathy.

If hypoglycaemia is detected on capillary glucose reading (send plasma sample to laboratory for confirmation, but do not delay treatment while awaiting result), IV glucose (25 mL 50% dextrose IV) should be given.

Once the patient's agitation and confusion have been controlled, careful clinical examination is needed to assess for other causes of confusion, as outlined above.

CASE 6.9 – **An 84-year-old woman brought to hospital after being found wandering in the street at night by the neighbours.**

A1: Give the most likely causes of the patient's confusional state.

The history is very suggestive of an acute-on-chronic confusional state, the former precipitated by acute illness(es). Underlying cognitive impairment as a result of early Alzheimer's diseases is quite likely in this setting but must not be assumed. A search for acute illnesses such as infection (UTI, infected bunion, respiratory), side effects of medication, heart failure and metabolic disturbance (e.g. diabetes, uraemia) is essential. The patient was found wandering at night, so hypothermia must be considered.

In addition to an acute illness, causes of chronic confusion must be considered, such as dementia (Alzheimer's or vascular brain disease), thyroid dysfunction, vitamin B12 deficiency and hypercalcaemia. If there is a poorly maintained gas appliance at home, chronic carbon monoxide (CO) poisoning may need to be excluded.

A2: What initial investigations should you perform?

- FBC – anaemia, infection
- urinalysis and MSU – infection, diabetes
- blood cultures and swab from infected bunion
- plasma electrolytes, glucose and renal function – metabolic disturbance and uraemia
- calcium – confusion caused by hypercalcaemia
- thyroid function tests – often difficult to interpret in acute illness, but in this case important to exclude thyroid dysfunction, particularly hyperthyroidism as a result of AF and heart failure
- chest radiograph – infection, heart failure
- ECG – to confirm AF
- arterial oxygen saturation (and spectrophotometry for carboxyhaemoglobin if CO poisoning suspected).

Once the acute illnesses have settled, and if chronic confusion persists, CT of the brain should be considered to exclude potentially treatable causes of chronic confusion such as hydrocephalus, meningioma and chronic subdural haematoma. Vitamin B12 and folate levels are needed if there is macrocytic anaemia.

A4: The patient's niece is worried about her aunt returning home alone at the conclusion of the hospital admission. How would you address this concern?

This is a difficult issue and there is insufficient information provided to formulate a full answer to this question. Once acute confusion has settled, the patient's cognitive and functional status should be reassessed by the multidisciplinary team (in particular, the occupational therapist and social worker). An old-age psychiatry consultation may be required, particularly if a new or former diagnosis of dementia is confirmed, so that an assessment of the patient's mental capacity can be made. If the patient insists on returning home alone, a formal judgement as per the Mental Capacity Act 2005 concerning her capacity to assess the risk involved will be important. If the patient is judged to have capacity regarding discharge destination, the risks associated with returning home should be minimized by her family and the multidisciplinary team, including social services if required. Assessment of the patient's home environment will also be important before a decision about discharge is finalized. If the patient lacks capacity to make decisions about her discharge destination, a formal 'best interests meeting' as per the Mental Capacity Act will need to be convened. Discharge home may still be the preferred option after full assessment. Acetylcholinesterase inhibitor therapy (e.g. donepezil) to enhance cognition is contraindicated in this patient because of significant cardiac disease.

OSCE counselling cases

OSCE COUNSELLING CASE 6.6 – What advice should be given to the matron of a local nursing home who telephones the local GP to report that one of her elderly residents, who has Alzheimer's disease, has become uncharacteristically agitated and restless?

This is a common scenario, often referred to as an acute-on-chronic confusional state, i.e. delirium complicating underlying dementia. Older people with impaired cognitive reserve are at greater risk of delirium, and this is often precipitated by events such as intercurrent illness (commonly infection), an adverse reaction to medication, emotional distress or pain/discomfort. The first priority is to ensure the patient's safety while identifying and correcting the offending precipitant.

The nurses should check for symptoms and signs of common infections such as UTI (fever, dysuria, incontinence, abnormalities on urinalysis) and respiratory infection (cough, wheezing, dyspnoea). A check for dehydration is important; if identified, dehydration can be corrected by giving regular drinks under supervision. Capillary glucose should be checked, even if there is no history of diabetes – a new diagnosis is always possible in this setting. The patient's medication chart should be reviewed to see whether there are any new medications or amended dosages. Physical distress resulting from urinary retention, faecal impaction, pain from injury (any recent fall?) or emotional upset should be identified and corrected. If there is any suspicion of underlying medical illness, a prompt medical assessment will be needed.

In the interim, the nurses should be advised to monitor the patient unobtrusively, enhance her orientation by using adequate soft lighting in familiar surroundings, and ensure any hearing aid is operational and spectacles are worn. A calm, confident approach is needed; the reassurance of a close family member or friend is helpful.

The nurses should be asked to watch the patient closely to prevent accidents and injury, and to encourage her to drink fluids to correct or prevent dehydration.

It is likely that the patient's confusional state will settle if the offending precipitant is identified and corrected, although it may take a few days or sometimes longer for the older person to settle back to 'normal'. In many instances, hospital admission (with its attendant hazards to a frail older person) can be avoided, but this will require close cooperation of the doctor, nursing staff and family and carers.

OSCE COUNSELLING CASE 6.7 – An 84-year-old woman has been brought to A&E, having been found wandering at night.

In discussion with the patient's daughter, you need to establish the following key aspects of the history.

- *Duration of confusion:* is this an acute, acute-on-chronic or chronic confusional state? Acute and acute-on-chronic confusion suggest the presence of delirium and warrant a diligent search for intercurrent general medical conditions that may have precipitated the current delirious state (e.g. infection, CNS event such as head injury, metabolic disturbance, hypothyroidism). The presence of chronic confusion (duration >6 months) is suggestive of a dementing illness such as Alzheimer's disease.
- *Systems enquiry:* the patient cannot give a coherent account of events, but while lucid she may have previously reported important symptoms to a close relative or carer. Enquiry along these lines may reveal, for example, a description of a recent head injury (subdural haematoma), urinary symptoms

(infection), thirst and urinary frequency (diabetes mellitus), or cold intolerance (hypothyroidism). Any predisposing factors for hypothermia should be sought.

- *Previous medical history:* this may give important information relevant to the patient's current presentation – e.g. a history of liver disease, cerebrovascular disease, chronic renal impairment or cardiopulmonary disease may cause or predispose to an acute confusional state. You need to find out if there is a previous formal diagnosis of dementia or other psychiatric history.
- *Drug history:* medications commonly cause confusion in older patients. Offending agents include anticholinergics (e.g. trihexyphenidyl for Parkinson's disease), tricyclic antidepressants (e.g. amitriptyline), opiates, hypoglycaemic agents (e.g. glibenclamide) and dopaminergic drugs (e.g. L-dopa). Alcohol should also be considered. Polypharmacy (more than five medications) can be the cause of a confusional state when many drugs, each with weak anticholinergic properties, combine to produce appreciable central anticholinergic side effects (e.g. digoxin, nitrates, warfarin, furosemide, ranitidine, cyclizine).
- *Social history:* this information is essential to gain a proper understanding of the context of the patient's presenting illness, potential for rehabilitation and, in due course, discharge planning.

INCONTINENCE

Questions

Clinical cases

For each of the case scenarios given, consider the following:

CASES 6.10 AND 6.11

Q1: What are the likely causes of urinary incontinence in this patient?
Q2: How should the problem be investigated?
Q3: What can be done to help?

CASE 6.12

Q4: What are the likely causes of urinary incontinence in this patient?
Q5: What treatments should be considered?
Q6: Suggest three reasons why the incontinence has gone unreported by the patient for so long.

CASE 6.10 – **A 78-year-old woman disabled by stroke and cared for by her daughter.**

Care at home is proving difficult as a result of persistent urinary incontinence, such that a nursing home placement is now being considered. The patient has a right hemiparesis and dysphasia and needs help to stand, transfer and walk. She receives treatment with aspirin (for stroke), amlodipine (for hypertension) and furosemide (for swollen ankles).

The patient is alert and responsive, but she has difficulty communicating as a result of her dysphasia. Sometimes she is able to indicate that she needs to use the lavatory, but she is usually wet before toileting can be achieved.

In addition to the signs of stroke, examination shows an excoriated perineum. There is no palpable bladder. Rectal examination is normal. There is no uterovaginal prolapse.

CASE 6.11 – **An 82-year-old man with advanced Parkinson's disease and dementia is cared for in a nursing home.**

His nursing needs are usually fairly predictable. Of late, he has become more agitated than usual. He seems uncomfortable and has started to shout and rattle the bedsides, and occasionally he hits out at the nurses. The on-call GP has prescribed a sedative to settle the patient at night. The patient is continuously wet with urine and, unusually for him, he is now incontinent of liquid faeces too. He has no fever and other vital signs are normal.

CASE 6.12 – **A 90-year-old woman who lives alone has slipped and fallen in her bathroom at home.**

She has escaped serious injury. Subsequent visits by the district nurse to assess the situation reveal that the elderly woman's clothing is always soaked in urine and the house has a strong smell of urine. The patient is reluctant to discuss the situation but does admit to a swelling 'down below'. She is sensible and independent in her activities of daily living. She is reluctant to be examined by the nurse, but in due course assessment reveals a swelling at the vaginal introitus, which on further examination is shown to be the cervix. When the patient stands up she leaks urine. Her bowel function is normal.

There are no other abnormal findings. In particular, there is no palpable bladder, neurological examination is normal and urinalysis is negative.

OSCE counselling cases

OSCE COUNSELLING CASE 6.8 – **An elderly woman with hypertension is attending the surgery for regular assessment of her blood pressure.**

On this occasion her daughter attends as well and mentions that the family is very concerned about the patient's apparent incontinence of urine. The daughter goes on to say that her mother's house and clothing have now developed a constant smell of urine. On direct questioning, the patient makes light of this problem. She seems sensible. How would you proceed?

OSCE COUNSELLING CASE 6.9 – **An 86-year-old woman is distressed by persistent incontinence of urine.**

Outline the key steps to establishing the cause of this problem in a primary care setting.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Urinary incontinence to some degree is common in older people, affecting about 12 per cent of men and 20 per cent of women aged 65 years and over, compared with 1 per cent of men and 6 per cent of women aged 15–64 years. Transient causes include confusional states, immobility, urine infection, diabetes, stroke, retention with overflow and drugs. Incontinence can persist if the above conditions remain unresolved. Established incontinence can also occur in many other chronic disorders – e.g. unstable bladder resulting from detrusor muscle instability (urge incontinence), pelvic floor incompetence (stress incontinence), neurogenic bladder (e.g. spinal cord lesions, cerebrovascular disease), incontinence associated with dementia, prostatism or bladder tumour or stone, and immobility from any cause.

Assessment must include a full history and examination, including per rectum and (if appropriate) per vagina examinations, and CNS and locomotor assessments. Investigations include urinalysis, MSU, U&Es, glucose, calcium, plain abdominal radiograph or ultrasonography and, in some patients, urodynamic studies.

Accurate diagnosis and treatment are essential. Effective treatments for urge incontinence include bladder retraining and drugs to stabilize the bladder (e.g. anticholinergics such as oxybutynin and solifenacin), but side effects can be problematic in elderly people. Stress incontinence can be helped by pelvic muscle exercises to strengthen the pelvic floor and surgical suspension procedures. Devices to ameliorate incontinence (pads, sheath drainage, urinals, intermittent self-catheterization) are effective to varying degrees and are appropriate steps to avoid permanent catheterization and its attendant hazards (e.g. infection, soreness, bypassing, embarrassment).

Faecal incontinence is less frequent than urinary incontinence but can be much more distressing to the patient and carers. Community-based studies reveal a 2 per cent prevalence of faecal incontinence in people aged over 65 years, rising to about 25 per cent in people aged over 85 years. Prevalence rates in nursing homes and hospital are even higher. In a British study, only half of people reporting faecal incontinence had discussed this with a health-care professional. Causes include underlying diseases in the rectum or anus (e.g. proctitis, tumour), faecal impaction with overflow diarrhoea (secondary to immobility caused by, for example, stroke or arthritis), neurological disorders affecting sphincter control (similar to those causing urinary incontinence), and cognitive disorders such as dementia or severe depression. Accurate diagnosis and treatment of remedial factors are essential (e.g. enemas for faecal impaction). When remedial measures fail or are inappropriate, faecal incontinence can be controlled by means of a drug-induced constipation regimen alternating with periodic planned bowel evacuation by enema or suppository.

Answers

Clinical cases

CASE 6.10 – **A 78-year-old woman disabled by stroke and cared for by her daughter.**

A1: What are the likely causes of urinary incontinence in this patient?

In this situation there are several factors responsible for the urinary incontinence.

- Damage to the CNS by a stroke will have impaired the central capacity to inhibit bladder (detrusor) contractions, resulting in frequency and urgency of micturition.
- Immobility and difficulty calling for help and perhaps cognitive dysfunction will precipitate urinary incontinence.
- Diuretic therapy will exacerbate the situation, as the patient will need to pass urine quickly.
- Immobility and incomplete bladder emptying both predispose to UTI, which can cause incontinence.

A2: How should the problem be investigated?

- urinalysis and MSU – to assess for infection, diabetes and occult renal disease
- U&Es – hypokalaemia, hyponatraemia and renal failure
- plasma glucose – polyuria caused by hyperglycaemia
- FBC – infection.

A3: What can be done to help?

- Discontinue the diuretic and observe. There are no history or signs of heart failure. Ankle swelling is a common side effect of calcium antagonist medication such as amlodipine. If this can be withdrawn, diuretic therapy may no longer be required. Persistent hypertension may be better managed by a beta-blocker, ACE inhibitor or angiotensin receptor blocker. In this situation, elastic hosiery is a more appropriate method for controlling dependent oedema.
- Assess communication and cognition with the help of a speech and language therapist. Try to improve the patient's ability to communicate the need to pass urine (e.g. bell, picture card, gestures).
- There should be an assessment of the patient's home environment and toilet facilities by an occupational therapist. Techniques to allow clothing to be removed quickly, assistance with transfers, and equipment to facilitate toileting (e.g. commode, grab-rails, raised toilet seat) will promote continence.
- The district nurse and carer need to work with the patient to establish a regular toileting regimen to anticipate and thus prevent incontinence. Pads and barrier cream are needed to protect the perineum.
- Antibiotics should be given if UTI is confirmed.
- If the above measures prove insufficient, consider stabilization of the bladder with anticholinergic medication, e.g. solifenacin or oxybutynin. Such treatment needs to be used with caution because of predictable anticholinergic side effects (e.g. confusion, glaucoma, constipation, dry mouth).
- The patient needs assistance with toileting and washing at home from the home-care service and regular monitoring of the situation by the district nursing team. Regular respite care should be considered to sustain the daughter in her caring role.

CASE 6.11 – **An 82-year-old man with advanced Parkinson's disease and dementia is cared for in a nursing home.**

A1: What are the likely causes of urinary incontinence in this patient?

Urinary and faecal incontinence are not uncommon in the setting of dementia and relative immobility caused by conditions such as Parkinson's disease. Nevertheless, regular toileting and maintenance of a daily bowel habit by appropriate diet, simple laxatives and, when necessary, suppositories are usually sufficient to maintain control of the situation. In this scenario, it is very likely that faecal impaction has supervened, with overflow of liquid stool. This is a most uncomfortable situation for the elderly man, who is unable, as a result of confusion, to draw attention to his predicament. Urinary retention with overflow of urine is also very common in this setting, particularly if there is pre-existing urinary outflow obstruction as a result of prostatic enlargement. Anticholinergic drugs, sometimes used (inappropriately) in older patients with Parkinson's disease, and opiate-based analgesics can also precipitate this problem.

Urinary infection is not infrequent in this setting but would usually be associated with fever and offensive urine. Infective diarrhoea would tend to produce profuse liquid stool associated with fever, abdominal tenderness and dehydration, and there may also be other affected residents in the home. *Clostridium difficile* enteritis should be considered, especially if the patient has received a broad-spectrum antibiotic.

A2: How should the problem be investigated?

A careful clinical examination (even if difficult) is essential, with particular reference to fever, hydration, abdominal tenderness or distension, bladder enlargement (often non-tender in chronic retention) and rectal examination (prostatic enlargement or impaction with hard stool).

Urinalysis and, if appropriate, stool culture should be done for evidence of infection. A bladder scan should be done to assess for urinary retention. Plasma U&Es should be sent if obstructive uropathy or dehydration is suspected.

A3: What can be done to help?

Faecal impaction should be relieved by regular enemas, with attention to regular bowel care as outlined above. Once constipation is relieved, urinary retention may resolve spontaneously, especially if the patient is able to sit or stand to pass urine. Failing this, temporary urinary catheterization (with measurement of residual urine to confirm the diagnosis) should be performed until the bowel function has normalized. Anticholinergic and opiate-based medication should be withdrawn whenever possible. Treatment for UTI should be guided by antibiotic therapy. Infectious diarrhoea will require 'barrier nursing' precautions to prevent the spread of infection. *Clostridium difficile* enteritis will require oral metronidazole or vancomycin.

CASE 6.12 – **A 90-year-old woman who lives alone has slipped and fallen in her bathroom at home.**

A4: What are the likely causes of urinary incontinence in this patient?

The patient has a third-degree uterine prolapse, resulting in stress incontinence as a result of pelvic floor (sphincter) incompetence. A history of leakage of urine when straining, coughing, laughing or standing is usual. There is a recognized relationship between stress incontinence and weakness of the pelvic floor musculature and sphincter tone. Ageing, oestrogen deficiency, previous multiparity and surgical interference at parturition are also predisposing factors.

A5: What treatments should be considered?

Lesser degrees of pelvic floor incompetence can be treated to good effect by pelvic floor exercises taught by a physiotherapist, in conjunction with oestrogen replacement therapy. The situation described in this scenario requires gynaecological referral and control of uterine descent by pessary or surgery.

A6: Suggest three reasons why the incontinence has gone unreported by the patient for so long.

Incontinence is often unreported by older patients. Embarrassment, social isolation, fear of investigation or treatment, and acceptance as a part of 'normal' ageing or that 'nothing can be done' are all factors to a greater or lesser degree.

OSCE counselling cases

OSCE COUNSELLING CASE 6.8 – **An elderly woman with hypertension is attending the surgery for regular assessment of her blood pressure.**

Urinary incontinence is a common problem in old age and is often unreported. The reasons for this reluctance to seek medical advice are multifactorial and include embarrassment and a belief that nothing can be done or that it is an inevitable consequence of ageing. Health-care professionals may fail to enquire about the symptom or, if it is mentioned, may feel unable to intervene in an effective manner.

The first step is to secure the patient's confidence and trust. An approach by the practice nurse may be a more successful first step to gain an initial history and preliminary assessment. It will be important for the nurse or doctor to emphasize that assessment is relatively simple and that an effective treatment is very likely. Even if cure is not feasible, improvement or containment of symptoms is certainly possible.

The initial assessment should include a thorough history and examination (note rectal and vaginal examinations), paying particular attention to medications and any gynaecological or neurological symptoms and signs. Urinalysis, urine culture and bladder scan (to assess bladder emptying and residual volume) are also essential steps in the assessment. Most assessments can be completed in a general practice setting, and measures can be instituted to improve the common conditions of urge and stress incontinence. The advice of a continence nurse specialist is useful for the treatment of complex cases and where a more detailed knowledge of containment devices and pads is required.

OSCE COUNSELLING CASE 6.9 – **An 86-year-old woman is distressed by persistent incontinence of urine.**

The key steps include a full history focusing on:

- precipitating factors
- pattern of voiding, including assessment of frequency and volume
- previous and current medical and surgical illnesses, including obstetric procedures and problems
- drug history, especially diuretics, anticholinergics, sedatives and opiates
- assessment of functional status and toileting arrangements
- corroborative details from carer or relative.

A full examination should be done, focusing on:

- abdomen – retention of urine, pelvic masses
- rectal examination – constipation, tumour, anal tone
- vaginal examination – prolapse, tumour, atrophic changes
- full neurological assessment – search for evidence of cognitive dysfunction and other CNS diseases, e.g. stroke, Parkinson's disease, spinal cord disease, autonomic dysfunction
- locomotor examination.

Simple, focused investigations in response to the findings on history and examination include:

- urinalysis
- MSU
- measurement of residual volume (by bladder scan or catheterization)
- capillary glucose
- plasma urea, creatinine and electrolytes
- plain radiograph or ultrasound scan of kidneys, ureters and bladder (for renal/bladder stone)
- urodynamic assessment if the above investigations fail to elucidate the cause.

IATROGENIC ILLNESS IN FRAIL OLDER PATIENTS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What iatrogenic illness may result from the given intervention?
Q2: What risk factors for iatrogenic illness are present in this case?
Q3: Suggest some alternative management strategies.
Q4: How can these complications be minimized?

CASE 6.13 – **An 84-year-old man is agitated and restless.**

The patient is disturbing other residents in the residential care home. He has a history of cardiac and cerebrovascular disease with vascular dementia. The on-call doctor who attends prescribes haloperidol 2.5 mg stat and then 1 mg three times a day to follow.

CASE 6.14 – **An 86-year-old woman who is a nursing home resident has become more drowsy than usual.**

The patient is immobile due to osteoarthritis and cerebrovascular disease. She also has cardiac failure and type 2 diabetes mellitus, with end-organ damage. She has an indwelling urinary catheter. The weather is hot and she is having difficulty drinking sufficient fluid. There is no fever. Her blood pressure is 106/52 mmHg and heart rate is 102/min. Urine dipstick testing shows positive + for protein, glucose and blood with nitrites present; there are no ketones. Several weeks ago the patient was unwell with a UTI, which was treated successfully with ciprofloxacin. The nurse in charge has suggested that you prescribe an antibiotic in case the patient has another UTI.

CASE 6.15 – **A 92-year-old woman is feeling dizzy and nauseated and is not her usual self.**

She has AF with cardiac failure and is receiving treatment with furosemide, digoxin, aspirin, spironolactone and ramipril. The dose of furosemide was increased 3 weeks ago following outpatient department attendance. Examination shows AF rate 54/min, blood pressure 106/64 mmHg, JVP not visible and no oedema. Blood tests show sodium 135 mmol/L, potassium 6.0 mmol/L, urea 18 mmol/L and creatinine 270 μmol/L. ECG confirms slow AF.

CASE 6.16 – **An 84-year-old woman with dementia is admitted from a residential home because she has had some falls.**

The patient is described as being frail. She is restless and agitated and has a respiratory infection. Her skin is fragile, with several small lacerations and bruises caused by her recent falls. The electronic prescribing process prompts the admitting medical team to assess for venous thromboembolism (VTE)

risk. She is considered at risk because of her age, dehydration and infection. Should she be prescribed VTE prophylaxis with subcutaneous enoxaparin?

CASE 6.17 – **A frail 92-year-old woman has fallen at home. The ambulance service has conveyed her to the local A&E department for further assessment.**

Further enquiry reveals the patient lives alone and has mild dementia and previous osteoporosis-related fragility fractures (wrist and thoracic vertebra). She has poor vision and hearing. She receives help from local family and the home-care service. She has not sustained any bone injury. Physiological parameters are stable. She is taking diuretics for ankle swelling. There are concerns about her safety at home. Should she be admitted to hospital?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Illness in frail older people often presents in a non-specific way, e.g. falls, functional decline, confusion, anorexia and weight loss, or following an observation from a family member or carer that the patient is not their 'usual self'. The older person may also underreport illness owing to cognitive decline, depression, anxiety, sensory impairments, decreased expectations and stoicism. Symptoms that are modified by age-related physiological decline or coexisting chronic disease(s) further complicate the diagnostic process.

Frailty itself is a physiological syndrome characterized by decreased reserve, diminished resistance to stress, cumulative decline across multiple systems and vulnerability to adverse outcomes. Such frailty is a marker of poor outcome, especially in relation to hospital admission. Compared with more robust older patients, those with markers of frailty are more likely to experience a longer length of hospital stay, are at increased risk of institutional care or social isolation, and are more likely to experience adverse outcomes following health-care interventions. The mortality in this patient group is substantially increased.

The assessment and management of illness in frail older patients require comprehensive assessment, attention to detail and knowledge of the background social situation. It is important to understand why the patient has presented now and their current and previous functional status. In the presence of multiple impairments and chronic illness, it is important to identify any remediable factors or conditions. When there is no cure, the focus should turn to modification of the situation and amelioration of symptoms. Creating a problem list and prioritizing the actions is a useful way to proceed. Bearing in mind the increased risk of adverse outcomes in such patients, any intervention should be weighted for risks and benefits, allowing the patient (and, where relevant, the patient's advocate) to be part of the decision-making process. Outcomes viewed from the ninth or tenth decade are sometimes very different from those considered best by younger professionals or carers. The relevance of rehabilitation and limitation of disability will also require focus from the multidisciplinary team. End-of-life situations are not uncommon. At this time in particular, the emphasis of care must be on comfort and dignity.

Answers

Clinical cases

CASE 6.13 – **An 84-year-old man is agitated and restless.**

A1: What iatrogenic illness may result from the given intervention?

Short-term side effects may include hypotension, sedation and immobility, increasing the risk of dehydration, poor nutrition and pressure sores. If continued for more than several days, there is a risk of drug-induced parkinsonism and falls. If continued long term, there is an increased risk of stroke, accelerated cognitive decline and continued parkinsonism. Mortality is increased when neuroleptics are continued long term in such situations.

A2: What risk factors for iatrogenic illness are present in this case?

Age, cardiac disease and vascular brain disease increase the risk of adverse events.

A3: Suggest some alternative management strategies.

If the agitation and restlessness are of recent onset, this is hyperactive delirium and there are underlying causes, such as infection, pain, discomfort or metabolic disturbance. Such precipitants should be carefully identified and treated as appropriate. Non-pharmacological means to settle the patient's agitation should be tried, including reorientation, the calming presence of a family member or familiar carer, encouraging the patient to wear his glasses and hearing aid if required, and hydration. Every opportunity to avoid pharmacological sedation should be considered.

A4: How can these complications be minimized?

If sedation is required, then the initial dose of haloperidol should be kept low (1 mg initially); if necessary, a further dose can be given 20–30 min later. Follow-on medication should be given only if necessary, and in this situation should be low dose (0.5 mg twice a day). Treatment should not be continued beyond 3 days and should never be continued indefinitely. If the patient has pre-existing parkinsonism, a small dose of lorazepam 0.5–1 mg can be considered as an alternative.

CASE 6.14 – **An 86-year-old woman who is a nursing home resident has become more drowsy than usual.**

A1: What iatrogenic illness may result from the given intervention?

There is a high risk of *C. difficile* colitis if antibiotics are used in this setting. Bowel colonization with *C. difficile* is not uncommon in residents of care homes (around 25 per cent of residents). Further disturbance of the normal large bowel bacterial flora by broad-spectrum antibiotics (especially ciprofloxacin) carries a high risk of precipitating *C. difficile* infection.

A2: What risk factors for iatrogenic illness are present in this case?

Age, comorbid illnesses, care-home settings and recent use of broad-spectrum antibiotics all increase the risk of *C. difficile* infection.

A3: Suggest some alternative management strategies.

In this scenario, there is no definite evidence of UTI. The abnormal urine dipstick result may be caused by (i) diabetic/hypertensive kidney disease, (ii) bladder irritation due to the urinary catheter or (iii) asymptomatic bacteriuria (present in up to 40–50 per cent of residents of care homes). The patient has hypoactive delirium, most likely caused by dehydration and hyperglycaemia. The dehydration should be corrected by giving regular oral fluids. Renal function, plasma electrolytes and capillary glucose should be checked and corrective action taken as necessary. The patient should be monitored regularly by the nursing staff, including charting of fluid balance and temperature. Resolution of the current symptoms and signs over the next 24 h will confirm that the management plan is working and that antibiotic treatment is not required.

A4: How can these complications be minimized?

If fever develops and there is no likely source of infection other than urine, then treatment for UTI must be considered. An elevated plasma white cell count or CRP will provide further support for UTI. Keeping the antibiotic course short (3–5 days) and using a narrow-spectrum agent (trimethoprim *v*. ciprofloxacin) where possible will minimize the risk of *C. difficile* colitis. A discussion with the patient and the nursing staff regarding removal of the urinary catheter and managing continence by other means (e.g. regular toileting, pads) will substantially reduce the risk of UTI in this setting.

CASE 6.15 – **A 92-year-old woman is feeling dizzy and nauseated and is not her usual self.**

A1: What iatrogenic illness may result from the given intervention?

A1: Digoxin toxicity, hypotension and renal failure may all result. Hypotension and renal failure are related to treatment with diuretics and ramipril. Hyperkalaemia is related to treatment with spironolactone (an aldosterone antagonist) and ramipril. The dizziness is multifactorial – digoxin toxicity, cardiac arrhythmia and hypotension are all possible causes.

A2: What risk factors for iatrogenic illness are present in this case?

Chronic renal failure – either disease- or age-associated – will cause digoxin accumulation as the drug is excreted via the kidneys and has a long half-life (36 h with normal renal function). A recent increase in diuretic dose can result in excessive diuresis, which will further compromise kidney function due to volume depletion. Nausea due to digoxin toxicity will reduce fluid intake and exacerbate the situation. Spironolactone is contraindicated in the presence of kidney disease because of the risk of hyperkalaemia, a situation aggravated by ACE inhibition.

A3: Suggest some alternative management strategies.

Adjustments in diuretic dose require close monitoring in this situation, ideally with serial weight, blood pressure and kidney function tests. Regular home assessments by a nurse specialist in cardiac failure are a valuable means of monitoring such treatment in frail older patients, rather than relying on frequent visits to the surgery or outpatient department.

A4: How can these complications be minimized?

Renal function declines progressively with age. The severity can be underestimated in frail older patients, as plasma creatinine is often lower than expected because of reduced muscle mass (estimated glomerular flow rate is a better guide to renal function in this situation). The digoxin dose should be reduced accordingly (62.5 μg/day or on alternate days in this scenario), and clinical effects and the digoxin level should be monitored carefully if events supervene that further compromise kidney function.

Spironolactone should be avoided in chronic kidney disease because hyperkalaemia is a predictable complication. ACE inhibition requires caution, as this medication can compromise renal perfusion.

CASE 6.16 – **An 84-year-old woman with dementia is admitted from a residential home because she has had some falls.**

A1: What iatrogenic illness may result from the given intervention?

Head injury and intracranial bleeding are a substantial risk because of the patient's frailty, confusion and risk of further falls. Low-dose enoxaparin will substantially increase this risk. The distress caused by subcutaneous injections may exacerbate the patient's delirium. There may be cutaneous bruising at injection sites and elsewhere due to the patient's restlessness and agitation and resulting minor trauma.

A2: What risk factors for iatrogenic illness are present in this case?

Fall-related head injury carries a higher than normal risk of intracranial bleeding, particularly subdural haemorrhage, because of age- and dementia-associated cerebral atrophy.

A3: Suggest some alternative management strategies.

The patient could be assessed for anti-thromboembolic stockings if peripheral circulation is satisfactory. Rehydration, treatment of respiratory infection and supervised mobilization will reduce the risk of VTE.

A4: How can these complications be minimized?

The risk of VTE has to be balanced against the substantial risk (in this case) of harm from increased bleeding. A supportive nursing environment and medical management aiming to reverse treatable conditions and resolve delirium are important. If the patient is judged not to have capacity to participate in treatment-related decisions, then the medical team should act in her best interests. Timely involvement of family members or any legally appointed representative (lasting power of attorney) is imperative.

CASE 6.17 – **A frail 92-year-old woman has fallen at home. The ambulance service has conveyed her to the local A&E department for further assessment.**

A1: What iatrogenic illness may result from the given intervention?

This a common scenario. The patient is frail and will be at substantial risk from hospital admission-related complications such as delirium, further falls, health-care-associated infection, deconditioning due to reduced activity and loss of functional skills. Local support networks will be destabilized by her admission. These risks have to be balanced against the hazards of returning to a potentially unsafe environment and occult illness.

A2: What risk factors for iatrogenic illness are present in this case?

The presence of frailty, cognitive impairment and sensory impairments substantially increases the risk of delirium and falls within the hospital environment. Any subsequent ward moves with unfamiliar routines and interventions will add to this risk.

A3: Suggest some alternative management strategies.

Assessment by a rapid-response therapy and nursing team skilled in the assessment of frail older people is essential in this A&E setting. The patient should have a supported discharge home with reinstatement

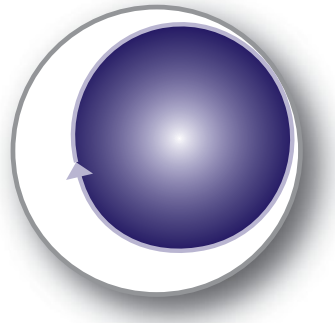
of her existing care plan, supplemented by short-term additional social and therapy support as necessary. There should be further early review at home or attendance at a community or day hospital-based falls clinic (depending on local availability of services) for further comprehensive geriatric assessment. This will identify modifiable conditions and implement treatment and support to enhance care at home and reduce risk of further falls.

A4: How can these complications be minimized?

Safe alternatives to hospital admission should always be considered in frail older people. A working knowledge of local services and community teams is essential. Close liaison and reassurance to the patient's family and carers are also important. The medical role in A&E is to quickly exclude life-threatening or serious illness, and this will provide focus to the rapid-response nursing/therapy team to permit early supported discharge. Many such teams are supported by elderly-care physicians who are able to give further confidence with respect to medical stability, immediate changes to medication and follow-up plans.

REVISION PANEL

- One-third of people aged over 65 years fall in a year, often repeatedly. Falls resulting in injury are a leading cause of death in older people, accounting for two-thirds of injury-related deaths in people aged 85 years and over.
- Falls in elderly people may be related to one or more underlying medical conditions, including aortic stenosis, cardiac arrhythmia, silent MI, postural hypotension, vasovagal episode, and hindbrain TIA.
- Osteomalacia (vitamin D deficiency) may occur due to lack of exposure to sunlight, poor diet if socially isolated or in poor health, and enhanced metabolism of vitamin D as a result of treatment with phenytoin (a liver enzyme inducer). Diseases causing malabsorption and chronic renal failure can also predispose to osteomalacia.
- There are many common causes of difficulty in walking in elderly people, including stroke, osteoarthritis, parkinsonism, dementia, visual impairment, chronic cardiorespiratory disease, injuries and complications of falling, and problems with feet and footwear.
- Acute confusion is more prevalent in elderly people. Common causes include metabolic and electrolyte problems, infection, medication and cerebrovascular disease.
- Drug toxicity (e.g. digoxin, phenytoin) is more common in elderly people due to polypharmacy and chronic renal and hepatic impairment.



7 Respiratory medicine

Malcolm Shepherd

DYSPNOEA

PLEURITIC CHEST PAIN

HAEMOPTYSIS

Answers

DYSPNOEA

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features of the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 7.1 – A 35-year-old woman with episodic breathlessness and wheeze.

A 35-year-old mother attends the medical outpatient clinic complaining of breathlessness with wheeze. This can occur at rest and has been getting worse over the past 2 years. Between episodes of breathlessness she feels better but does not feel that she ever returns to 'normal'. Occasionally she wakes with shortness of breath and coughing in the early hours of the morning.

CASE 7.2 – A 66-year-old man with chronic dyspnoea and cough.

A 66-year-old retired publican attends the respiratory outpatient clinic complaining of severe exercise limitation as a result of breathlessness. He has trouble moving about the house and rarely goes outside. He feels worse in the mornings and describes wheeze. His symptoms have developed over 3 years. His general practitioner (GP) has tried inhalers, but they have not helped. He has had a cough with sputum for more than 10 years. He has been a smoker for more than 40 years and has smoked five to ten cigarettes per day over this time.

CASE 7.3 – A 66-year-old man with progressive dyspnoea and weight loss.

A 66-year-old man presents complaining of worsening exercise tolerance as a result of breathlessness. He can walk 200 m on a flat road, whereas a year ago he could manage at least a mile. He describes feeling short of breath at rest. He is severely restricted on hills and stairways. He denies cough, but he has lost 3 kg over the past 6 months. He is a lifelong non-smoker. He worked in the shipbuilding industry, where he was exposed to asbestos fibres. His GP describes inspiratory crackles at both lung bases.

OSCE counselling case

OSCE COUNSELLING CASE 7.1 – **'Can I have oxygen at home? I'm sure it would help me'.**

A 72-year-old man with cryptogenic fibrosing alveolitis (CFA) attends the clinic with his daughter. They both feel that he requires oxygen to help him with his daily activities. What criteria should you assess before prescribing oxygen? What advice would you give to him about the use of oxygen?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

SPIROMETRY

This is a useful test that is quick to perform and has good reproducibility. Spirometry measures the volume and velocity of a forced exhalation over approximately 5 s. Two important values are derived: the volume of air expired in the first second, known as the forced expiratory volume in 1 s (FEV_1), and the total volume exhaled in 5 s, known as the forced vital capacity (FVC). In the context of dyspnoea, two patterns are frequently found: if both values are lower than predicted for an individual's size, age and gender, then the pattern is described as 'restrictive'; if the FEV_1 is disproportionately smaller than the FVC (FEV_1/FVC ≤ 75 per cent), then the pattern is described as 'obstructive'.

Answers

Clinical cases

CASE 7.1 – A 35-year-old woman with episodic breathlessness and wheeze.

A1: What is the likely differential diagnosis?

The differential diagnoses are asthma, hyperventilation and recurrent pulmonary embolism (PE).

A2: What issues in the given history support the diagnosis?

Episodic breathlessness, wheeze and cough with spontaneous resolution are typical of asthma. Symptoms tend to occur at night, first thing in the morning or after exercise, but none of these clinical features is specific for asthma. Progression over 2 years may suggest insufficient treatment of asthma.

A3: What additional features of the history would you seek to support a particular diagnosis?

A smoking history should be taken. It would be useful to assess the likelihood of other associated atopic diseases by enquiring about allergic rhinitis and eczema. Any environmental or other factors that exacerbate the patient's breathlessness should be identified, such as occupational asthma. A chronic cough without wheeze, currently or in the past, may suggest cough variant asthma. A family or personal history of thromboembolic disease may suggest pulmonary thromboembolism (PTE).

A4: What clinical examination would you perform, and why?

Examination is likely to be normal unless the patient is suffering from an exacerbation. General examination should look for evidence of eczema (dermatitis, ichthyoid skin). Respiratory examination may reveal wheeze or hyperinflated lung fields.

A5: What investigations would be most helpful, and why?

The metacholine or histamine provocation test is the recommended test to diagnose asthma. A fall in FEV_1 of more than 20 per cent (PC20) after inhalation of 25 mg/mL or less of metacholine is considered a positive test. A negative test has a high negative predictive value.

A 2-week recording of the peak expiratory flow (PEF) measured twice a day can identify diurnal variation that is characteristic of asthma (≥20 per cent from baseline). This is a specific but insensitive diagnostic test.

A single spirometry measurement may be normal or may demonstrate a low FEV_1/FVC ratio (an obstructive pattern). An improvement in FEV_1 of more than 15 per cent and 200 mL after inhalation of a bronchodilator or a 2-week course of corticosteroid therapy is highly suggestive of asthma.

Chest radiograph is unhelpful in diagnosing asthma but may rule out alternative diagnoses or pneumothorax. A full blood count (FBC) is not useful, although blood eosinophilia may occur occasionally in asthma.

Common allergen tests may identify specific agents to which the patient is sensitive that could trigger asthmatic reactions. Common allergens include cat and dog hair, house-dust mite and grass pollen.

A6: What treatment options are appropriate?

- Assess asthma control – pattern and severity of symptoms and exacerbations, supplemented where appropriate with serial PEF recording. An oral steroid trial (as above) may be required to demonstrate the patient's best spirometry.
- Eliminate trigger factors.
- Patient education – ensure understanding of medications and how to alter treatment in the event of deterioration, and check inhaler technique. Provide a written asthma action plan.

Stepwise drug treatment is as follows.

1. Mild intermittent asthma – inhaled short-acting $beta_2$ agonist as required.
2. Regular preventer therapy – add inhaled steroid 200–800 µg daily for patients with recent exacerbations, nocturnal asthma or using short-acting $beta_2$ agonists more than once a day.
3. Add-on therapy – add inhaled long-acting $beta_2$ agonist twice a day.
4. Persistent poor control – increase inhaled steroid dose up to 2000 µg daily, or consider trial of leukotriene receptor antagonist, theophylline preparation or oral beta-agonist.
5. Continuous or frequent use of oral steroids – use daily steroid tablets in lowest dose tolerated. Consider anti-immunoglobulin E (IgE) therapy if appropriate, based on total and specific IgE.

CASE 7.2 – **A 66-year-old man with chronic dyspnoea and cough.**

A1: What is the likely differential diagnosis?

The differential diagnoses are chronic obstructive pulmonary disease (COPD), asthma and bronchiectasis.

A2: What issues in the given history support the diagnosis?

Chronic progressive breathlessness on the background of a long smoking history suggests COPD. Typical features include lack of spontaneous improvement or response to inhaled therapy, relentless progression of symptoms, and a combination of productive cough and dyspnoea. Although the patient has only a 20 pack-year smoking history, his occupation and the variable effects of cigarette smoking make COPD the most likely diagnosis.

A3: What additional features of the history would you seek to support a particular diagnosis?

A history of previous reversible wheeze and dyspnoea may suggest chronic asthma. Productive sputum can accompany bronchiectasis, and predisposing features such as childhood infections should be sought. Assessment of severity in terms of lifestyle and exercise impairment should be made. Chronic lung disease can precipitate depression, and the patient's mood should be assessed because antidepressants can help.

A4: What clinical examination would you perform, and why?

Physical examination is rarely diagnostic in COPD. Look for signs of respiratory failure (central cyanosis), hypercapnia (bounding high-volume pulse, flapping tremor) and cor pulmonale (raised jugular venous pressure [JVP], ankle or sacral oedema). Physical signs of airflow obstruction usually occur only when severe airflow obstruction is present, such as pursed-lipped breathing, hyperinflated thorax, paradoxical in-drawing of the intercostal spaces, resonant percussion note, poor breath sounds and wheeze.

A5: What investigations would be most helpful, and why?

- *Spirometry:* baseline spirometry with reversibility to bronchodilators should be performed in all patients suspected of having COPD. The FEV_1 is typically less than 80 per cent of the predicted value, and the FEV_1/FVC ratio is less than 70 per cent; these values do not return to normal with a bronchodilator. A short course of oral steroids can be used to help distinguish chronic asthma from COPD. Post-bronchodilator FEV_1 is used to classify the severity of COPD.
- *Chest radiograph:* no specific features, but upper-zone emphysema, hyperinflation (more than six ribs anteriorly) and a flattened diaphragm would support the diagnosis. It is useful to exclude an alternative diagnosis such as bronchial carcinoma.
- *Arterial blood gases (ABGs)/pulse oximetry:* these should be measured in patients with severe disease. Oxygen saturation of 92 per cent or less should lead to ABG measurement.
- *FBC:* this is useful to exclude anaemia or polycythaemia.
- *Alpha$_1$-antitrypsin:* this may identify deficiency in rare cases; check in patients aged under 45 years.

A6: What treatment options are appropriate?

The aims of management are to lessen dyspnoea, reduce exacerbations and improve exercise tolerance, with minimal side effects, normally using both pharmacological and behavioural components. Smoking cessation is the most effective way to reduce the risk of developing COPD and slow or halt its progression.

Although no objective improvement in spirometry is seen in response to bronchodilator therapy in COPD, patients may derive symptomatic benefit. The patient should therefore be provided with an inhaled bronchodilator, either a short-acting $beta_2$ agonist or anticholinergic therapy. Patients with more severe symptoms should be given a trial with an inhaled long-acting $beta_2$ agonist or anticholinergic agent. Other agents may be tried on a symptomatic trial basis, including oral theophyllines.

Inhaled steroids result in small reductions in the frequency of exacerbation in severe COPD. Combination therapy of an inhaled long-acting $beta_2$ agonist and an inhaled steroid may reduce the frequency of exacerbations more effectively than either drug alone.

Long-term oxygen therapy is recommended for patients who have stopped smoking and who have chronic respiratory failure (PaO_2 <7.3 kPa, where PaO_2 is the partial pressure of oxygen in arterial blood). Pulmonary rehabilitation is useful to maximize the patient's functional capacity.

The patient should be immunized against influenza yearly. A mood assessment should be made with intervention for depression where appropriate.

CASE 7.3 – A 66-year-old man with progressive dyspnoea and weight loss.

A1: What is the likely differential diagnosis?

The differential diagnoses are CFA, pulmonary asbestosis and cardiogenic pulmonary oedema.

A2: What issues in the given history support the diagnosis?

Progressive dyspnoea in a non-smoker with no history of cough may suggest fibrotic (interstitial) lung disease. Dyspnoea is frequently first encountered on effort, but progression to dyspnoea at rest is common. The history of occupational exposure to asbestos may suggest an industrial component to this disease, but formal diagnosis requires further investigations. Crackles are typical of some forms of interstitial lung disease and are frequently confused with pulmonary oedema.

A3: What additional features of the history would you seek to support a particular diagnosis?

An attempt should be made to quantify the degree of functional impairment experienced by the patient. The degree of exposure to asbestos fibres should be enquired about. The history should also include information on any systemic disease, drug therapy, travel and environmental exposures, such as agents known to cause extrinsic allergic alveolitis (EAA; e.g. bird protein, mouldy hay). A history of ischaemic heart disease (IHD) or hypertension makes pulmonary oedema more likely.

A4: What clinical examination would you perform, and why?

General examination should look for evidence of respiratory or cardiac failure. Ankle oedema, cyanosis, tachycardia and respiratory rate should all be examined. Finger clubbing is frequently associated with CFA but is seen less often in asbestosis. Respiratory examination may reveal poor thoracic excursion, normal percussion note and widespread inspiratory crackles. Weight loss frequently accompanies interstitial lung disease, but assessment for bronchial carcinoma should be made.

A5: What investigations would be most helpful, and why?

- *chest radiograph* – may be normal or reveal shrunken lungs with coarse vascular markings (honeycomb lung) or patchy areas of consolidation; evidence of asbestos exposure may be found such as pleural calcification or plaques
- *high-resolution computed tomography (HRCT)* – may reveal long-standing changes of fibrosis (honeycombing) or the more acute changes associated with active inflammation (ground-glass intra-alveolar shadowing)
- *pulmonary function tests* – typically a restrictive pattern of spirometry would be expected (FEV_1/FVC ratio normal, but both values less than predicted); total lung volumes and static volumes are reduced and the CO diffusion gradient is also reduced
- *oxygen saturation/tension* – it is useful to assess the degree of hypoxaemia, because this helps to quantify the severity of disease and may indicate patients who will benefit from the administration of domiciliary oxygen therapy; a 6 min walk test with oxygen saturation measurements is a sensitive test of early interstitial lung disease
- *serum markers of EAA* – serum precipitins to avian proteins and other causes of EAA should be sought
- *FBC* – of little use, although an elevated haematocrit may develop in response to chronic hypoxia
- *autoimmune antibodies* – may reveal coexistence of connective tissue diseases that may present with interstitial lung disease such as rheumatoid arthritis, systemic lupus erythematosus (SLE) or systemic sclerosis.

A6: What treatment options are appropriate?

The patient should avoid any causal agents. Advice on seeking industrial compensation is appropriate in the case of pulmonary asbestosis.

Controlling the progression of pulmonary fibrosis may be achieved in CFA by systemic corticosteroid therapy or immunosuppressive treatment, although the response to treatment is often disappointing. Domiciliary oxygen may be prescribed for patients with end-stage disease.

OSCE counselling case

OSCE COUNSELLING CASE 7.1 – **'Can I have oxygen at home? I'm sure it would help me'.**

There is concern over the use of oxygen supplementation in the context of possible exposure to naked flames. Oxygen can promote combustion and may make house fires more likely. It is recommended that patients who smoke are not prescribed oxygen and that oxygen is not used in homes heated by open-flame fires.

Patients with interstitial pulmonary disease may benefit from oxygen as a palliative measure at later stages of the disease. The degree of alveolar hypoxia should be estimated by ABG measurement, and the secondary consequences of hypoxaemia should be assessed. If PaO_2 is less than 8 kPa and symptoms of dyspnoea are disabling to the patient, oxygen may be prescribed on an as-required basis.

Oxygen is administered from either constant-flow cylinders or concentrators, both of which must be delivered to the patient's home. The patient's capacity to use the device should be assessed; where necessary, training or additional support from, for example, a specialist nursing service should be arranged.

There is concern over the safety of overreliance on domiciliary oxygen. Patients should be advised that oxygen is safe in stable respiratory disease but is not a substitute for medical intervention in the event of a sudden deterioration. Therefore, if dyspnoea gets worse despite normal use of oxygen, medical advice should be sought.

There is concern about excess oxygen in COPD. Patients who have COPD may become dependent on hypoxic drive to stimulate respiration, and COPD can complicate many respiratory conditions, including fibrosing alveolitis. Although supplementary oxygen is safe if assessed properly, increasing the supply of oxygen may depress the patient's respiratory drive. Patients are advised not to make changes to the flow settings on their concentrators or cylinders without seeking advice.

PLEURITIC CHEST PAIN

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features of the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 7.4 – A 35-year-old woman with sudden pleuritic chest pain and haemoptysis.

A 35-year-old woman is brought to the accident and emergency (A&E) department complaining of acute onset of chest pain the preceding evening and collapsing that afternoon. She is shocked and dyspnoeic. This pain is described as 'sharp', located posteriorly on the left hemi-thorax, and worse on inspiration and coughing. On the morning of admission there was some haemoptysis. She has recently been in hospital for treatment and investigation of recurrent miscarriage.

CASE 7.5 – A 73-year-old man with gradual-onset pleuritic chest pain and haemoptysis.

A 73-year-old man attends his GP complaining of left-sided 'sharp' chest pain. The pain is worse on inspiration, does not radiate and has appeared in the past 2 days. He has not felt well for a week, with uncontrollable shivering bouts and sweats. He has had a cough with red-tinged sputum for 3 days. He smokes 20 cigarettes a day, and he has angina complicated by a myocardial infarction (MI) 2 years previously. He has recently felt increasingly short of breath with effort.

CASE 7.6 – A 30-year-old man with sudden pleuritic chest pain and dyspnoea.

A 30-year-old man attends A&E complaining of chest pain and breathlessness. The pain developed suddenly, 16 hours before attendance, and he has gradually become increasingly short of breath since. The pain is described as 'sharp', worse on inspiration or coughing, and located on the right thoracic chest wall. He denies new cough or sputum production.

OSCE counselling case

OSCE COUNSELLING CASE 7.2 – **'Should I take oral contraceptives rather than risk a further pregnancy?'**

This 35-year-old woman was finally diagnosed as having a life-threatening PE. Having received 6 months of anticoagulation therapy, she returns to her doctor for advice. Her main concerns surround whether she should now consider oral contraception rather than risk further pregnancy. What risks exist, and how should the GP advise her?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

PLEURITIC PAIN

Pleuritic pain is pain usually localized to the thoracic wall, whose severity varies with respiration. Typically the pain will be worse on inspiration and relieved by expiration. Commonly, coughing exacerbates this type of pain. The pain normally derives from inflamed layers of pleura moving over each other.

THROMBOEMBOLISM

Thromboembolism is the passage of blood clots from a peripheral source to a more proximal vascular bed. Typically the origin of thromboembolism is the deep veins of the leg. Clots frequently lodge in the pulmonary arterial circulation.

COMMUNITY-ACQUIRED PNEUMONIA

Community-acquired pneumonia is infective pneumonia that has developed in the community. It is distinguished from conditions that develop in a hospital setting, which are caused by different organisms and carry different prognoses.

ADDITIONAL FACTORS ASSOCIATED WITH PULMONARY THROMBOEMBOLISM

Pre-test probability scores are designed to calculate the numerical risk of PE, based on clinical assessment, to guide the interpretation of more detailed investigation. The score includes the patient's age, history of thrombotic disease, predisposing condition such as malignancy, the presence of tachypnoea (respiratory rate >30/min), tachycardia, chest pain, clinical evidence of deep venous thrombosis (DVT), abnormal electrocardiogram (ECG; as a new finding) and abnormal chest radiograph. The presence of one or more clinical features plus one of the baseline investigations is said to have a sensitivity for PE of more than 80 per cent.

ADDITIONAL FEATURES IN COMMUNITY-ACQUIRED PNEUMONIA

The British Thoracic Society guidelines for assessment of confusion score each of the following questions 1 mark, with a maximum score of 10 marks. A score of 8 or less indicates mental confusion:

- age
- date of birth
- time (nearest hour)
- year
- hospital name
- recall address (e.g. 24 West Street)
- date of First World War
- name of monarch
- count backwards from 20
- recognition of two people (e.g. doctor or nurse).

Answers

Clinical cases

CASE 7.4 – **A 35-year-old woman with sudden pleuritic chest pain and haemoptysis.**

A1: What is the likely differential diagnosis?

The differential diagnoses are PE, community-acquired pneumonia with septic shock, and tension pneumothorax.

A2: What issues in the given history support the diagnosis?

Pleuritic chest pain with dyspnoea and haemoptysis is typical of PE. A recent spell in hospital where the patient may have been relatively immobile, and the history of recurrent miscarriages, which may be associated with thrombophilia, are potential risk factors for PE. The sequence of a small embolic event followed by a more clinically significant episode with haemodynamic compromise is typical of PE.

A3: What additional features of the history would you seek to support a particular diagnosis?

Further enquiry should attempt to identify risk factors for DVT, such as smoking, history of DVT, PE or malignancy, recent long-haul airline flight, family history of DVT or PE, and recent surgical procedures and use of DVT prophylaxis. A history of leg swelling may indicate current DVT.

A4: What clinical examination would you perform, and why?

The clinical presentation demands urgent emergency assessment and should follow the standard advanced life support ABC (A – airway, B – breathing, C – circulation) protocol.

Further clinical assessment should be aimed at identifying the presence of DVT and assessing the severity of respiratory and haemodynamic compromise. The respiratory rate, pulse rate, blood pressure (typically low in PE) and presence of cyanosis should be recorded. Calves should be examined for swelling or tenderness, and any circumferential differences should be measured and documented. Detailed respiratory examination, including auscultation, which may reveal localized wheeze or a pleural rub or be normal, should be performed. A loud pulmonary second heart sound is rarely heard in acute PE.

A5: What investigations would be most helpful, and why?

- *chest radiograph* – may be normal or show oligaemia or pleural-based wedge-shaped shadowing
- *ECG* – tachycardia, atrial fibrillation, rarely S1, Q3, T3 pattern
- *oxygenation* – saturation or PaO_2 by arterial puncture is useful to assess severity
- *blood D-dimers* – have high negative predictive value; measure only when there is a reasonable suspicion of PE
- *computed tomography pulmonary angiogram (CTPA)* – replaced pulmonary angiogram as the imaging of choice
- *ventilation/perfusion isotope lung scan* – normal scans reliably exclude PTE; positive or negative scans are diagnostic in 30–50 per cent of cases, but rely on a normal chest radiograph appearance

- *thrombophilia screen* – important in this case, given the history of recurrent miscarriage; protein S, protein C, von Willebrand's factor, lupus anticoagulant and factor V Leiden should all be measured.

A6: What treatment options are appropriate?

The initial management of this patient depends on the degree of haemodynamic compromise. Immediate steps should be made to stabilize her condition, including supplementary oxygen therapy, IV fluid resuscitation and transfer to a location where intensive monitoring can be performed.

If she remains haemodynamically unstable, thrombolytic therapy should be administered intravenously. Thrombolysis is the first-line treatment for massive PE.

If the patient is stable, a pre-test probability of PE should be made before investigation, and further management should be directed by the likelihood of PE based on this pre-test probability score and the appropriate investigations. If clinical suspicion of PTE is high, full-dose anticoagulation should be initiated with low-molecular-weight (LMW) heparin, while oral anticoagulant therapy (warfarin) is commenced at a loading regimen. Anticoagulation should be continued for a minimum of 6 months and discontinued if there are no obvious predisposing factors remaining. Consideration of life-long therapy should be made in the light of ongoing risk factors.

CASE 7.5 – **A 73-year-old man with gradual-onset pleuritic chest pain and haemoptysis.**

A1: What is the likely differential diagnosis?

The differential diagnoses are community-acquired streptococcal pneumonia, community-acquired pneumonia caused by 'atypical pathogen', PE and tuberculosis (TB).

A2: What issues in the given history support the diagnosis?

Symptoms typical of infection (fevers or sweats) with pleuritic chest pain suggest pneumonia, but they can be associated with PE. Although there are no clinical features specific for a given pathogen, *Streptococcus pneumoniae* remains the most common cause of community-acquired pneumonia. The so-called 'atypical' pathogens such as *Mycoplasma* species, *Legionella pneumophila* and *Chlamydia* species represent a substantial minority. In this patient, the age, presence of pleuritic chest pain and cardiovascular comorbidity are all associated with streptococcal infections. The red-tinged or rusty sputum is said to typify streptococcal infections, but haemoptysis may occur with other pulmonary infections, especially TB.

A3: What additional features of the history would you seek to support a particular diagnosis?

Comorbid conditions, associated with a poor outcome in community-acquired pneumonia, should be sought, such as diabetes mellitus, cystic fibrosis and chronic lung disease. If the patient has been bedridden or confused since the onset of symptoms, his prognosis is worse. It is very difficult to reliably determine the cause of pulmonary infections by history alone. Contact with TB should be enquired after.

A4: What clinical examination would you perform, and why?

Clinical examination in community-acquired pneumonia is directed at confirming the diagnosis and measuring a severity score. The latter informs management decisions, including the best location for treatment (home, ward or intensive care unit) and the likely prognosis.

General examination should identify cachexia, pyrexia (absence of fever in community-acquired pneumonia carries a poor prognosis), cyanosis and peripheral lymphadenopathy, and the presence of labial herpes simplex. A Mini-Mental State Examination (MMSE) should be performed and recorded (a score below 8/10 is associated with a poor prognosis). Respiratory rate, pulse rate and blood pressure

should be recorded. Respiratory examination should look for the typical features of consolidation, including dull percussion note, bronchial breathing, increased vocal fremitus and whispering pectoriloquy.

A5: What investigations would be most helpful, and why?

Investigations are used to confirm the diagnosis and assess likely prognosis. Chest radiograph is the most useful investigation in confirming the diagnosis. Unfortunately, no single feature can identify the causative organism. Multilobar involvement or pleural effusions are more frequent in bacteriological pathogens, and cavitation is more common with *Staphylococcus aureus* or *Klebsiella pneumoniae* infections. Multilobar involvement carries a poor prognosis.

- *FBC* – high leucocytosis ($>20\times10^9$/L) or leucopenia ($<4\times10^9$/L) carries a poor prognosis
- *urea and electrolytes (U&Es)* – high urea has a worse prognosis, and renal failure suggests severe sepsis
- *liver function tests (LFTs) and creatine kinase* – commonly abnormal in *Legionella* infections
- *sputum culture* – unless previous antibiotics have been administered
- *blood cultures and sensitivities* – very sensitive marker for aetiology if positive
- *serum for serology* – paired samples for atypical serology
- *urine and blood samples* – for pathogen antigens.

A6: What treatment options are appropriate?

Initial management decisions should be informed by a severity assessment score. The CURB-65 is commonly used. This score addresses confusion (MMSE <8/10), serum urea elevated >7 mmol/L, respiratory rate >30/min, abnormal blood pressure (systolic <90 mmHg, diastolic <60 mmHg) and age >65 years. Community treatment is likely to be safe if none or only one of these markers is present; the presence of two or more markers requires hospital assessment and may require admission to a ward or an intensive care setting.

Medical treatment should include supplementary oxygen if required, IV fluids and antibiotic therapy. Initially an empirical choice is required, but this should not be delayed because the time to first dose of antibiotic correlates with outcome. It is rare to have sufficient clues to the identity of the infecting organism to guide initial choice. In the UK, most streptococcal infections remain sensitive to beta-lactam antibiotics, whereas most atypical organisms are sensitive to macrolides. It is reasonable therefore to prescribe co-amoxiclav and clarithromycin in the first instance, and then to await sensitivities or treatment failure to guide further selection. In a hospital setting, an initial IV dose and a choice of IV or oral medication thereafter is frequently used. In the community, both penicillin and macrolide antibiotics are well absorbed orally.

CASE 7.6 – A 30-year-old man with sudden pleuritic chest pain and dyspnoea.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are left-sided pneumothorax and PE.

A2: What issues in the given history support the diagnosis?

Sudden onset of chest pain suggests either trauma or spontaneous pneumothorax. As no history of a precipitating event is given, spontaneous pneumothorax is the most likely diagnosis. Frequently the pneumothorax will enlarge over time, and thus dyspnoea may develop relatively late. Pulmonary embolus should always be considered; however, there is no supporting history given.

A3: What additional features of the history would you seek to support a particular diagnosis?

The previous history of similar events is important because recurrent disease (even if not picked up clinically) is likely to lead to further episodes and will usually be treated by a definitive procedure. Employment history is important because professional diving and flying are banned after a pneumothorax. Recreational diving is also not recommended and should be enquired about.

A4: What clinical examination would you perform, and why?

The patient should be assessed for severity: ABC (A – airway, B – breathing, C – circulation). Occasionally pneumothoraces may develop 'tension' and precipitate haemodynamic compromise. Cyanosis, tachycardia, hypotension and evidence of mediastinal shift (away from the side of the chest pain) are indications of severity. Respiratory examination may reveal tracheal shift (away from pneumothorax), hyperresonant percussion note on the side of the pneumothorax and normal on the opposite side; reduced or normal breath sounds may be present.

Assessment for predisposing conditions should be made, e.g. Marfan's syndrome may present with pneumothorax, and so it is worth examining arm span, palate and eyes for lens dislocation, and examining carefully for an ejection systolic murmur.

A5: What investigations would be most helpful, and why?

- *chest radiograph* – if clinical suspicion of tension pneumothorax is high, treatment should not await radiological examination
- *oxygenation* – either saturation (if >93 per cent) or ABGs
- *FBC* – not useful in a pneumothorax
- *U&Es* – not useful in a pneumothorax
- *cardiac echocardiogram* – if clinical suspicion of aortic incompetence (in Marfan's syndrome).

A6: What treatment options are appropriate?

If there is haemodynamic compromise, immediate puncture of the chest wall in the second intercostal space anteriorly with a large-bore Venflon should be done, releasing air from the pleural space. Attach a 50 mL syringe and a three-way tap after release of air and perform underwater-sealed aspiration of remaining air.

If there is no compromise and chest radiograph confirms the diagnosis, the first step is to perform aspiration under water seal. If there is no obvious predisposing lung disease, this should be sufficient to treat the pneumothorax. This procedure is less likely to be successful if there is underlying disease such as COPD or bullous disease (secondary pneumothorax).

For failed aspiration or secondary pneumothorax, a chest drain should be inserted and attached to an underwater seal to allow the gradual reinflation of the lung and removal of pleural gas. Administration of supplemental oxygen is said to hasten reabsorption of pleural gas.

If a second or recurrent pneumothorax is present, a pleural sealing procedure should be performed such as talc pleurodesis or video-assisted pleurectomy.

OSCE counselling case

OSCE COUNSELLING CASE 7.2 – **'Should I take oral contraceptives rather than risk a further pregnancy?'**

Pulmonary embolus is a rare condition affecting 1–4/1000 people in the UK per year. This risk is increased in pregnant women tenfold over non-pregnant women. This risk is increased further if known risk factors coexist. Such risk factors include age >35 years, thrombophilia, obesity (body mass index >30 kg/m^2), paraplegia and inflammatory bowel disease.

In this case, the history of life-threatening PE and recurrent miscarriage makes the presence of a thrombophilia more likely. The precise risk depends on the nature of each thrombophilia. This patient carries three risk factors: age, history and a likely thrombophilia.

Pre-pregnancy advice from a specialist should be sought. Extensive investigation of a thrombophilia is important. Treatment with LMW heparin can be instituted throughout pregnancy, so investigation before pregnancy is helpful.

The oestrogen content of the oral contraceptive pill is associated with a thrombotic risk. The history of life-threatening PE contraindicates the oral contraceptive in this case, and alternative methods of contraception should be used.

HAEMOPTYSIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features of the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 7.7 – A 60-year-old man with 2 weeks of trivial haemoptysis and weight loss.

A 60-year-old man attends the medical outpatient clinic complaining of 4 weeks of cough productive of white sputum and 2 weeks of haemoptysis. The haemoptysis is described as 'streaks of old blood through the spit' and is trivial in volume. It has remained constant throughout the 2-week period. There is no dyspnoea or chest pain, but the patient is a life-long smoker. He has noticed his clothes being looser over the previous 6 months and describes a loss of appetite, but he denies dysphagia or altered bowel habit. He is easily tired and notices his voice becoming hoarse in the evenings. He is a bookmaker and is married with two daughters, one of whom attends the clinic with him. She adds that her father appears slightly confused at times, particularly in the evenings.

CASE 7.8 – A 45-year-old woman with chronic cough and massive haemoptysis.

A 45-year-old mother of two presents at A&E on a Sunday night, complaining of coughing large volumes of fresh red blood for the past 2 days. She estimates she has coughed up five mugs of fresh blood. She describes a cough with purulent sputum for the past month, but she cannot remember a time when she did not have a cough. She frequently receives antibiotics from her GP when the sputum turns green or increases in volume. She has been increasingly breathless for the past 2 weeks, although she has noticed increasing breathlessness for 3 years.

CASE 7.9 – A 62-year-old man with 2 months of fevers and haemoptysis.

A 62-year-old man attends the respiratory clinic complaining of worsening cough, spit and haemoptysis. This has been of 2 months' duration and is associated with weight loss, anorexia, fevers, night sweats and purulent sputum. He denies chest discomfort or dyspnoea. He lives alone, smokes 20 cigarettes a day, and admits to drinking in excess of 40 units of alcohol a week. As a child he was treated for TB at the same time as his father. He was a welder in a shipyard before being made redundant.

OSCE counselling case

OSCE COUNSELLING CASE 7.3 – **'My father tends to drink too much and often forgets to take his tablets – is it important?'**

The patient's daughter tells you that her father is an alcoholic and returns a large number of anti-TB tablets that he has not taken.

What are the risks of poor compliance with treatment in 'open TB'? What options are available to improve the patient's compliance?

Answers

Clinical cases

CASE 7.7 – **A 60-year-old man with 2 weeks of trivial haemoptysis and weight loss.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are bronchial carcinoma, TB and upper respiratory tract infection.

A2: What issues in the given history support the diagnosis?

Haemoptysis associated with weight loss suggests a systemic disease of uncertain duration. Bronchial carcinoma may present late with haemoptysis after a lengthy period of weight loss and cough. Smoking is associated with most cases of bronchial carcinoma, and a non-smoking history should suggest other causes. Associated features of fatigue are non-specific but frequently associated with pulmonary malignancy, whereas hoarseness and confusion should raise suspicions about complications of the disease, such as recurrent laryngeal nerve palsy or syndrome of inappropriate antidiuretic hormone secretion (SIADH).

A3: What additional features of the history would you seek to support a particular diagnosis?

Employment with a history of asbestos exposure may support pulmonary malignancy. The cumulative lifetime amount of tobacco smoked should be noted, and the presence of constitutional features of fever and sweating may point towards an infective origin of haemoptysis. Pain is an important complication of bronchial carcinoma and can be effectively palliated. Thus, bone or chest wall pain (suggesting advanced disease) should specifically be addressed. An assessment of quality of life and the World Health Organization's 'performance status' is helpful to decide appropriate future management.

A4: What clinical examination would you perform, and why?

Assessment of peripheral (hand–T1 root) muscle wasting, peripheral lymphadenopathy, hepatic enlargement and any unusual or new skin lesions helps to identify distant metastases. Finger clubbing is common but non-specific. Respiratory examination to identify lobar or lung collapse from a central obstructing tumour (tracheal deviation, apex beat, loss of breath sounds) or pleural metastases (signs of effusion) is helpful for baseline assessment of the extent of disease. An assessment of paraneoplastic syndromes can be helpful, e.g. blood pressure (autonomic neuropathy), skin rash (pigmentation [adrenocorticotrophic hormone] or dermatomyositis) or joint stiffness or discomfort (hypertrophic pulmonary osteoarthropathy).

A5: What investigations would be most helpful, and why?

- *chest radiograph* – most important and may reveal diagnosis and complications
- *computed tomography (CT)* – may identify non-carcinoma causes of haemoptysis, and help staging and biopsy of peripheral lesions seen on chest radiograph; ideally performed before bronchoscopy to guide biopsy
- *bronchoscopy with lavage or biopsy* – important to provide histology, particularly in central tumours

- *sputum cytology* – generally unhelpful, with only 5 per cent sensitivity
- *U&Es* – helpful to exclude SIADH and assess fitness for treatment
- *serum calcium* – elevated in some cases of bronchial carcinoma
- *LFTs* – help exclude liver metastases
- *pulmonary function tests* – assess fitness for thoracic surgery.

A6: What treatment options are appropriate?

Palliate the patient's symptoms, including haemoptysis, pain and anxiety. Then treat the underlying disease.

- *Small cell carcinoma:* chemotherapy-based treatment, either as palliation of symptoms (reduced dose) or with curative intent (full dose), may be given. Cisplatin-based regimens are now the usual treatment option.
- *Non-small cell carcinoma:* chemotherapy regimens are used only to downstage extensive disease and allow more definitive therapy to be instituted. Such options include surgical resection (pneumonectomy or lobectomy) and radiotherapy (radical or high-dose palliative).
- Fully palliative radiotherapy can be used for symptomatic control.

CASE 7.8 – **A 45-year-old woman with chronic cough and massive haemoptysis.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are bronchiectasis, PE and pulmonary TB.

A2: What issues in the given history support the diagnosis?

Chronic productive cough is a feature of bronchiectasis, which occasionally presents with massive haemoptysis. Chest discomfort with haemoptysis may simply be associated with coughing-induced musculoskeletal discomfort, but PE should be considered. A change in the volume or purulence of sputum associated with the constitutional features suggests chest infection, which can herald haemoptysis in bronchiectasis.

A3: What additional features of the history would you seek to support a particular diagnosis?

A history of a predisposing condition (childhood pneumonias, whooping cough, measles) should be sought, but its absence does not exclude bronchiectasis. Evidence of immunodeficiency may be suggested by recurrent infections outwith the chest. A history of fertility problems, such as assisted conception, and bowel irregularities throughout life may suggest cystic fibrosis.

A4: What clinical examination would you perform, and why?

An initial cardiovascular examination should be performed to assess the degree of blood loss. Pulse rate, blood pressure and evidence of peripheral circulation should be measured to exclude shock.

A respiratory examination should be done, particularly searching for crackles in any region of the lungs. Palpation of the painful region should be done to confirm the musculoskeletal nature of the pain. Finger clubbing is not present in most cases of bronchiectasis. Wheeze occurs in 75 per cent and crackles in 60 per cent.

A5: What investigations would be most helpful, and why?

- *chest radiograph* – very important; in one series 20 per cent of patients of haemoptysis with a normal chest radiograph had bronchiectasis
- *bronchoscopy* – only if haemodynamically significant volumes of blood or to exclude bronchial carcinoma
- *sputum* – helpful for microbiological identification, especially *Pseudomonas* species
- *HRCT* – diagnostic investigation of choice with 87–97 per cent sensitivity and 93–100 per cent specificity
- *bronchial angiography* – helpful if radiological treatment of haemoptysis is warranted
- *FBC* – for assessment of anaemia.

A6: What treatment options are appropriate?

Resuscitation if required. Antitussives can be used if cough is severe. Sedation is sometimes used to control cough and anxiety. Treatment for infection should be guided by sputum sensitivities. Haemoptysis usually needs no specific treatment; if very severe and persistent, consider bronchial artery embolization or, as a last resort, surgical resection.

Bronchiectasis is a life-long condition that can result in chronic respiratory impairment. The patient should be warned that she may deteriorate over time and require frequent courses of antibiotics. Physiotherapy for lung hygiene may be helpful to reduce the frequency of infective exacerbations and preserve lung function. The evidence for the latter is currently lacking, but the patient should be taught the appropriate exercises tailored to her own specific capacity. The patient should be taught to look out for signs of infection, because prompt and appropriate antibiotic therapy may slow the decline in lung function often associated with bronchiectasis. Specialist therapies may be tried in individual patients, including nebulized antibiotic therapy or long-term rotational antibiotics (in which a series of antibiotics are taken chronically to keep bacterial levels to a minimum, with regular changes in the antibiotic to prevent drug resistance).

CASE 7.9 – A 62-year-old man with 2 months of fevers and haemoptysis.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are TB, bronchial carcinoma, pneumonia, mycetoma and bronchiectasis.

A2: What issues in the given history support the diagnosis?

A previous history of TB and the consumption of large quantities of alcohol suggest reactivation of old TB. The constitutional symptoms support this diagnosis, but bronchial carcinoma should also be excluded in a smoker with haemoptysis. Previous TB can give rise to mycetoma and bronchiectasis, both of which should be borne in mind. In case series where bronchial carcinoma is rare or excluded, bronchiectasis and TB represent the greatest cause of haemoptysis.

A3: What additional features of the history would you seek to support a particular diagnosis?

Contact with other people with similar symptoms, and with close family members, should be ascertained. The type of therapy used for the historical TB may suggest inadequate treatment.

A4: What clinical examination would you perform, and why?

Clinical examination should attempt to exclude TB. Respiratory examination may suggest focal signs of old TB, such as crackles in the upper lobes, but may be normal in active TB. Evidence of liver disease should be sought, given the patient's alcohol consumption and the possible need for anti-TB therapy.

A5: What investigations would be most helpful, and why?

- *chest radiograph* – important
- *sputum* – three samples on different days for smears looking for acid- and alcohol-fast bacilli (AAFB) and culture of organisms (for up to 8 weeks)
- *bronchoscopy* – to exclude malignancy and allow bronchoalveolar lavage and biopsy
- *enzyme-linked immunosorbent spot assay* – lymphocyte activation testing has increased the rapidity of screening for TB
- *U&Es* – baseline
- *FBC* – assesses anaemia
- *LFTs* – baseline.

A6: What treatment options are appropriate?

Assess infectivity and risk:

- sputum for AAFB – urgent consideration
- likely contact with children or others – if high risk of contact spread, admit patient for isolation until sputum is negative for organisms.

The patient should be assessed for likelihood of multidrug-resistant TB (human immunodeficiency virus [HIV], foreign contact). If the patient is at high risk, institute quadruple therapy; otherwise, start triple therapy with rifampicin, isoniazid and pyrazinamide (add ethambutol for quadruple therapy).

It is important in this case to include pyridoxine and multi-B vitamins to reduce the peripheral neuropathic complications of the anti-TB chemotherapy.

The patient's compliance with therapy should be assessed; if compliance is poor, consider starting directly observed therapy (DOT).

Try to find the trace, by contacting likely contacts, family members and regular contacts.

OSCE counselling case

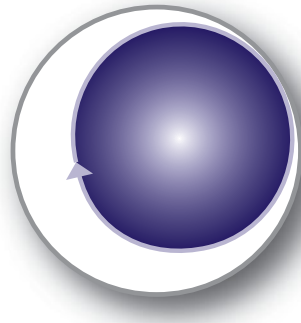
OSCE COUNSELLING CASE 7.3 – **'My father tends to drink too much and often forgets to take his tablets – is it important?'**

Tuberculosis diagnosed by sputum examination is likely to be infectious. Although it may be safe to treat this man in the community if his contacts are known, screened and limited, incomplete or no treatment increases the risk to the general public of infectious spread. Before effective antibiotic treatment, TB was a fatal disease; failure to take appropriate anti-TB chemotherapy puts the patient's own health at risk. Incomplete or intermittent treatment increases the risk of developing drug-resistant TB. This can lead to chronic infection and the risk of community dissemination of multidrug-resistant TB.

Alcohol-related liver impairment may worsen the side-effect profile of some anti-TB drugs and may explain the patient's poor compliance. Such a problem should be sought and alternative drugs administered. Usually it is best to admit such a patient to a ward or clinic and reintroduce regular triple therapy in a stepwise manner until the problem can be identified. It is likely that this patient's lifestyle is 'chaotic', and therefore regular compliance with treatment is likely to be poor. In these circumstances, DOT may be instituted. Directly observed therapy requires that a trained health-care professional, e.g. TB specialist nurse or equivalent, visits the patient at a prearranged location, either daily or three times a week, and observes the treatment being taken. Such practice has been found to reduce the incidence of drug-resistant TB in areas with a relatively high prevalence. In very rare cases, compulsory admission can be arranged under public health law. This can be done only in the context of respiratory TB, where there is a considerable risk to public health. Compulsory administration of medications is not permissible, however, and it is therefore best to develop a concordant rather than a coercive relationship with the patient.

REVISION PANEL

- The volume of air expired in the first second is known as the forced expiratory volume in 1 s (FEV_1). The total volume exhaled in 5 s is the forced vital capacity (FVC).
- Episodic breathlessness, wheeze and cough with spontaneous resolution are typical of asthma. Symptoms tend to occur at night, first thing in the morning or after exercise, but none of these clinical features is specific for asthma.
- Chronic progressive breathlessness on the background of a long smoking history suggests COPD. Typical features include lack of spontaneous improvement or response to inhaled therapy, relentless progression of symptoms, and a combination of productive cough and dyspnoea.
- Progressive dyspnoea in a non-smoker with no history of cough may suggest fibrotic (interstitial) lung disease.
- Pleuritic chest pain with dyspnoea and haemoptysis is typical of PE. Diagnosis can be confirmed by CTPA. Full-dose anticoagulation should be initiated with LMW heparin, while oral anticoagulant therapy (warfarin) is commenced at a loading regimen. Anticoagulation should be continued for a minimum of 6 months.
- Symptoms typical of infection (fevers or sweats) with pleuritic chest pain suggest pneumonia. *Streptococcus pneumoniae* remains the most common cause of community-acquired pneumonia. The so-called 'atypical' pathogens such as *Mycoplasma* species, *L. pneumophila* and *Chlamydia* species represent a substantial minority. The red-tinged or rusty sputum is said to typify streptococcal infections, but haemoptysis may occur with other pulmonary infections, especially TB.
- Sudden onset of chest pain suggests either trauma or spontaneous pneumothorax. Pulmonary embolus should always be considered.
- Bronchial carcinoma may present late with haemoptysis after a lengthy period of weight loss and cough. Smoking is associated with most cases of bronchial carcinoma, and a non-smoking history should suggest other causes.



8 Gastroenterology

C.S. Probert

GASTROENTEROLOGICAL EMERGENCIES

PANCREATITIS

INFLAMMATORY BOWEL DISEASE

PEPTIC ULCER DISEASE

CIRRHOSIS

CONSTIPATION

HEPATITIS

IRRITABLE BOWEL SYNDROME

COELIAC DISEASE

GASTROENTEROLOGICAL EMERGENCIES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What specific questions would you ask the patient?
Q2: What is the most likely diagnosis?
Q3: What examination would you perform?
Q4: What would be the initial management?
Q5: What investigations would you request to confirm a diagnosis?
Q6: What other issues should be addressed?

CASE 8.1 – **A 73-year-old man with melaena.**

A 73-year-old man presents with a 5-day history of passing black stools. On the fifth day he began to feel breathless and tired, particularly on climbing stairs.

CASE 8.2 – **A 26-year-old woman with bloody diarrhoea.**

A 26-year-old woman presents with a 3-week history of bloody diarrhoea. The blood is fresh and mixed in the liquid stool. Initially, she thought she may have food poisoning, but she cannot recall eating anything unusual and has eaten the same food as her unaffected partner.

CASE 8.3 – **A 46-year-old man with alcohol problems and haematemesis.**

A 46-year-old man with alcohol problems presents with haematemesis and shock.

OSCE counselling cases

OSCE COUNSELLING CASE 8.1 – **'Are my symptoms caused by an infection, or is it all down to the colitis?'**

You have determined that the woman in Case 8.2 has ulcerative colitis and tell her that you can treat it. She would like to know whether she could have passed it on to the children in the school where she is a catering assistant.

OSCE COUNSELLING CASE 8.2 – **'Will my children get inflammatory bowel disease?'**

The woman in Case 8.2 is worried that she may pass inflammatory bowel disease (IBD) on to her own children.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

- Initial assessment of the cause of gastrointestinal (GI) emergencies such as bleeding or severe diarrhoea should be carried out at the same time as resuscitation.
- Most patients with haematemesis or melaena will have bled from a peptic ulcer, most cases of which are painless.
- Initiating proton pump inhibitor (PPI) therapy before endoscopic assessment is not evidence based.
- Although stigmata of chronic liver disease may suggest varices as the cause of haematemesis, endoscopic assessment should be made before 'blind' treatment using a Sengstaken–Blakemore tube.
- Any form of colitis may be life-threatening.
- Infections should always be sought in parallel with treatment.

Answers

Clinical cases

CASE 8.1 – **A 73-year-old man with melaena.**

A1: What specific questions would you ask the patient?

The presence of black stools indicates GI bleeding above the ligament of Trietz. The likely sources include benign and malignant ulceration of the stomach and peptic duodenal ulceration. The history should determine whether there are any symptoms suggestive of ulceration and risk factors and clues to whether the lesion is malignant. Postprandial and nocturnal burning epigastric pains are classic symptoms of peptic ulceration, particularly if the pain radiates to the back. These symptoms differentiate poorly between gastric and duodenal ulcers, however (20 per cent of patients with bleeding peptic ulcers have ulcer-like dyspepsia). Risk factors to seek include:

- past history of peptic ulceration or surgery for such disease
- recent ingestion of non-steroidal anti-inflammatory drug (NSAID) of any type, warfarin or antiplatelet drugs
- smoking
- alcohol use
- diabetes
- heart failure.

The last four of these are likely to relate to poor mucosal healing. Clues to malignancy include weight loss, anorexia and anaemia before the presenting gastrointestinal haemorrhage.

A2: What is the most likely diagnosis?

The most likely diagnosis is a bleeding duodenal ulcer. It is unlikely that the patient is bleeding from an oesophageal lesion (carcinoma or oesophagitis) because, in most cases, haematemesis will occur at the same time. Of all patients with acute upper GI bleeding, 40 per cent have benign peptic ulcer disease. Duodenal ulcers appear to be more common than gastric ulcers.

A3: What examination would you perform?

A full physical examination is necessary, with particular attention being paid to shock. In a patient of this age, however, a systolic blood pressure of 110 mmHg may be considered to be shock. Of secondary importance is the examination of the abdomen, during which an epigastric mass and palpable liver should be sought.

A4: What would be the initial management?

The first step in the management is resuscitation. The patient should be laid flat and given oxygen via a facemask, while two large-bore cannulae are inserted, one of which ought to be a central line if the patient is shocked. As the cannulae are inserted, blood samples should be taken for full blood count (FBC), cross-match (4–6 units), and urea and electrolytes (U&Es) (urea is a marker of the amount of blood lost). Liver function tests (LFTs) are not of immediate importance. Clotting abnormalities need to be sought if the patient is taking warfarin or has jaundice. Fluid replacement should start as soon as the cannulae are in place. There is no advantage to using colloids. Blood transfusion should start as soon as

possible if the patient is shocked or has a haemoglobin (Hb) level below 10 g/dL. A urinary catheter is desirable.

A5: What investigations would you request to confirm a diagnosis?

Oesophagogastroduodenoscopy (endoscopy) should be performed within 24 h of admission. If the patient is shocked or has Hb ≤ 10 g/dL, this should be performed as soon as the patient has been resuscitated, or immediately if urgent surgery is contemplated (i.e. if resuscitation attempts are failing).

A6: What other issues should be addressed?

The ulcer is likely to be *Helicobacter pylori*-related. Triple therapy should be instituted. This is typically a PPI with two antibiotics from amoxicillin, clarithromycin and metronidazole. If aspirin was being used, then clopidogrel may be substituted.

CASE 8.2 – **A 26-year-old woman with bloody diarrhoea.**

A1: What specific questions would you ask the patient?

The duration of the disease suggests that the cause is acute colitis. The differential diagnoses include microbial diarrhoea – *Clostridium difficile* (so a drug history is needed) or protozoa (a travel history should be taken) – side effects of medications such as NSAIDs, and familial adenomatous polyps (bleeding usually occurs in the context of normal stool, so a family history should be taken). Lifestyle and past medical history should be considered in case the patient is immunocompromised.

A2: What is the most likely diagnosis?

The most likely diagnosis is acute colitis, most probably as a result of ulcerative colitis. Other forms of colitis caused by Crohn's colitis, drug side effects and *C. difficile* are possible. Cytomegalovirus (CMV) proctitis and amoebic dysentery are unlikely.

A3: What examination would you perform?

A full physical examination is necessary, with particular attention to examination of the abdomen. Distension and tenderness are particularly worrying physical signs in such a patient. Shock caused by colitis is uncommon but critically important. Anaemia and a fever should be sought. Severe colitis is defined by the presence of tachycardia, fever and anaemia. Tenderness may indicate toxic dilation or perforation.

A4: What would be the initial management?

The patient may require admission or at least discussion with a senior colleague. Assuming that the patient meets the criteria for admission (i.e. she has severe disease), the initial management includes bedrest, hydrocortisone 100 mg IV four times a day, transfusion to correct anaemia, and nutritional support (typically high-energy food cartons). Occasionally IV fluid replacement is required. Heparin is used in most centres: full anticoagulation may treat the disease, whereas prophylactic doses prevent thromboembolism, to which such patients are prone. It is important to confirm the diagnosis rapidly, however. At least three stool cultures should be taken. *Clostridium difficile* toxin must be sought if antibiotics have been consumed recently. Microscopy is often negative, but protozoa must be considered. A plain abdominal radiograph is necessary to assess the diameter of the transverse colon and to look for the distribution of faeces, which may be used to determine the extent of the disease.

A5: What investigations would you request to confirm a diagnosis?

A limited sigmoidoscopy should be performed by a trained operator. This is a hazardous procedure in untrained hands, but assessment of the rectal mucosa often helps determine the aetiology of the colitis.

A6: What other issues should be addressed?

The management of severe ulcerative colitis has two phases: control of the attack and maintenance of remission. If the patient does not respond to IV hydrocortisone by the fifth day, a surgical opinion should be sought, with a view to performing colectomy on day 7. An alternative approach is to initiate rescue therapy with IV ciclosporin or, in some situations, infliximab. Any patient who deteriorates despite IV hydrocortisone should also be considered for emergency colectomy. If hydrocortisone controls the attack, the patient should be weaned on to oral steroids and, probably, a 5-aminosalicylic acid (5-ASA) compound. Steroids should later be discontinued, with a view to controlling remission with the 5-ASA compound.

CASE 8.3 – A 46-year-old man with alcohol problems with haematemesis.

A1: What specific questions would you ask the patient?

This is bleeding oesophageal varices until proven otherwise. Although people with alcohol problems may bleed from all the same lesions as people who do not have this problem, a person with alcohol problems who has bled sufficiently to become shocked is most likely to have varices. If the patient is shocked, treatment must be started before a full history is obtained; indeed, the patient may be unable to give a history. If a history is available, ask for previous episodes of GI bleeding and treatment for varices.

A2: What is the most likely diagnosis?

The most likely diagnosis is bleeding oesophageal varices.

A3: What examination would you perform?

Shock should be evaluated quickly: blood pressure, heart rate and state of peripheral perfusion. Signs of portal hypertension would support the diagnosis: ascites, spider naevi, umbilical hernia. Other evidence of decompensated liver disease should be documented: Glasgow coma score (GCS), fetor, flapping tremor and bruising.

A4: What would be the initial management?

The patient must be resuscitated as quickly as possible. The patient should be laid flat and given oxygen via a facemask while two large-bore cannulae are inserted, one of which should be a central line. As the cannulae are inserted, blood samples should be taken for FBC, cross-match (4–6 units) and U&Es (urea is a marker of the amount of blood lost). Albumin and clotting factors (prothrombin time, PT) can be measured to assess synthetic function; other tests, such as alanine transaminase and alkaline phosphatase, assess hepatocyte damage and biliary tract disease/cholestasis, respectively. Synthetic function is an important prognostic indicator. Fluid replacement should start as soon as the cannulae are in place. The central venous pressure (CVP) should be monitored and blood or albumin given to maintain a pressure of 10–12 cmH_2O. A urinary catheter is desirable. If the patient is in renal failure despite an adequate CVP, call for senior help. Vasopressin analogues are desirable, with senior guidance. If the patient remains shocked, a Sengstaken–Blakemore tube may be necessary.

A5: What investigations would you request to confirm a diagnosis?

Urgent endoscopy is both diagnostic and therapeutic. This should be performed as soon as the patient is cardiovascularly stable. If such stability cannot be achieved, endoscopy may be performed while resuscitation is continued, provided that the airway is protected.

A6: What other issues should be addressed?

Broad-spectrum antibiotics should be given because bacteraemia is common at the time of variceal haemorrhage. Anti-encephalopathy treatment (lactulose, metronidazole) should be started as soon as possible. Intravenous thiamine should be replaced before dextrose is given; without this, there is a risk of precipitating Wernicke's encephalopathy.

OSCE counselling cases

OSCE COUNSELLING CASE 8.1 – 'Are my symptoms caused by an infection, or is it all down to the colitis?'

The answer is, fortunately, colitis. There are similarities in the symptoms between ulcerative colitis and infectious diarrhoea; this is because some infections damage the colon and cause a different kind of colitis. In this patient's case, however, infection has been ruled out by the stool tests. Furthermore, other tests (sigmoidoscopy ± biopsy) have shown that the patient's symptoms are caused by ulcerative colitis. In the acute phase, most forms of colitis are very similar. Infection should be ruled out in new patients with acute disease. Three sets of stool analysis are often necessary to exclude *C. difficile* with confidence. Campylobacter infection causes acute colitis with bloody diarrhoea, but myalgia and abdominal pain are conspicuous. Gastrointestinal infection may occur in patients with ulcerative colitis. Microbiological tests should be performed in patients with an established diagnosis if the attack is atypical or refractory to the usual treatment.

OSCE COUNSELLING CASE 8.2 – 'Will my children get inflammatory bowel disease?'

The answer is, fortunately, 'no'. Although IBD can appear to run in families, the risk is comparatively small. The chances of the patient's children getting IBD are raised ten times, but the risk is still only 1 in 100 – i.e. their chances of getting IBD are less than their risk of getting diabetes or asthma. This is an important test of communication skills. The key is to explain relative and absolute risks. There is a genetic component to the risk of acquiring IBD. The risk to first-degree relatives is 10–20 times greater than that in unaffected families, but this raises the prevalence only from 1 in 1000 to 1 in 100. There is a wealth of literature describing genetic loci in IBD. Although few undergraduates will have read such literature, all should be aware that loci have been described, that the disease is not sporadic, and that there is not a simple mendelian inheritance.

PANCREATITIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What specific questions would you ask the patient?
Q2: What is the most likely diagnosis?
Q3: What examination would you perform?
Q4: What would be the initial management?
Q5: What investigations would you request to confirm a diagnosis?
Q6: What other issues should be addressed?

CASE 8.4 – **A 67-year-old woman with pale stools and weight loss.**

A 67-year-old woman presents with diarrhoea. She describes her stools as pale. You discover that she has lost weight and has nocturia and thirst.

CASE 8.5 – **A 26-year-old woman with abdominal pain and vomiting.**

A 26-year-old woman presents with upper abdominal pain and vomiting. Previously she has experienced episodes of right upper quadrant colicky pain that had lasted several hours at a time. On one of these occasions she experienced a brief episode of jaundice accompanied by dark urine. The present episode is different, however. The pain has lasted for 2 days and appears to be worsening and, this time, it is non-colicky.

CASE 8.6 – **A 48-year-old man with alcohol problems with chronic abdominal pain.**

A 48-year-old man with alcohol problems presents with upper abdominal pain with some radiation to the back.

OSCE counselling cases

OSCE COUNSELLING CASE 8.3 – **'Why have I got pancreatitis?'**

A 26-year-old woman with pancreatitis secondary to gallstones asks 'Why have I got pancreatitis?'.

OSCE COUNSELLING CASE 8.4 – **'Why should I stop drinking?'**

A 46-year-old man with alcohol problems presents with chronic relapsing pancreatitis and asks 'Why should I stop drinking?'.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

- Acute pancreatitis is a significant cause of mortality. It should be considered in the differential diagnosis of all cases of acute abdominal pain.
- The diagnosis can generally be confirmed by an elevated serum amylase.
- Risk factors for acute pancreatitis include alcohol abuse and gallstones.
- Chronic pancreatitis, in general, has an insidious onset.
- Presenting features arise from exocrine failure, later with endocrine failure, accompanied by epigastric pain that usually radiates to the back.
- Diagnosis is reached by assessment of exocrine function or imaging.

Answers

Clinical cases

CASE 8.4 – **A 67-year-old woman with pale stools and weight loss.**

A1: What specific questions would you ask the patient?

The pale stool should prompt questions about malabsorption and obstructive jaundice. After asking about jaundice, itching and dark urine – which should all be absent – direct questions to the patient's stool. Look for fluffy, offensive, floating stools. Blood and mucus will be absent. The duration of the symptoms should be noted along with exacerbating and relieving factors. Abdominal pain should be sought, in particular epigastric pain. Such pain is unusual in coeliac disease (although bloating is curiously common) but common in patients with chronic pancreatitis. With regard to the nocturia, the volume should be assessed (small amounts suggest a urinary tract infection [UTI]; larger amounts suggest a diuresis – osmotic or drug-induced). Large-volume nocturia accompanied by thirst suggests diabetes or hypercalcaemia.

A2: What is the most likely diagnosis?

The most likely diagnosis is chronic pancreatitis. The patient exhibits both exocrine and endocrine failure. Pain is absent in 50 per cent of older patients with chronic pancreatitis.

A3: What examination would you perform?

A full physical examination is necessary, with particular attention being paid to the state of nutrition and the cause of the pancreatic failure. Alcoholism and haemochromatosis are associated with signs of liver disease and pigmentation, respectively. Most patients with alcohol problems, however, have either liver or pancreatic damage. Alcoholism and haemochromatosis are both associated with atrial fibrillation (AF) and cardiomyopathy. A per rectal examination should confirm the colour of the stool.

A4: What would be the initial management?

The first step in the management is to corroborate the clinical diagnosis. Blood samples should be taken for calcium, glucose and urea. This will rapidly explain the source of the nocturia. Diabetes should be managed appropriately (see Chapter 1). Early dietetic input should be obtained.

A5: What investigations would you request to confirm a diagnosis?

The pancreas should be imaged and its exocrine function assessed. Imaging modalities to consider include abdominal radiograph (to show calcification – present in 30 per cent of cases), ultrasonography and computed tomography (CT). The latter two have similar specificities (85–90 per cent), but CT is more sensitive than ultrasonography (75 per cent *v.* 65 per cent). Exocrine function is currently best tested by the pancreolauryl test, which is non-invasive, cheap and easy to perform. Faecal fats are no longer routinely available.

A6: What other issues should be addressed?

After confirming the diagnosis, the diet should be modified – fats can be eaten and should not be avoided because the patient will continue to lose weight. Adequate pancreatic replacement therapy should be prescribed, along with acid-suppressing drugs. Pancreatic enzymes are usually buffered by

bicarbonate secretion; however, in chronic pancreatitis, there may be too little bicarbonate and so acid suppression is essential.

CASE 8.5 – **A 26-year-old woman with abdominal pain and vomiting.**

A1: What specific questions would you ask the patient?

Earlier episodes of right upper quadrant pain suggest biliary colic. The episode accompanied by jaundice and dark urine suggests that a stone may have obstructed the common bile duct. The present problem suggests acute gallstone pancreatitis. As with any abdominal pain, the site, radiation, and exacerbating and relieving factors should be sought. Acute pancreatitis should always be considered in patients with acute abdominal pain.

A2: What is the most likely diagnosis?

The most likely diagnosis is acute pancreatitis. The differential diagnosis for its aetiology is gallstone pancreatitis, hereditary hypertriglyceridaemia and drug-induced pancreatitis. The differential diagnosis of the pain is cholecystitis, peptic ulcer disease (perforation) and Crohn's disease.

A3: What examination would you perform?

A full physical examination is necessary with particular attention being paid to the abdomen. Signs range from epigastric tenderness to a full-blown acute abdomen with distension and rigidity. The Grey–Turner and Cullen signs should be sought. An epigastric mass (pseudo-cyst) may be present. Shock may also be present.

A4: What would be the initial management?

The first step in the management is to confirm the clinical diagnosis. Blood samples should be taken for amylase, calcium, glucose and blood gases. Amylase is elevated threefold in most cases of acute pancreatitis; occasionally, however, very shocked patients have a normal amylase. Acidosis, hyperglycaemia and hypocalcaemia are all poor prognostic indicators. The patient should receive analgesia (pethidine), an antiemetic, resuscitation with oxygen and IV fluids. Hyperglycaemia should be corrected with an insulin infusion. Early senior review of patients who are shocked or have other poor prognostic indicators is imperative.

A5: What investigations would you request to confirm a diagnosis?

The pancreas should be imaged. Imaging modalities to consider include abdominal radiograph (to exclude a perforated viscus and possibly to show a sentinel loop). Ultrasonography and CT are preferable. Ultrasonography is useful because it can show gallstones and pancreatic necrosis; bowel gas may obscure the view, however. Computed tomography is more accurate than ultrasonography for grading the pancreatic damage (90 per cent *v.* 73 per cent). Endoscopic retrograde cholangiopancreatography (ERCP) has a role to play, primarily in treating the underlying pathology; magnetic resonance cholangiopancreatography (MRCP) is preferred for diagnosis, however, as ERCP can cause pancreatitis. Without intervention, 30– 50 per cent of patients with gallstone pancreatitis have further episodes.

A6: What other issues should be addressed?

After confirming the diagnosis, the patient should undergo supportive therapy. An underlying cause should be sought. Endoscopic retrograde cholangiopancreatography is recommended.

CASE 8.6 – **A 48-year-old man with alcohol problems with chronic abdominal pain.**

A1: What specific questions would you ask the patient?

Epigastric pain may arise from pathology in three main sites: stomach/duodenum, gallbladder and pancreas. An accurate description of the pain may help to differentiate biliary colic from pancreatic and gastroduodenal pain, as the latter two are not colicky. Pancreatic pain tends to last for days or weeks rather than hours, as in the case of peptic ulceration. The relationship to food, lack of relief with antacids, and so on should be sought.

A2: What is the most likely diagnosis?

The most likely diagnosis is alcoholic chronic pancreatitis. Pain often precedes exocrine failure in people with alcohol problems.

A3: What examination would you perform?

A full physical examination is necessary, with particular attention being paid to the abdomen and the nutritional status.

A4: What would be the initial management?

The first step is to confirm the clinical diagnosis. This can be problematic in the absence of exo- and endocrine failure. The diagnosis is largely clinical, supported by anatomical changes when the pancreas is imaged and in the absence of other pathology such as duodenal ulcer disease.

A5: What investigations would you request to confirm the diagnosis?

The pancreas should be imaged. Imaging modalities to consider include abdominal radiograph (to show calcification – present in 30 per cent of cases), ultrasonography and CT. Ultrasonography and CT have similar specificities (85–90 per cent), although CT is more sensitive than ultrasonography (75 per cent *v.* 65 per cent). Exocrine failure is not clinically apparent until 90 per cent of the exocrine function has been lost. Faecal elastase may be measured to assess exocrine failure; the enzyme levels are lowered in patients with pancreatic insufficiency. Pancreolauryl test and faecal fats measurement are no longer routinely available.

A6: What other issues should be addressed?

After confirming the diagnosis, the patient should receive pain relief in line with the World Health Organization's (WHO's) 'pain ladder'. Most patients require opiates, and these should not be withheld because of concerns about their long-term use. Fifty per cent of patients respond to a nerve block. Surgery is seldom indicated.

OSCE counselling cases

OSCE COUNSELLING CASE 8.3 – **'Why have I got pancreatitis?'**

An appropriate answer is: 'Unfortunately, your pancreas has become inflamed; this is called pancreatitis. The pancreas is an organ that lies beside the gallbladder. Stones have grown in your gallbladder. One (or some) of these stones has passed into the tube that links the gallbladder to the intestine. In this site, the same tube joins to the pancreas. As a result of the stone lying in these tubes, the pancreas has become inflamed. Pancreatitis may also be caused by alcohol and drugs; there is no suggestion that this is the case for you.'

This is an important test of communication skills. The key is to explain the anatomy of the biliary tree and how the gallstones lead to pancreatitis. It is important to explain that pancreatitis is a result of gallstones. As it can be a result of alcohol abuse, the patient should be reassured that you understand that her pancreatitis is not so caused. The explanation of diseases that may or may not be confused with those that are associated with social stigma requires particular skill and tact. Be prepared to discuss the management of any condition, the nature of which you have been asked to explain.

OSCE COUNSELLING CASE 8.4 – **'Why should I stop drinking?'**

An appropriate answer is: 'Your drinking has led to a serious disorder of your pancreas. This disorder may cause severe abdominal pain and failure to digest your food (resulting in weight loss); if severe, you may need surgery. In some patients it can be fatal. As alcohol is the cause, it is important that you stop drinking to reduce the risk of further severe attacks. If you continue to drink, the problem is likely to get worse. If you stop drinking, the disease may not progress.'

In answering this question, it is crucial to be honest and understanding. Patients may continue to have pain even if they do stop drinking. There is no place for blaming the patient if the pain continues. Supportive measures should be offered. Additional means of controlling the pain are likely to be called for, including long-term analgesics, nerve blocks and even surgery.

INFLAMMATORY BOWEL DISEASE

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What specific questions would you ask the patient?
Q2: What is the most likely diagnosis?
Q3: What examination would you perform?
Q4: What would be the initial management?
Q5: What investigations would you request to confirm a diagnosis?
Q6: What other issues should be addressed?

CASE 8.7 – **A 20-year-old woman with ulcerative colitis.**

A 20-year-old woman with ulcerative colitis has had symptoms for several weeks, so she presents to the accident and emergency (A&E) department.

CASE 8.8 – **An 18-year-old man with colicky central abdominal pain and vomiting after meals.**

An 18-year-old male smoker presents with colicky central abdominal pain and vomiting 30–60 min after meals. He has been told that he may have IBD, but his mother is concerned because he has lost weight.

CASE 8.9 – **A 21-year-old man with diarrhoea and a perianal abscess.**

A 21-year-old man has noted episodes of colicky lower abdominal pain over several months. It has been suggested that he may have IBD.

OSCE counselling cases

OSCE COUNSELLING CASE 8.5 – **'Will I get cancer?'**

A 36-year-old man with established ulcerative colitis has heard that there is a risk of bowel cancer in patients with the condition.

OSCE COUNSELLING CASE 8.6 – **'Will I need to have the bag?'**

A 20-year-old woman with refractory ulcerative colitis is concerned that surgery is imminent.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Patients with IBD often present with symptoms that have been present for several weeks or months. Many will have been told that they have irritable bowel syndrome (IBS). A history and examination will often point to the correct diagnosis by the time the patient presents.

Patients should be counselled about the need for potentially embarrassing invasive investigations and the probable long-term nature of IBD. They should be encouraged to seek help from reputable sources such as Crohn's and Colitis UK (CCUK), formerly the National Association for Colitis and Crohn's Disease (NACC).

Answers

Clinical cases

CASE 8.7 – **A 20-year-old woman with ulcerative colitis.**

A1: What specific questions would you ask the patient?

The severity of the attack should be assessed. Specifically, the frequency and consistency of the stool should be assessed. The presence of blood should be sought. The presence, periodicity and site of abdominal pain, and any weight loss, should be assessed.

A2: What is the most likely diagnosis?

The most likely diagnosis is acute severe ulcerative colitis. The assessment of severity is based upon clinical observation. The differential diagnosis is infectious diarrhoea and hypersensitivity to her treatment.

A3: What examination would you perform?

A full physical examination is necessary, with particular attention being paid to the signs of disease severity (fever, anaemia, tachycardia) and to abdominal signs. Fever, anaemia and tachycardia define severe disease.

A4: What would be the initial management?

The first step is to corroborate the clinical diagnosis. Blood samples should be taken for FBC, C-reactive protein (CRP) and albumin. A plain abdominal radiograph should be performed to assess colonic diameter and to look for mucosal islands. Stool cultures should be performed. The patient should be admitted and commenced on IV hydrocortisone 100 mg four times a day and subcutaneous heparin 5000 U three times a day. A stool chart should be commenced, recording the frequency and amount of stool and the presence of blood. The patient's weight should be recorded.

A5: What investigations would you request to confirm a diagnosis?

Senior review should be sought, with a view to considering a cautious limited sigmoidoscopy. Sigmoidoscopy is potentially dangerous.

A6: What other issues should be addressed?

If after 3–5 days the CRP and stool frequency have not improved, a surgical opinion should be sought, with a view to colectomy on day 7. An alternative approach is to initiate rescue therapy on days 3–5 with IV ciclosporin or, in some situations, infliximab. Some centres recommend abdominal radiograph on alternate days. A deterioration in the abdominal radiograph or physical signs should prompt earlier surgical review.

CASE 8.8 – **An 18-year-old man with colicky central abdominal pain and vomiting after meals.**

A1: What specific questions would you ask the patient?

The pain should be assessed, looking for site, radiation, exacerbating and relieving factors, and special precipitating factors, particularly foods. The frequency of the vomiting and its relationship to the pain

and meals should be clarified. The amount of weight lost and the duration of this symptom should be documented. A family and travel history should be taken. Medication should be recorded.

A2: What is the most likely diagnosis?

The symptoms suggest subacute obstruction. The differential diagnoses include adhesions, Crohn's disease and intussusception.

A3: What examination would you perform?

A full physical examination is necessary, with particular attention being paid to the nutritional state, signs of inflammatory disease (fever, anaemia, tachycardia) and abdominal signs, specifically looking for a mass.

A4: What would be the initial management?

The patient may warrant admission if he is malnourished, dehydrated or in pain, but subacute obstruction is often investigated in the outpatient setting. If the patient is admitted he will need analgesia, IV fluid replacement (2–3 L/day) and a nasogastric tube (to decompress the upper GI tract). Initial investigation of the admitted patient should include abdominal radiograph (for obstruction), U&Es, LFTs and FBC with CRP and plasma viscosity. If he is not admitted, he should be investigated as in A5 below.

A5: What investigations would you request to confirm a diagnosis?

After resuscitation or in the outpatient setting, urgent barium follow-through (or small bowel enema) should be performed. Computed tomography or ultrasonography may be indicated if there is a mass. Computed tomography will show the 'pseudo-kidney sign' if intussusception is present. In general, magnetic resonance imaging (MRI) should not be used in this setting, as there is inadequate experience in interpreting this test.

A6: What other issues should be addressed?

Subacute obstruction may be managed conservatively while the diagnosis is reached. Most cases come to surgery in the long term.

CASE 8.9 – **A 21-year-old man with diarrhoea and a perianal abscess.**

A1: What specific questions would you ask the patient?

The diarrhoea should be assessed with regard to frequency, duration, the presence of blood and mucus, and its relationship to the abdominal pain. Constitutional symptoms (fever, weight loss) should be sought. With regard to the patient's abscess, the duration of symptoms and the site and radiation of the pain should be determined. Previous episodes and their treatment should be recorded. Lifestyle, travel and a family history should be noted.

A2: What is the most likely diagnosis?

The most likely diagnosis is Crohn's disease. Diarrhoea is not always accompanied by blood in patients with Crohn's disease. Perianal abscess may accompany ulcerative colitis.

A3: What examination would you perform?

A full physical examination is necessary, with particular attention being paid to the abdomen, nutritional status, evidence of systemic illness (fever, tachycardia, anaemia) and the perineum. Per

rectal examination is not indicated because the abscess encroaches on the anus. An examination under anaesthetic is preferred.

A4: What would be the initial management?

The first steps in the management are to relieve suffering and confirm the clinical diagnosis. Pain should be relieved by analgesia while a prompt surgical opinion is sought. Investigations to support the diagnosis should be performed with FBC, LFTs, CRP and plasma viscosity as a prelude to a surgical review.

A5: What investigations would you request to confirm a diagnosis?

Generally, an examination under anaesthetic is the preferred approach to such patients. During this procedure, the abscess may be drained, a sigmoidoscopy and rectal biopsy performed, and probing performed for a fistula. A stent may be placed if the fistula is found.

A6: What other issues should be addressed?

After managing the abscess, the diagnosis of Crohn's disease should be confirmed. Imaging options include MRI and CT; MRI is the investigation of choice for imaging the soft tissues around the rectum and demonstrating fistulas, which usually underlie abscesses in Crohn's disease. Crohn's disease should be managed by draining the abscess, seeking out and treating other foci of infection, and treating the disease itself.

OSCE counselling cases

OSCE COUNSELLING CASE 8.5 – **'Will I get cancer?'**

An appropriate answer is: 'There is an increased risk of bowel cancer in some patients with ulcerative colitis. This risk does not apply to all patients. Young patients with extensive disease that has a grumbling course seem to be at greatest risk. The medication that is given for the treatment of colitis (mesalazine) appears to lower the risk of bowel cancer. We will assess your risk by plotting your disease extent. If the risk appears to be increased, we will discuss measures that may enable us to detect it at an early stage. We will check your bowel by performing a colonoscopy from time to time – perhaps as rarely as once every 5 years. Although the risk to patients with ulcerative colitis of getting bowel cancer is greater than that of people without colitis, the risk to an individual patient remains relatively small.'

It is important to be honest but to offer reassurance at the same time. Relative risk and absolute risk may be difficult concepts to explain to patients. It is worth planning your answer to such common questions.

OSCE COUNSELLING CASE 8.6 – **'Will I need to have the bag?'**

An appropriate answer is: 'Yes, at least in the short term'. Patients with refractory disease are often taking steroids at the time of surgery, and so the surgery is kept as simple as possible. The operation of choice is to remove as much diseased bowel as possible without operating deep in the pelvis (subtotal colectomy, oversewing the rectum). A stoma will be necessary. Most patients feel better very quickly, and many soon adapt to the stoma. These patients will later need a second operation to remove the rectum (proctectomy). Other patients may prefer an ileoanal pouch. The pouch brings about improved body image but is associated with the need to pass stool frequently (typically four to six times a day). Of patients, 15–20 per cent lose their bowel (undergo colectomy) in the long term. It is important to differentiate the emergency situation, in which the priority is to keep the patient alive and healthy, from the elective situation, where the aim is to restore quality of life. Ileoanal pouches are not a panacea. The quality of life of a patient with a pouch is only as good as that in a patient with mild ulcerative colitis. The stool of a patient with a pouch is likely to be loose and passed frequently. Pouchitis with bloody looser stools occurs in 5–20 per cent of patients; it can often be managed medically but may result in a reversal of the pouch and recreation of the stoma.

PEPTIC ULCER DISEASE

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What in the given history supports the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 8.10 – **A 70-year-old man with indigestion.**

A 70-year-old man with arthritis and ischaemic heart disease presents with indigestion. He has epigastric pain radiating to his back. He has been taking aspirin for his heart and ibuprofen for his arthritis.

CASE 8.11 – **A 35-year-old woman with indigestion and a feeling of discomfort after eating meals.**

A 35-year-old woman presents with a feeling of discomfort after eating meals. She describes a fullness after eating a modest amount and can no longer finish the meal that she used to eat. The indigestion is also troublesome.

CASE 8.12 – **A 60-year-old man losing weight and vomiting.**

A 60-year-old man is brought to see you accompanied by his wife. Together they describe that he has had progressively worsening vomiting for some months. He has lost a stone in weight. He finds that the vomiting is worse after a full meal, but liquids trouble him less than solid food. In the past he has suffered from indigestion and has taken over-the-counter remedies for this.

OSCE counselling cases

OSCE COUNSELLING CASE 8.7 – **'Can I take aspirin for my heart now that I have an ulcer?'**

OSCE COUNSELLING CASE 8.8 – **'The tablets for my ulcer were wonderful. Should I continue to take them?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Helicobacter pylori is found in more than 90 per cent of patients with duodenal ulcers and 70 per cent of patients with gastric ulcers. Non-steroidal anti-inflammatory drugs contribute to the aetiology of peptic ulcer disease. Smoking and alcohol are minor contributory factors.

The gold standard diagnosis is the demonstration of an ulcer by endoscopy or barium meal. Endoscopy is preferable because gastric ulcers can be biopsied, to look for malignancy, and *H. pylori* can be sought in the stomach of patients with peptic ulcers, whether gastric or duodenal.

As most ulcers are related to *H. pylori*, eradication of *H. pylori* should be prescribed. This consists of a PPI and two antibiotics from metronidazole, amoxicillin and clarithromycin.

Answers

Clinical cases

CASE 8.10 – **A 70-year-old man with indigestion.**

A1: What is the likely differential diagnosis?

The differential diagnoses are peptic ulcer disease, carcinoma of the stomach and carcinoma of the pancreas.

A2: What in the given history supports the diagnosis?

Indigestion-like symptoms are usually a result of gastroduodenal disease. The diseases include mucosal inflammation (gastritis, duodenitis) and ulceration. Most duodenal ulcer disease is associated with *H. pylori*; NSAIDs, including aspirin and ibuprofen, enhance the risk of ulcer disease occurring in patients without *H. pylori* infection. This man is of an age where ulcer-complicating *H. pylori* is quite common. His consumption of NSAIDs increases his risk.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important to ask the patient about weight loss, because this may indicate that the patient has a carcinoma. His NSAID medication should be reviewed. Evidence from his history of earlier ulcer symptoms before the current episode should be sought.

A4: What clinical examination would you perform, and why?

A full physical examination should be performed, with particular attention being paid to lymphadenopathy in the neck, which may indicate metastatic disease from carcinoma of the stomach. The epigastrium should be examined with particular care for a mass. The liver edge should be identified. An irregular edge may indicate a carcinoma.

A5: What investigations would be most helpful, and why?

An endoscopy (oesophagogastroduodenoscopy) should be performed to look for peptic ulcer disease and to rule out carcinoma of the stomach. Histology should be obtained for *H. pylori*.

A6: What treatment options are appropriate?

If the patient has *H. pylori*, triple therapy should be prescribed, followed by a long-term PPI to protect him against future non-NSAID-associated risks. If he is *H. pylori*-negative, a PPI should be used alone. If the patient is found to have carcinoma of the stomach, it should be staged and surgery considered. Patients with a gastric ulcer should undergo repeat endoscopy after 6 weeks to ensure healing and to facilitate repeat biopsy to obtain further histological samples.

CASE 8.11 – **A 35-year-old woman with indigestion and a feeling of discomfort after eating meals.**

A1: What is the likely differential diagnosis?

The differential diagnoses are non-ulcer dyspepsia and peptic ulcer disease. Gastric cancer is very unlikely in a patient of this age. The role of *H. pylori* in the absence of ulceration in such patients is not clear.

Early satiety (feeling full before completing a meal) is associated with non-ulcer dyspepsia, but it may also occur in patients with gastric outlet obstruction and carcinoma of the stomach. The patient's age make these considerations unlikely.

A2: What in the given history supports the diagnosis?

Non-ulcer dyspepsia is a functional disorder often exacerbated by stress. Stressors should be investigated. The early satiety means that non-ulcer dyspepsia is the most likely explanation, although if vomiting is present, carcinoma of the stomach or other sinister pathology should be considered.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important, in the history, to look for the patient's ethnic background and family history, either of which may increase the risk of peptic ulcer disease. Exposure to NSAIDs should be sought in the history – these may be over-the-counter remedies. Consumption of alcohol and cigarettes should be investigated, although these are small contributory factors to peptic ulcer disease compared with *H. pylori*.

A4: What clinical examination would you perform, and why?

A full examination should be performed, with consideration given to lymphadenopathy and epigastric mass. Such features are not expected in patients with non-ulcer dyspepsia.

A5: What investigations would be most helpful, and why?

It is useful to look for *H. pylori* in young patients with dyspepsia. There are several ways in which this can be conducted: *H. pylori* can be identified by a urease breath test, necessitating a trip to the local hospital; *H. pylori* infection can also be sought using serology – most general practitioners (GPs) can perform this test and send the sample to a reference laboratory; or endoscopy may be used, although in a patient of this age, it is not usually indicated.

A6: What treatment options are appropriate?

Triple therapy may be prescribed for the patient if she is *H. pylori*-positive: a PPI with two antibiotics from metronidazole, amoxicillin and clarithromycin (typically one is metronidazole). It is important to stop PPI therapy after *H. pylori* has been eradicated. Domperidone may also be prescribed to aid gastric emptying by increasing its motility.

CASE 8.12 – **A 60-year-old man losing weight and vomiting.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are pyloric stenosis secondary to *H. pylori*-associated peptic ulcer disease, carcinoma of the stomach, rare duodenal tumours, polyps, Crohn's disease and dysmotility syndrome.

A2: What in the given history supports the diagnosis?

The clue to the diagnosis in this patient is previous use of over-the-counter remedies for indigestion, mainly in a patient with undertreated peptic ulcer. The vomiting suggests gastric outlet obstruction.

A3: What additional features in the history would you seek to support a particular diagnosis?

Pyloric stenosis and carcinoma of the stomach may present in a similar manner. Duodenal Crohn's disease, polyps, and so on usually have a longer history. Dysmotility syndrome is unusual, except in patients with diabetes.

A4: What clinical examination would you perform, and why?

On examination anaemia, lymphadenopathy, epigastric mass and irregular liver edge should be sought.

A5: What investigations would be most helpful, and why?

Investigation is mandatory. Endoscopy or barium meal should be performed urgently. Computed tomography of the upper abdomen should be considered. If these investigations are negative, gastric emptying studies should be performed.

A6: What treatment options are appropriate?

If the patient is found to have benign peptic stricture, endoscopic balloon dilation should be considered. Surgery is called for if balloon dilation fails. If the patient has carcinoma, staging should be performed and surgery considered. If the patient has duodenal obstruction, a gastroenterostomy should be performed. If the patient has dysmotility syndrome, domperidone or erythromycin should be prescribed.

OSCE counselling cases

OSCE COUNSELLING CASE 8.7 – **'Can I take aspirin for my heart now that I have an ulcer?'**

In a patient who has a good indication for non-steroidal therapy such as coronary disease, transient ischaemic attack (TIA) or inflammatory arthritis, aspirin or non-steroidal therapy should be resumed after the ulcer has been treated appropriately, typically with triple therapy. A PPI should be co-prescribed with the non-steroidal drugs. Consider alternative use of clopidogrel, which may be safer.

OSCE COUNSELLING CASE 8.8 – **'The tablets for my ulcer were wonderful. Should I continue to take them?'**

The short answer to this patient is 'no'. He should be told that the *H. pylori* infection caused the ulcer. Eradicating infection will mean that the ulcer is unlikely to return. It is important to discontinue PPI therapy because of the problems of atrophic gastritis, achlorhydria and bacterial overgrowth.

CIRRHOSIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What in the given history supports the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 8.13 – **A retired publican says he has 'turned yellow' and his 'stomach is swollen'.**

A retired publican presents with progressive jaundice and abdominal swelling. He drinks more than 40 units of alcohol per week. Previously he has been admitted with fever and vomiting, which he was told was caused by alcohol.

CASE 8.14 – **The same patient has become confused.**

After several days in hospital, the patient with jaundice and ascites becomes confused, disoriented and aggressive.

CASE 8.15 – **The same patient is vomiting blood.**

A couple of days after showing evidence of encephalopathy, the patient with chronic liver disease has haematemesis.

OSCE counselling cases

OSCE COUNSELLING CASE 8.9 – **'Should my husband have a transplant?'**

OSCE COUNSELLING CASE 8.10 – **'Why is my husband confused?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Decompensated liver disease is recognized from the following:

- *history* – jaundice, abdominal swelling, drowsiness, GI bleeding
- *examination* – jaundice, fetor, flapping tremor, ascites, oedema, impaired consciousness
- *laboratory investigations* – poor synthetic function – falling albumin and prolonging clotting times.

Bleeding varices are managed first by resuscitating with IV fluids (preferably blood products) and oxygen. Endoscopy is done with a view to injection sclerotherapy or band ligation. Finally, a Sengstaken tube may be placed or IV glypressin given.

Ascites caused by decompensated liver disease is managed first by analysing the ascitic fluid for spontaneous bacterial peritonitis. If the white cell count is >250/mL, spontaneous bacterial peritonitis is likely and should be treated with cephalosporins or ciprofloxacin. Therapy should be initiated:

- water restriction to <1.5 L/day or even <1 L/day with salt restriction
- spironolactone should be started at 50 mg, with a slow increase in dose
- therapeutic paracentesis should be considered with IV replacement – 100 mL 20% human albumin solution per 2–2.5 L ascites drained.

Answers

Clinical cases

CASE 8.13 – **A retired publican says he has 'turned yellow' and his 'stomach is swollen'.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are decompensated cirrhosis secondary to alcohol consumption or other causes of chronic liver disease, and carcinoma of the pancreas (or similar upper GI cancer with liver metastases) and peritoneal spread.

A2: What in the given history supports the diagnosis?

This man has a high-risk profession for alcoholic liver disease. His previous admission suggests that he may have had alcoholic hepatitis. He is still drinking. The abdominal swelling is likely to be the result of ascites. Together, the jaundice and ascites indicate that he has decompensated cirrhosis.

A3: What additional features in the history would you seek to support a particular diagnosis?

In the history it should be established whether he has been told that he has cirrhosis. Look for weight gain to support the diagnosis of ascites (weight loss may indicate a malignant process). Swelling of the ankles is common in cirrhosis at this stage. A history should be sought of previous ulcer disease, which may indicate gastric cancer. Previous bowel surgery may indicate a malignant process.

A4: What clinical examination would you perform, and why?

The signs of decompensated alcoholic liver disease should be sought, including Dupuytren's contracture, palmar erythema, spider naevi, gynaecomastia, hepatosplenomegaly and ascites.

A5: What investigations would be most helpful, and why?

Ultrasonography of the abdomen with liver biopsy should be performed at an early stage. Paracentesis should be carried out to look for a malignant process causing the ascites. The liver investigations should include hepatitis serology, autoimmune profile, serum ferritin, alpha-fetoprotein, anti-trypsin and caeruloplasmin.

A6: What treatment options are appropriate?

The ascites should be treated with fluid restriction and spironolactone. If these measures do not work, paracentesis with terlipressin and albumin (human albumin solution) cover should be instituted.

CASE 8.14 – **The same patient has become confused.**

A1: What is the likely differential diagnosis?

The likely diagnosis is encephalopathy secondary to decompensation, sepsis, electrolyte disturbance or GI bleeding.

A2: What in the given history supports the diagnosis?

Patients admitted with decompensated liver disease are at high risk of encephalopathy. The instrumentation for paracentesis may increase the risk of bacterial peritonitis. Venous access and urethral catheterization will increase the risk of sepsis in those sites. Treatment of ascites may precipitate encephalopathy as a result of electrolyte disturbance.

A3: What additional features in the history would you seek to support a particular diagnosis?

From the patient's wife and the nurses, clues should be sought for the portal of entry of infection. The nurses should be asked whether the patient has had haematemesis or melaena. Charts should be checked for undue diuresis.

A4: What clinical examination would you perform, and why?

A full physical examination with a view to finding a focus of infection should be carried out. This must include the chest and Venflon sites and careful abdominal palpation. Rectal examination may be necessary to rule out melaena.

A5: What investigations would be most helpful, and why?

A full septic screen should be performed, with paracentesis, blood cultures, chest radiograph and urine cultures. Electrolytes should be assessed. Haemoglobin may be measured to look for evidence of sepsis (raised white cell count) and anaemia (indicating GI bleed).

A6: What treatment options are appropriate?

The most likely explanation for the deterioration is sepsis. Cephalosporins or ciprofloxacin should be commenced. Consideration should be given to staphylococcal infection, which will require gentamicin or flucloxacillin. If methicillin-resistant *Staphylococcus aureus* (MRSA) is present, vancomycin may be used. Lactulose should be started immediately. Neomycin, or more probably metronidazole, should be used to suppress bacterial growth within the bowel. Electrolyte disturbance and hypoglycaemia should be corrected.

CASE 8.15 – **The same patient is vomiting blood.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are bleeding oesophageal varices and bleeding peptic ulcer disease.

A2: What in the given history supports the diagnosis?

Patients with decompensated liver disease are at high risk of variceal bleeding, having demonstrated evidence of portal hypertension (through the ascites). Encephalopathy may have been precipitated by a GI bleed. Fifty per cent of patients with GI bleed on the background of cirrhosis actually bleed from non-variceal sources.

A3: What additional features in the history would you seek to support a particular diagnosis?

No further features could be obtained in the history of this patient.

A4: What clinical examination would you perform, and why?

Evidence of GI bleeding should be assessed, including observation of melaena and assessment of blood pressure and pulse, and sweating and anaemia should be sought.

A5: What investigations would be most helpful, and why?

Urgent endoscopy should be performed, with a view to finding and treating the varices. Full blood count is likely to show anaemia. Clotting tests (international normalized ratio, [INR]) and a cross-match should be undertaken.

A6: What treatment options are appropriate?

At endoscopy, banding or sclerotherapy should be used to stop variceal bleeding. Patients with peptic ulcer haemorrhage should receive the preferred treatment in the unit. In most hospitals this is adrenaline (epinephrine) injection; it is good practice to add a second measure such as applying a clip to the bleeding point or a heater probe. Resuscitation with blood or clotting factors is mandatory. The treatment for encephalopathy should be continued and possibly increased.

OSCE counselling cases

OSCE COUNSELLING CASE 8.9 – **'Should my husband have a transplant?'**

Liver transplantation is not indicated in patients who are still drinking alcohol. The consensus of opinion is that patients should be abstinent from alcohol for 6 months before surgery. In the 6 months between stopping drinking and surgery, full liver support and psychological assessment should be offered.

OSCE COUNSELLING CASE 8.10 – **'Why is my husband confused?'**

Patients with liver disease become confused when the liver does not work properly. In this situation, the risk of infection is increased and chemical upsets now occur as part of the treatment. In addition, patients with this problem can bleed internally. All of these factors lead to a disturbance of brain chemical function; in most patients, however, this can be put right.

CONSTIPATION

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What in the given history supports the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 8.16 – **A 50-year-old man with squamous carcinoma of the bronchus and bony metastases cannot open his bowels.**

A 50-year-old man with squamous carcinoma of the bronchus and bony metastases is referred complaining of abdominal distension. He has not opened his bowels for 8 days. His abdominal pain has worsened and he has increased his morphine sulphate tablets, which previously he took only for bone pain.

CASE 8.17 – **A teenage girl who feels she does not empty her bowel.**

A teenage girl presents with abdominal discomfort and a story of passing pellet-like stools. She experiences abdominal bloating before defaecation and after defaecation feels that she has not adequately emptied her bowels.

CASE 8.18 – **A 78-year-old man with faecal incontinence.**

A 78-year-old man with Parkinson's disease is admitted from a nursing home with faecal incontinence. Previously he had been noted to have stubborn bowels. Both he and the nurses were surprised when he began staining his clothing.

OSCE counselling cases

OSCE COUNSELLING CASE 8.11 – **'What can be done to stop my husband who needs to take painkillers becoming constipated again?'**

OSCE COUNSELLING CASE 8.12 – **'Why can't my daughter simply take senna when she has constipation?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Constipation is a consequence of slow or interrupted transit through the intestine, in particular the large bowel. In most patients it is a result of either drugs (anticholinergic side effects or opiates) or diet. Occasionally bowel motility is impaired by hormonal or colonic neuromuscular disorders.

A careful history should be obtained. Drugs causing constipation should be stopped or further drugs given to counter the side effects. Diet should be improved with the addition of fresh fruit and vegetables.

Answers

Clinical cases

CASE 8.16 – **A 50-year-old man with squamous carcinoma of the bronchus and bony metastases cannot open his bowels.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are opiate-induced constipation and hypercalcaemia-induced constipation secondary to squamous carcinoma or bony metastases.

A2: What in the given history supports the diagnosis?

Constipation is a symptom, not a disease. In this patient the risk factor for constipation is treatment with opiates. In addition, patients with bony metastases and squamous carcinoma are at risk of hypercalcaemia. This needs to be considered.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important to see whether the patient appears dehydrated or confused, which may suggest hypercalcaemia. In the history it should be determined whether the patient is taking laxatives while consuming morphine sulphate tablets.

A4: What clinical examination would you perform, and why?

Look for evidence of dehydration, which may accompany confusion, because this also indicates hypercalcaemia. This is an insidious problem and should be specifically looked for on examination. The abdomen should be palpated and a rectal examination performed.

A5: What investigations would be most helpful, and why?

The main investigations include biochemistry for hypercalcaemia and uraemia. Abdominal examination may be necessary to look for faecal loading if the patient has an empty rectum on physical examination.

A6: What treatment options are appropriate?

Most patients will respond to enemas and stimulant laxatives such as senna, accompanied by softeners such as docusate sodium. Co-danthramer is specifically indicated in patients with opiate-induced constipation in the terminal setting. A new preparation combining oxycodone and naloxone is useful as the patient will absorb the oxycodone while the naloxone will prevent the gastrointestinal side effects. If the patient has hypercalcaemia, fluids should be replaced intravenously and bisphosphonate treatment considered.

CASE 8.17 – **A teenage girl who feels she does not empty her bowel.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are poor dietary habit, constipation-predominant IBS and dysmotility. Myxoedema, hypercalcaemia and Hirschsprung's disease are rare causes.

A2: What in the given history supports the diagnosis?

This girl is a prime candidate for poor dietary intake. Girls of this age can have fickle diets. Breakfast is often avoided. The most likely explanation for her bowel disorder is poor dietary intake with an element of IBS.

A3: What additional features in the history would you seek to support a particular diagnosis?

A full dietary history should be taken, with particular attention being paid to fruit, fibre and breakfast consumption. A history of stress should be sought. A history of sexual abuse should also be sought, which is more prevalent in girls with IBS than other patients. If the patient has vomiting or a family history, an underlying motility disorder may be the problem.

A4: What clinical examination would you perform, and why?

On examination, look for evidence of hypothyroidism, demonstrated by dry skin and goitre, perhaps with a bradycardia. On examination of the abdomen, faecal loading should be sought. Rectal examination should be considered only after a history of sexual abuse has been sought.

A5: What investigations would be most helpful, and why?

Thyroid-stimulating hormone (TSH) and calcium may be measured, but in most patients this is unnecessary. Consider transit time studies and full-thickness rectal biopsy.

A6: What treatment options are appropriate?

Dietary advice should be given, with particular reference to fruit, fibre and breakfast consumption. It may be necessary to add linseed, kiwi or other dietary laxatives to her diet. Regular medication (laxatives) should not be prescribed.

Occasionally a barium enema can be therapeutic and provide reassurance.

CASE 8.18 – **A 78-year-old man with faecal incontinence.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are overflow diarrhoea (secondary to medication, immobility, depression or colonic dysmotility) and infection (e.g. norovirus, rotavirus, *C. difficile*).

A2: What in the given history supports the diagnosis?

Parkinson's disease causes immobility but can also cause smooth muscle dysfunction of the GI tract. Dysphagia and constipation are common. The most common cause of faecal incontinence in this kind of patient is overflow diarrhoea.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important to look for drugs that may contribute to constipation, including traditional anticholinergic medication for Parkinson's disease. The patient's immobility should be assessed. Patients who are bed- or chair-bound have a greater risk of constipation. Depression can also exacerbate immobility and is not uncommon in people with Parkinson's disease. A source of infectious diarrhoea should also be considered in a patient living in a nursing home.

A4: What clinical examination would you perform, and why?

Signs of Parkinson's disease should be sought, along with signs of faecal loading on abdominal and rectal examinations.

A5: What investigations would be most helpful, and why?

If the patient has a loaded colon on physical examination, no investigation is called for. If the patient has an empty rectum and no faecal loading on abdominal radiograph, an infection screen should be performed.

A6: What treatment options are appropriate?

An enema followed by oral laxative should be prescribed. Consideration should be given to stopping anticholinergic drugs and dealing with any depression.

OSCE counselling cases

OSCE COUNSELLING CASE 8.11 – 'What can be done to stop my husband who needs to take painkillers becoming constipated again?'

Stimulant laxatives should be prescribed in all patients receiving opiate medication. The frequency and strength of the laxative should match the strength of the opiate. A prescription with such laxatives should prevent further problems.

OSCE COUNSELLING CASE 8.12 – 'Why can't my daughter simply take senna when she has constipation?'

It is important to treat the cause rather than the effect of the constipation. Senna is a stimulant laxative that can lead to problems later in life if started in such young patients. It is better to have a healthy mixed diet to help with normal GI function than to use laxatives.

HEPATITIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What in the given history supports the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 8.19 – **An 18-year-old student returns from India with jaundice.**

An 18-year-old student has returned from a gap year spent in India with a short history of diarrhoea, abdominal discomfort and jaundice.

CASE 8.20 – **A 30-year-old man who previously misused drugs presents with mildly abnormal LFTs.**

A 30-year-old who previously misused drugs presents with feeling vaguely unwell. His GP has obtained LFTs, which are mildly abnormal with an alanine aminotransferase of 50 IU/L (normal <40 IU/L).

OSCE counselling cases

OSCE COUNSELLING CASE 8.13 – **'I have given up my drug habit, but I have hepatitis C. Do I need to be treated?'**

OSCE COUNSELLING CASE 8.14 – **'I have hepatitis A. Is there a risk I will pass it on?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Hepatitis B and C may both become chronic.

Treatment is determined by the grade and stage of liver disease (activity and fibrosis). In addition, the patient must have no ongoing lifestyle risk factors (e.g. using IV drugs) for reinfection or other forms of liver disease (e.g. due to alcohol use).

For hepatitis B, therapy with interferon alpha or lamivudine is recommended. For hepatitis C, combination therapy with pegylated interferon alpha and ribavirin is recommended.

Answers

Clinical cases

CASE 8.19 – **An 18-year-old student returns from India with jaundice.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are hepatitis A or B, amoebic abscess, Weil's disease, side effects of medication and autoimmune hepatitis.

A2: What in the given history supports the diagnosis?

The key to the diagnosis in this patient is the trip to India. Infectious (A) hepatitis is not uncommon in people returning from this part of the world. The pain and jaundice make a hepatobiliary problem most likely. The patient is too young to have gallstones unless she has a haemolytic disorder.

A3: What additional features in the history would you seek to support a particular diagnosis?

In the history, attention should be paid to dark urine and pale stools, which may suggest cholestatic jaundice. If the patient has abdominal pain, its site should be elicited. It is expected that hepatobiliary pain will be epigastric and right upper quadrant in site. A history of dysentery should be sought, as this may predispose the patient to amoebic liver abscess. The patient's use of drugs (medical and recreational) should be considered.

A4: What clinical examination would you perform, and why?

Full examination should be performed, including temperature, pulse, respiration and blood pressure. The degree of jaundice should be elicited. Anaemia should be sought. The size and texture of the liver should be found on examination. If the diaphragm appears to be raised on the right side, consideration should be given to amoebic abscess.

A5: What investigations would be most helpful, and why?

Hepatitis serology should be performed urgently (hepatitis A and B). Amoebic serology may be considered. Ultrasonography of the liver should be performed to look for an abscess. Autoimmune profile should be obtained. Liver function tests, FBC, INR and a malaria screen should also be obtained.

A6: What treatment options are appropriate?

The treatment of hepatitis A and B is supportive. Weil's disease is treated with penicillin-based antibiotics. Liver abscess requires drainage and treatment of the underlying infection. Autoimmune hepatitis should be treated with steroids.

CASE 8.20 – **A 30-year-old man who previously misused drugs presents with mildly abnormal LFTs.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are hepatitis C, non-alcoholic steatohepatitis (NASH) and hepatitis B.

A2: What in the given history supports the diagnosis?

The patient's lifestyle predisposes him to hepatitis B and C, particularly hepatitis C. Modest elevation of alanine aminotransferase is more suggestive of hepatitis C than anything else, but NASH can give a similar picture.

A3: What additional features in the history would you seek to support a particular diagnosis?

Previous jaundice should be sought in the history, which would suggest hepatitis B. If the patient is obese, NASH is a possibility. A history of alcohol consumption should be sought.

A4: What clinical examination would you perform, and why?

On examination, stigmata of chronic liver disease should be sought for patients with hepatitis. If there are no signs other than simple obesity, NASH is likely.

A5: What investigations would be most helpful, and why?

For hepatitis C, the investigations are serology (antibody to hepatitis C) and polymerase chain reaction for viral load, followed by liver biopsy, preferably guided by ultrasonography. Hepatitis B serology and liver biopsy are required. For NASH (patients negative for hepatitis B and C), an ultrasound-guided liver biopsy should be obtained.

A6: What treatment options are appropriate?

If the patient is no longer taking drugs and the liver biopsy shows viral hepatitis of sufficient stage and grade, antiviral therapy should be undertaken: interferon and either ribavirin or lamivudine for hepatitis B and C, respectively. If the patient has NASH, weight reduction should be encouraged. If the patient appears to be drinking more alcohol than was apparent initially, abstinence should be encouraged.

OSCE counselling cases

OSCE COUNSELLING CASE 8.13 – **'I have given up my drug habit, but I have hepatitis C. Do I need to be treated?'**

Treatment for hepatitis C is determined by the stage and grade of the disease (severity). This is determined by a liver biopsy. Any patients with active inflammation but no cirrhosis are candidates for antiviral therapy. Some patients require no therapy but need repeat biopsy instead.

OSCE COUNSELLING CASE 8.14 – **'I have hepatitis A. Is there a risk I will pass it on?'**

Hepatitis A is transmitted through poor hygiene. With good hand-washing, there is no chance of passing the virus. The virus appears only in faeces, and very good hygiene will prevent its transmission.

IRRITABLE BOWEL SYNDROME

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What in the given history supports the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 8.21 – **A 24-year-old housewife with abdominal bloating.**

A 24-year-old housewife complains of abdominal bloating, which gets progressively worse during the day.

CASE 8.22 – **After an elective period in India, a medical student returns to the UK with diarrhoea.**

The diarrhoea initially appeared to settle but has gradually worsened over the 2 months before coming to see you.

CASE 8.23 – **A 42-year-old social worker presents with straining to pass stool.**

A 42-year-old social worker presents with a story of straining to pass stool, passage of mucus and perhaps blood on the tissue paper.

OSCE counselling cases

OSCE COUNSELLING CASE 8.15 – **'I have severe bloating. Is it the result of food allergy?'**

OSCE COUNSELLING CASE 8.16 – **'I have been told that I have IBS. Should I take a fibre supplement?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

The aetiology of IBS is largely unknown. Irritable bowel syndrome falls under the umbrella of 'functional illness'. Most research points to a role for stress – sexual abuse seems particularly important. Post-infectious IBS is well recognized following 'food poisoning'. Food intolerance is rarely the explanation.

Irritable bowel syndrome is diagnosed clinically, based on the Manning or Rome criteria. It is not a diagnosis of exclusion.

Stressors need to be identified and managed. Counselling may be necessary. Antidepressants are sometimes helpful. Specific drug therapy based on serotonin is not licensed.

Answers

Clinical cases

CASE 8.21 – **A 24-year-old housewife with abdominal bloating.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are IBS, bacterial overgrowth, lactose intolerance and IBD.

A2: What in the given history supports the diagnosis?

Bacterial overgrowth, lactose intolerance and IBS can be difficult to separate from history alone. If the patient reports that certain foods (milk-based) exacerbate her symptoms and there is diarrhoea at the same time, then lactose intolerance is a possibility. Bacterial overgrowth can mimic this.

If the patient experiences relief of abdominal pain with passing flatus or faeces, it is likely to be IBS, particularly if the symptoms are episodic.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important to look for duration of the illness. Irritable bowel syndrome often has insidious onset for many months before patients seek help. Weight gain is often the case, although weight loss may be a consequence of stress. Weight loss is, however, more likely to indicate organic disorder such as IBD or coeliac disease. Abdominal pain that is worse on the day that the stool form is different suggests IBS. Straining to finish defaecation and mucus are often found in patients with IBS. No blood should be present.

A4: What clinical examination would you perform, and why?

On examination, there should be no abnormal findings. In IBD, tenderness, abdominal mass or perianal abnormalities may be found.

A5: What investigations would be most helpful, and why?

No investigations are needed if a clinical diagnosis of IBS is made. Normal CRP and plasma viscosity may be reassuring, however. NICE guidelines recommend a serological test to exclude coeliac disease.

A6: What treatment options are appropriate?

Irritable bowel syndrome is usually a consequence of stress. A careful social history should be obtained and attention paid to counselling around the issues described by the patient. Lactose exclusion may be helpful in some patients.

CASE 8.22 – **After an elective period in India, a medical student returns to the UK with diarrhoea.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are post-infectious IBS and giardiasis.

A2: What in the given history supports the diagnosis?

It is hard to distinguish between the differential diagnoses, but the history suggests that an infection was acquired in India, which has led to a subtle change in the bowel habit, giving chronic diarrhoea.

A3: What additional features in the history would you seek to support a particular diagnosis?

Weight loss may suggest that the patient has ongoing giardiasis. Most patients with IBS have episodic symptoms, with some easing from time to time. If these symptoms do not wax and wane, it is likely that the patient has giardiasis rather than IBS.

A4: What clinical examination would you perform, and why?

No abnormal findings are expected.

A5: What investigations would be most helpful, and why?

Stool culture and duodenal biopsy should be undertaken to look for *Giardia lamblia*. A therapeutic trial of metronidazole may be considered.

A6: What treatment options are appropriate?

If the patient has giardiasis, metronidazole will cure the problem. If *G. lamblia* is not present, it is likely that the problem is post-infectious IBS and the symptoms will gradually improve over time. Lactose avoidance may help ease the symptoms.

CASE 8.23 – **A 42-year-old social worker presents with straining to pass stool.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are IBS, mucosal prolapse, solitary rectal ulcer syndrome, gonorrhoea and haemorrhoids.

A2: What in the given history supports the diagnosis?

The passage of mucus with an urge to strain suggests that the patient has rectal disease. Infrequent blood that is present only on the tissue paper makes it unlikely that the patient has proctitis, but this is not completely ruled out.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important to determine whether there is an urge to strain at the start or the end of defaecation. Both are often present in IBS. If blood is present only on days when the patient strains, this suggests that the patient has haemorrhoids or solitary rectal ulcer syndrome. Proctitis tends to give rise to frequent passage of blood in the absence of the need to strain. Sexual practice should be investigated tactfully. Anal intercourse in either sex can cause local trauma and transmit a sexually transmitted infection. Some patients self-digitate when they feel they have inadequately emptied the bowel; this can traumatize the bowel.

A4: What clinical examination would you perform, and why?

On examination, nothing is expected. Sigmoidoscopy should be performed. This may show proctitis or solitary rectal ulcer in the anterior wall of the rectum. Haemorrhoids may be seen prolapsing through the anus, but proctoscopy may be necessary to visualize them.

A5: What investigations would be most helpful, and why?

Flexible sigmoidoscopy should be considered. Swabs should be considered if there has been anal intercourse. Physiological studies may be necessary in patients in whom tenesmus is severe.

A6: What treatment options are appropriate?

Treatment is difficult. Stool softeners may help patients with haemorrhoids, but some patients require a surgical assessment with a view to band ligation or sclerotherapy. If proctitis is present, it should be treated with topical therapy (steroids or 5-ASA compound). Any local infection should be treated with appropriate antibiotics or antiviral agents.

Most patients will have IBS. This may respond to hypnotherapy and, in certain situations, biofeedback, which teaches the patient to respond differently to symptoms they perceive from their rectums and 'retrains' the manner in which they defaecate.

OSCE counselling cases

OSCE COUNSELLING CASE 8.15 – **'I have severe bloating. Is it the result of food allergy?'**

Bloating is unlikely to be caused by food allergy, although food intolerance (especially wheat) may aggravate bloating. Milk sugar (lactose) intolerance is a possibility; the patient should try avoiding all milk products (including goat's and sheep's milk) for 2 weeks and see whether this improves the symptoms.

OSCE COUNSELLING CASE 8.16 – **'I have been told that I have IBS. Should I take a fibre supplement?'**

The short answer is 'no'. High-fibre diets often worsen abdominal pain in IBS. The patient should eat a well-balanced diet including a mixture of fruit and vegetables.

COELIAC DISEASE

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What in the given history supports the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 8.24 – **A 44-year-old woman with anaemia.**

A 44-year-old woman presents with lethargy, breathlessness on exertion and a little chest tightness on walking uphill. She was turned down as a blood donor because of anaemia.

CASE 8.25 – **A 23-year-old woman with impaired fertility and loose stools.**

She had loose stools throughout her teenage years. She is slightly built and has noted that it is difficult to increase her weight.

CASE 8.26 – **A man with coeliac disease who infrequently attends clinic but has weight loss and anaemia.**

The patient presents with weight loss and anaemia at the insistence of his wife.

OSCE counselling cases

OSCE COUNSELLING CASE 8.17 – **'I feel well. Why should I eat a gluten-free diet?'**

OSCE COUNSELLING CASE 8.18 – **'I have coeliac disease. Are my children at risk?'**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Coeliac disease is a true food allergy. An immune response to the alpha-gliadin component of gluten leads to an immune infiltrate in the mucosa of the proximal small intestine, with secondary crypt hyperplasia and villous atrophy.

Antibodies to gliadin, endomysium and tissue transglutaminase are often found in the serum of patients with coeliac disease, but these antibodies lack the sensitivity and specificity to be the gold standard for making the diagnosis. The gold standard remains the proximal small intestinal biopsy, typically obtained from the third part of the duodenum at endoscopy.

Untreated coeliac disease leads to complications associated with malabsorption, including anaemia (folate and iron deficiency), rickets, osteomalacia, bleeding disorders and subfertility.

Late complications include small bowel lymphoma and carcinomas arising in the small intestine, oesophagus, pharynx and colon.

Answers

Clinical cases

CASE 8.24 – **A 44-year-old woman with anaemia.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are menorrhagia, dietary insufficiency (vegetarian) and coeliac disease.

A2: What in the given history supports the diagnosis?

The history is consistent with progressive iron-deficiency anaemia; lack of overt blood loss in the presenting complaint suggests malabsorption or menorrhagia as likely causes.

A3: What additional features in the history would you seek to support a particular diagnosis?

A dietary history should be obtained to exclude vegetarianism. Gynaecological history should be pursued to look for menorrhagia. A subtle change in the bowel habit should be sought that may suggest coeliac disease.

A4: What clinical examination would you perform, and why?

Nothing is expected on examination, except evidence of anaemia, perhaps with cheilosis or mouth ulcers.

A5: What investigations would be most helpful, and why?

Duodenal biopsy may be done; some clinicians use anti-endomysial or anti-tissue transglutaminase antibodies as a justification for duodenal biopsy. If the dietary history is non-contributory and the gynaecological history unremarkable, coeliac disease is the most likely explanation. Further investigations may be called for, however, if coeliac disease is not found.

A6: What treatment options are appropriate?

Treatment of coeliac disease is a gluten-free diet with possible mineral and vitamin supplements. The patient should be encouraged to join the Coeliac Society.

CASE 8.25 – **A 23-year-old woman presents with impaired fertility and loose stools.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are coeliac disease, Crohn's disease, hormone disturbance (e.g. thyrotoxicosis) and anorexia nervosa.

A2: What in the given history supports the diagnosis?

The clue is the loose stool; without this, the differential diagnosis would be quite broad. People with anorexia rarely complain of inability to gain weight, so anorexia is unlikely. Crohn's disease, thyrotoxicosis and coeliac disease are all genuine differential diagnoses of diarrhoea and subfertility.

A3: What additional features in the history would you seek to support a particular diagnosis?

The nature of the stool should be investigated: pale, bulky, floating stools suggest steatorrhoea, while bloody diarrhoea suggests Crohn's disease. Features of thyrotoxicosis (tremors and sweats) should be sought to rule out thyroid disease. Abdominal pain is unlikely in coeliac disease but common in Crohn's disease.

A4: What clinical examination would you perform, and why?

On examination, little is expected in patients with coeliac disease, although clubbing and anaemia may be present. Mouth ulcers are also relatively common. A goitre would point to thyroid dysfunction, and proptosis would suggest Graves' disease.

A5: What investigations would be most helpful, and why?

Anti-endomysial or anti-tissue transglutaminase antibodies or duodenal biopsy should be obtained. Duodenal biopsies are the standard investigation. Thyroid function should be assessed if the duodenal biopsy is normal. Consideration should be given to a barium follow-through.

A6: What treatment options are appropriate?

The treatment for coeliac disease is a gluten-free diet. The treatment for thyrotoxicosis is carbimazole or radiotherapy with thyroxine replacement. Crohn's disease is treated according to symptoms; a 5-ASA compound may be used as maintenance medication.

CASE 8.26 – A man with coeliac disease who infrequently attends clinic but has weight loss and anaemia.

A1: What is the likely differential diagnosis?

The likely diagnosis is poor treatment compliance, with relapse of coeliac disease. Lymphoma or small bowel carcinoma complicating poorly controlled coeliac disease should also be considered.

A2: What in the given history supports the diagnosis?

Poor clinic attendance suggests non-compliance. A history from the patient's wife would be useful to support this.

A3: What additional features in the history would you seek to support a particular diagnosis?

The patient's diet should be reviewed, and barium follow-through and duodenal biopsy considered.

A4: What clinical examination would you perform, and why?

Lymphadenopathy may be present, but often lymphoma in the GI tract does not present with lymphadenopathy.

A5: What investigations would be most helpful, and why?

Duodenal biopsy, barium follow-through and CT scan of the abdomen would be most helpful.

A6: What treatment options are appropriate?

The patient should be encouraged to reintroduce a gluten-free diet for coeliac disease. Oncological assessment with radiotherapy or chemotherapy is necessary if the patient has lymphoma.

OSCE counselling cases

OSCE COUNSELLING CASE 8.17 – **'I feel well. Why should I eat a gluten-free diet?'**

Most patients with coeliac disease have insidious symptoms, gradually leading to presentation with diarrhoea or anaemia. Without control of coeliac disease, malabsorption as a consequence will occur in most patients. Untreated coeliac disease increases the risk of lymphoma and gastrointestinal malignancy.

OSCE COUNSELLING CASE 8.18 – **'I have coeliac disease. Are my children at risk?'**

There is a weak association. This is not simple inheritance such as that found in patients with haemophilia or cystic fibrosis. Although the risk to the children is small, a delay in weaning or prolonged breastfeeding is thought to be helpful. If the child fails to thrive, coeliac disease should be considered.

REVISION PANEL

- Most patients with haematemesis or melaena will have bled from a peptic ulcer, most cases of which are painless.
- The differential diagnoses for acute bloody diarrhoea are acute colitis, microbial diarrhoea (*C. difficile* – a drug history is needed; protozoa – a travel history should be taken), side effects of medications such as NSAIDs, and familial adenomatous polyps (bleeding usually occurs in the context of normal stool, so a family history should be taken).
- Acute pancreatitis is a significant cause of mortality. It should be considered in the differential diagnosis of all cases of acute abdominal pain. The diagnosis can generally be confirmed by an elevated serum amylase. Risk factors for acute pancreatitis include alcohol abuse and gallstones.
- Patients with IBD often present with symptoms that have been present for several weeks or months. Many will have been told that they have IBS.
- *Helicobacter pylori* is found in over 90 per cent of patients with duodenal ulcers and 70 per cent of patients with gastric ulcers. Non-steroidal anti-inflammatory drugs contribute to the aetiology of peptic ulcer disease. Smoking and alcohol are minor contributory factors.
- Decompensation is recognized from jaundice, abdominal swelling, drowsiness, GI bleeding, fetor, flapping tremor, ascites, oedema, impaired consciousness, falling albumin and prolonged clotting times.
- Constipation may be related to poor dietary habit, IBS and dysmotility. Myxoedema, hypercalcaemia and Hirschsprung's disease are rare causes.
- Coeliac disease is a food allergy to gluten that leads to an immune infiltrate in the mucosa of the proximal small intestine, with secondary crypt hyperplasia and villous atrophy. Antibodies to gliadin, endomysium and tissue transglutaminase are often found in the serum of patients with coeliac disease. The gold standard diagnostic test remains the proximal small intestinal biopsy, typically obtained from the third part of the duodenum at endoscopy.

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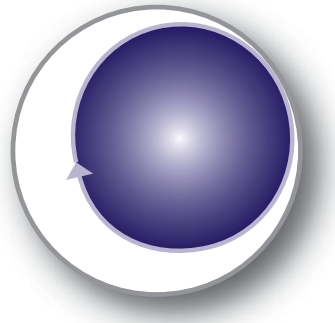

9 Haematology

Christopher Fegan

ANAEMIA

ABNORMAL FULL BLOOD COUNT

HAEMOGLOBINOPATHIES

Answers

ANAEMIA

Questions

Clinical cases

For the case scenarios given, consider the following:

Q1: What are the likely diagnosis and the possible differential diagnoses?
Q2: What are the relevant points to elicit from the history?
Q3: What are the possible clinical signs?
Q4: What additional investigations are indicated?
Q5: What is the treatment?
Q6: What is the long-term outcome?

CASE 9.1 – A 27-year-old woman is referred with palpitations and shortness of breath.

Her haemoglobin (Hb) is 8.2 g/dL (normal range 11.5–16 g/dL), white cell count (WCC) is 5.2×10^9/L (normal range 4–11×10^9/L) and platelets are 513×10^9/L (normal range 150–400×10^9/L). The mean cell volume (MCV) is 69 fL (normal range 80–100 fL) and the mean cell haemoglobin (MCH) is 23 pg (normal range 27–33 pg). She has a life-long history of menorrhagia but has declined therapeutic investigations and intervention. The serum ferritin is 3 ng/mL (normal range 6–81 ng/mL).

CASE 9.2 – A 58-year-old woman is referred with a 12-month history of increasing difficulty in walking.

The patient has been relatively well throughout her life, and her only medication is thyroxine 150 µg once a day for hypothyroidism diagnosed many years earlier. Over recent months she has noticed increasing shortness of breath on exertion, although her decreased mobility has meant that this has not been a particular problem. She works as a clerical officer, smokes five cigarettes a day but drinks no alcohol.

On examination, the positive clinical signs elicited were pallor, tachycardia (100/min, regular), decreased sensation in both legs below the knee, absent ankle jerks and up-going plantar responses. Investigations reveal the following:

- Hb 8.2 g/dL (normal range 11.5–16 g/dL)
- MCV 124 fL (normal range 80–100 fL)
- WCC 2.4×10^9/L (normal range 4–11×10^9/L)
- platelets 102×10^9/L (normal range 150–400×10^9/L).
- urea and electrolytes (U&Es) are normal, as are the liver function tests (LFTs), apart from a slightly raised bilirubin of 45 µmol/L (normal <25 µmol/L) and a lactate dehydrogenase (LDH) level of 2374 U/L (normal range 200–500 U/L).

CASE 9.3 – **A 78-year-old woman is referred with a 6-month history of general deterioration.**

On admission the patient is confused. Her daughter reports that she has been very thirsty for the past 4 weeks. Apart from back pain, there have been no other new symptoms. Clinical examination is unremarkable, except for signs of dehydration. Her full blood count (FBC) shows the following:

- Hb 9.5 g/dL (normal range 11.5–16 g/dL)
- WCC 4.2×10^9/L (normal range 4–11×10^9/L)
- platelet count 127×10^9/L (normal range 150–400×10^9/L).

The biochemistry profile reveals the following:

- sodium 126 mmol/L (normal range 133–147 mmol/L)
- potassium 4.8 mmol/L (normal range 3.5–5.0 mmol/L)
- urea 17 mmol/L (normal 2.5–7.5 mmol/L)
- creatinine 201 μmol/L (normal range 50–120 μmol/L)
- total protein 117 g/dL (normal range 60–80 g/dL)
- albumin 28 g/dL (normal range 35–48 g/dL)
- aspartate aminotransferase (AST) 39 U/L (normal <35 U/L)
- alkaline phosphatase (ALP) 214 U/L (normal range 90–430 U/L)
- calcium 3.4 mmol/L (normal range 2.05–2.6 mmol/L)
- glucose 4.0 mmol/L.

OSCE counselling case

OSCE COUNSELLING CASE 9.1 – **A colleague phones asking whether or not to transfuse a 24-year-old Asian woman who is 34 weeks pregnant with a haemoglobin of 7.8 g/dL secondary to iron deficiency.**

What further information would you require, and what are the most salient points you would like to bring to your colleague's attention?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Anaemia is a very common topic because it impinges on all areas of medical care. A basic knowledge of the physiology of red cell production (erythropoiesis) is essential in understanding the causes of anaemia. There are several ways of classifying anaemia, the simplest of which is based on the red cell size: microcytic (MCV <80 fL), normocytic (MCV 80–100 fL) and macrocytic (MCV >100 fL). One can also consider anaemia as either a failure of red cell production or a reduction in red cell survival. The age at which anaemia develops, a good dietary and clinical history, and the knowledge of how to interpret the data given by the FBC are essential in narrowing down the differential diagnoses and requesting relevant investigations. The management of anaemia, and in particular the indications for blood transfusion, are a must-know area for any doctor.

Answers

Clinical cases

CASE 9.1 – **A 27-year-old woman is referred with palpitations and shortness of breath.**

A1: What are the likely diagnosis and the possible differential diagnoses?

This woman presents with symptomatic, hypochromic (low MCH)/microcytic (low MCV) anaemia. There are only four conditions giving rise to hypochromic/microcytic anaemia: iron deficiency, thalassaemia, anaemia of chronic disease, and some rare (usually hereditary) types of sideroblastic anaemia. The low ferritin in this woman indicates that she has iron deficiency anaemia, probably secondary to excess menstrual blood loss.

A2: What are the relevant points to elicit from the history?

It is likely that the iron deficiency is secondary to the excess menstrual blood loss. It is important to ask about diet, however, to ensure that her oral iron intake is adequate and to check whether she is taking any non-steroidal anti-inflammatory drugs. Sufficient quantities of dietary iron are found in red meat (less in pork or chicken) and, therefore, iron deficiency is common in vegetarians. The patient should be asked about other routes of bleeding (especially gastrointestinal and urinary tract symptoms). The platelet count rises in any form of iron deficiency and is not necessarily a sign of blood loss. Oesophageal webs causing dysphagia are a rare associated feature.

A3: What are the possible clinical signs?

Clinical signs include pallor (difficult sign seen as pale conjunctivae), tachycardia, brittle hair and nails, koilonychia (spoon-shaped nails), smooth atrophic tongue and angular stomatitis.

A4: What additional investigations are indicated?

Depending on any symptoms elicited from the history, one might consider performing a rectal examination, upper and lower gastrointestinal endoscopy and faecal occult blood estimation. Coeliac disease is also possible, so anti-tissue transglutaminase or anti-endomysial antibodies should be requested. Given the long history of menorrhagia, thyroid function tests should be performed, together with consideration of referral to a gynaecologist for more specific tests and investigations.

A5: What is the treatment?

Treatment is with iron. Ideally patients should receive 6 months of ferrous sulphate 200 mg three times a day. Side effects, usually constipation or more rarely diarrhoea, can occur, in which case intravenous or more rarely intramuscular iron can be used; the latter is very painful, however. Intravenous iron can be given but may lead to severe anaphylactic reactions. In this patient, one could also consider using oral tranexamic acid or the combined oral contraceptive pill to reduce menstrual blood loss.

A6: What is the long-term outcome?

On the assumption that menstrual loss is the underlying cause of this anaemia, the outcome should be excellent.

CASE 9.2 – **A 58-year-old woman is referred with a 12-month history of increasing difficulty in walking.**

A1: What are the likely diagnosis and the possible differential diagnoses?

The patient's neurological examination reveals a combination of peripheral neuropathy and an upper motor neuron lesion in the lower limbs. In addition, there are symptoms and signs of anaemia, pancytopenia (all three cell lineages reduced) and macrocytosis. All these point to vitamin B12 deficiency and a diagnosis of pernicious anaemia with subacute combined degeneration of the spinal cord and peripheral neuropathy. Potentially reversible dementia can also occur. All dividing cells require vitamin B12; the bone marrow, as one of the tissues with the fastest turnover, is often affected first. The raised bilirubin and LDH are a result of ineffective erythropoiesis within the bone marrow (so-called intramedullary haemolysis). Folate deficiency can give rise to a similar blood and bone marrow picture, but neurological deficit does not occur.

A2: What are the relevant points to elicit from the history?

Pernicious anaemia is an autoimmune disease, and so a personal and family history of other autoimmune diseases should be sought (e.g. type 1 diabetes, thyroid disease, Addison's disease, vitiligo). The patient should be asked if she has ever undergone any gastric surgery. Rarely, there is associated subfertility (but this would not apply in this age group) and visual loss. Vitamin B12 is present in foods of animal origin, including meat, eggs and milk products. Daily requirements of vitamin B12 are very low, and so it is very unusual for vegans to develop clinical vitamin B12 deficiency, but a dietary history should always be taken.

A3: What are the possible clinical signs?

The tongue is said to be 'big and beefy' in contrast to the atrophic tongue seen in iron deficiency. The skin has a lemon tinge (caused by the mildly elevated bilirubin). Optic atrophy can also occur, and anecdotally patients are often said to be white-haired.

A4: What additional investigations are indicated?

Measuring the serum vitamin B12 levels easily makes the diagnosis. Other useful tests are anti-parietal and intrinsic factor antibodies, which are present in 90 per cent and 60 per cent of patients, respectively. It may also be prudent to look for evidence of the other autoimmune disorders that are associated with pernicious anaemia. Historically, a Schilling test was performed to confirm vitamin B12 malabsorption, but this is rarely performed today because it exposes patients to radiation and does not usually alter the clinical management.

A bone marrow examination would confirm a megaloblastic anaemia but does not distinguish between vitamin B12 and folate deficiency and hence is not routinely performed.

A5: What is the treatment?

Management is vitamin B12, usually given as 1 mg intramuscular injections for six doses over 2 weeks and then every 3 months for life. If required, the response to therapy can be assessed by the rise in reticulocytes and Hb and the fall in LDH.

A6: What is the long-term outcome?

The blood and marrow changes will improve over the following few weeks, but the neurological deficit may take many, many months and if severe at diagnosis may not resolve completely.

CASE 9.3 – **A 78-year-old woman is referred with a 6-month history of general deterioration.**

A1: What are the likely diagnosis and the possible differential diagnoses?

The blood count shows mild pancytopenia; this, taken together with bony pain and hypercalcaemia, could indicate secondary cancer in the bone or possibly a primary haematological cancer of the bone marrow. The total protein is very high and the albumin low, meaning that the globulin level (total protein minus albumin) is very high. Supported by the presence of renal impairment, the diagnosis is likely to be multiple myeloma. When a very high globulin level occurs, a low sodium level is often seen (so-called pseudo-hyponatraemia).

A2: What are the relevant points to elicit from the history?

Multiple myeloma is a disease of elderly people, and symptoms are often non-specific and attributed to old age. Symptoms caused by anaemia and bony pain (especially back) are typical, and myeloma should always be considered with this combination. There are relatively few causes of thirst, but the most common are diabetes (mellitus and insipidus), dehydration and hypercalcaemia. Hypercalcaemia also causes the confusion and polyuria that lead to dehydration (this will contribute to the raised creatinine in this patient). Renal impairment in myeloma is caused by dehydration, hypercalcaemia and paraprotein deposition in the kidney.

A3: What are the possible clinical signs?

Back pain is common as a result of pressure on spinal nerve roots or pathological fractures. Vertebral collapse can lead to paraplegia. Note that there is usually no enlargement of the liver, spleen or lymph nodes, unless secondary amyloidosis has occurred.

A4: What additional investigations are indicated?

Multiple myeloma is a cancer of the plasma cells. Immunoglobulins are normally produced by plasma cells, and therefore a malignant proliferation of plasma cells leads to uncontrolled production of a single type of immunoglobulin – so-called paraprotein. The plasma cells proliferate within the bone marrow, damaging normal bone marrow cells and bone and leading to anaemia and other blood cell cytopenias, hypercalcaemia and lytic lesions on radiographs.

The diagnosis of multiple myeloma depends on four tests:

- serum immunoglobulin estimation and protein electrophoresis
- urinary sample for Bence Jones protein (light chain) analysis
- skeletal survey looking for lytic lesions.
- bone marrow examination to assess malignant plasma cell infiltration.

A5: What is the treatment?

In this case, treatment of the hypercalcaemia would be of most immediate priority because this may reduce the confusion and alleviate symptoms of dehydration. Local irradiation may be indicated for bony pain. The anaemia can be treated with blood transfusion in the short term, and possibly with erythropoietin therapy thereafter. Treatment for myeloma consists of chemotherapy with autologous stem cell transplantation for younger patients. Steroids and anti-angiogenic agents also have a role as upfront or palliative therapy. Regular bisphosphonate therapy reduces the risk of bony fracture and hypercalcaemia and has been shown to prolong overall survival.

A6: What is the long-term outcome?

The prognosis is poor, with death usually within 2–3 years of diagnosis for patients not fit enough for autologous stem cell transplantation and around 5 years for those who are fit enough.

OSCE counselling case

OSCE COUNSELLING CASE 9.1 – **A colleague phones asking whether or not to transfuse a 24-year-old Asian woman who is 34 weeks pregnant with a haemoglobin of 7.8 g/dL secondary to iron deficiency.**

This is a common clinical scenario. It is imperative that you treat the patient and not the Hb level, and so first you need to know whether the patient is clinically compromised by her anaemia. You also need to know whether or not the patient has been taking iron supplements and if so what dose and for how long. It would also be helpful to know whether this is her first child or if there have been previous pregnancies, and the plans for delivery of this baby. In addition, it would be reassuring to be informed that this woman and her partner have been screened for thalassaemia and that she has no red cell antibodies that are likely to lead to haemolytic disease of the newborn.

In general terms, patients with iron deficiency anaemia should be treated with iron therapy and not blood transfusion. If the patient cannot tolerate oral iron, consideration should be given to parenteral iron. Adequate iron therapy raises the Hb by about 1 g/dL per week of therapy – within 3 weeks, therefore, the Hb should be >10 g/dL in this patient. Apart from the usual risks of blood transfusion (reactions, infections, fluid overload), this patient is of Asian origin and therefore blood transfusion has a much higher risk of leading to the development of alloantibodies, which may lead to future problems when cross-matching blood and can also predispose to haemolytic disease of the newborn (possibly in this pregnancy, but certainly in future pregnancies). Blood transfusion should be given only if the patient is clinically compromised by her anaemia and there is a need for 'urgent' delivery of the baby or if she is allergic to iron therapy, i.e. previous anaphylaxis with parenteral iron. It would be prudent to genotype the blood for cross-match to minimize the risk of alloantibody production. The patient should be counselled about the risks of blood transfusion and the fact that, although all reasonable steps have been taken to avoid alloantibodies, nothing can be guaranteed.

ABNORMAL FULL BLOOD COUNT

Questions

Clinical cases

For the case scenarios given, consider the following:

Q1: What are the likely diagnosis and the possible differential diagnoses?
Q2: What are the relevant points to elicit from the history?
Q3: What are the possible clinical signs?
Q4: What additional investigations are indicated?
Q5: What is the treatment?
Q6: What is the long-term outcome?

CASE 9.4 – A 78-year-old retired mechanic is admitted with increasing left hypochondrial pain of a stabbing character over the previous 12 h.

The patient has not felt well for 3 months. He has lost 5 kg in weight and recently noticed night sweats. Clinical examination reveals hepatomegaly of 5 cm and splenomegaly of 15 cm. There is no lymphadenopathy.

The FBC reveals the following:

- Hb 10.1 g/dL (normal range 13.0–16.5 g/dL)
- WCC 227×10^9/L (normal range 4–11×10^9/L) with prominent eosinophilia and basophilia
- platelets 741×10^9/L (normal range 150–400×10^9/L).

Urea and electrolytes and LFTs are normal, except for a uric acid level of 490 μmol/L (normal range 110–420 μmol/L).

CASE 9.5 – A 63 year-old-man presents with a left-sided transient ischaemic attack (TIA).

The TIA follows on from a similar episode 1 week earlier that had been labelled a TIA. After the first TIA, the general practitioner (GP) performed some blood tests, the results of which are as follows:

- Hb 21.2 g/dL (normal range 13.0–16.5 g/dL)
- red cell count 6.7–10^{12}/L (normal range 3.8–5.6–10^{12}/L)
- haematocrit 0.61
- WCC 15.3×10^9/L (normal range 4–10.5×10^9/L)
- increased neutrophils and eosinophils
- platelets 897×10^9/L (normal range 150–400×10^9/L)
- sodium 142 mmol/L (normal range 135–145 mmol/L)
- potassium 4.8 mmol/L (normal range 3.4–5.0 mmol/L)
- urea 5.0 mmol/L (normal range 2.5–7.0 mmol/L)

- creatinine 79 μmol/L (normal range 50–100 μmol/L)
- total protein 71 g/dL (normal range 60–80 g/dL)
- albumin 43 g/dL (normal range 35–50 g/dL)
- bilirubin 8 μmol/L (normal range 1–22 μmol/L)
- AST 30 IU/L (normal range 19–48 IU/L)
- ALP 71 IU/L (normal range 30–115 IU/L)
- cholesterol 3.6 mmol/L (normal range 2.5–6.2 mmol/L)
- triglyceride 1.9 mmol/L (normal range 0.1–1.6 mmol/L).

CASE 9.6 – **A 23-year-old man is brought into the accident and emergency (A&E) department having become acutely unwell while shopping.**

On admission the patient is barely rousable and unable to provide a history. His Glasgow coma score (GCS) is 12, with no obviously localizing signs. His temperature is 39.5 °C, his pulse is regular with a rate of 130/min and his blood pressure is 60/35 mmHg. His respiratory rate is 25/min, but on auscultation there are no added sounds. Abdominal examination is unremarkable, with no obvious tenderness, rigidity or guarding, and bowel sounds are present. An FBC was performed by his GP 2 days before this episode and shows the following:

- Hb 5.2 g/dL (normal range 13.0–16.5 g/dL)
- red cell count 1.9×10^{12}/L (normal range $3.8–5.6\times10^{12}$/L)
- WCC 93.3×10^{9}/L (normal range $4–10.5\times10^{9}$/L)
- neutrophils 0.1×10^{9}/L (normal range $2.0–8.0\times10^{9}$/L)
- platelets 7×10^{9}/L (normal range 150–400×109/L).

OSCE counselling case

OSCE COUNSELLING CASE 9.2 – **What advice would you give a GP who writes to you about a 37-year-old African Caribbean woman with mild fluctuating neutropenia (0.8–1.5$\times10^9$/L; normal range 2.0–8.0$\times10^9$/L) over the past 4 years?**

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

The FBC is basically a measure of the quantity and size of the blood cells circulating at that time. If a particular blood cell count is raised, the question is whether this is the result of something inherently wrong with the bone marrow or whether the bone marrow is simply reacting to something else going on within the body, such as inflammation, infection or malignancy. The answer may be obvious from the FBC but if it is not clear, a raised C-reactive protein (CRP) typically indicates a reactive process. An invaluable aid to diagnosis is a previous FBC, because this may show whether the changes are recent or old. A common scenario is a patient whose Hb rises over a few days during admission; assuming the patient has not received a red blood cell transfusion, a reduction in plasma volume (i.e. dehydration) is the usual cause. Likewise, a rapidly falling Hb does not necessarily indicate bleeding; one would expect the Hb to fall in a patient admitted with dehydration once rehydration is complete.

A blood film should be examined to ascertain the exact nature of any cells raised in the peripheral blood, such as leukaemia cells.

Low blood counts indicate either a failure of production by the bone marrow or reduced survival of that particular cell. In bone marrow failure, one would expect to see all normal blood cells eventually affected, i.e. falling white cells, red cells and platelets. Typically, the neutrophil count falls first because this has the shortest survival in the circulation – 24 h.

Answers

Clinical cases

CASE 9.4 – A 78-year-old retired mechanic is admitted with increasing left hypochondrial pain of a stabbing character over the previous 12 h.

A1: What are the likely diagnosis and the possible differential diagnoses?

This patient presents with hepatosplenomegaly, leucocytosis (with eosinophilia and basophilia) and thrombocytosis. This, taken together with the constitutional symptoms, indicates chronic myeloid leukaemia.

A2: What are the relevant points to elicit from the history?

During the history, direct evidence of hyperleucostasis should be sought, notably dizziness, headaches and visual loss.

A3: What are the possible clinical signs?

Splenic infarction leads to acute stabbing pain, and this may be elicited on examination. Infarction can occur during splenic enlargement, probably as a result of the very high WCC and hyperleucostasis. In the acute event, one may hear a splenic rub. Note that the gradual enlargement of the spleen is not, in itself, usually painful. Other signs of hyperleucostasis are retinal haemorrhages and retinal vein thrombosis.

A4: What additional investigations are indicated?

The diagnosis is easily confirmed by cytogenetic analysis of peripheral blood cells, where a translocation between chromosome 9 and 22 is found – the so-called Philadelphia chromosome.

A5: What is the treatment?

If there are symptoms or signs of hyperleucostasis, leucopheresis should be undertaken to lower the WCC. Immediate care should include analgesia, allopurinol or rasburicase (to prevent acute gout), hydration and chemotherapy. The WCC can be rapidly reduced using hydroxycarbamide (usually) or cytosine arabinoside (rarely required). Having reduced the WCC sufficiently, further therapy should be with the tyrosine kinase inhibitor imatinib. Patients who present with accelerated phase or blast crisis should be treated with combination therapy, including imatinib, interferon alpha or chemotherapy.

The age of this patient makes allogeneic stem cell transplantation from a donor too risky a procedure to be considered.

A6: What is the long-term outcome?

Chronic myeloid leukaemia consists of three distinct phases.

- *Chronic phase:* relatively easy to control blood counts with imatinib monotherapy. Patient remains relatively well with few symptoms.
- *Accelerated phase:* the blood counts become more difficult to control, often swinging from too low to too high.

- *Blast crisis:* the clinical picture becomes more akin to acute leukaemia, with increasing constitutional symptoms and marrow failure, i.e. low platelets, anaemia and high WCC. Further chromosomal abnormalities, in addition to the Philadelphia chromosome, often occur at this stage. Patients at this stage become resistant to conventional therapies and the prognosis is very poor.

Overall survival without transplantation has historically been around 5–6 years, but survival is much longer in patients who have a good response to imatinib. If there is a poor initial response to imatinib, the dose can be increased or interferon or cytosine arabinoside can be added; alternatively, one can switch from imatinib to one of the other tyrosine kinase inhibitors – dasatinib or nilotinib. With the exception of allogeneic stem cell transplantation, none of the therapies is thought to be curative, but transplantation is now reserved for patients who fail to respond to tyrosine kinase inhibitors.

CASE 9.5 – **A 63-year-old-man presents with a left-sided TIA.**

A1: What are the likely diagnosis and the possible differential diagnoses?

This patient is suffering from recurrent TIAs and has a high Hb, red cell count (erythrocytosis), WCC (leucocytosis) and platelet count (thrombocythaemia). This combination is highly suggestive of polycythaemia rubra vera (PRV); in this condition TIAs occur because of high whole blood viscosity caused by increased red cells and also increased platelet 'stickiness'. One still needs to consider the common causes of TIAs (systemic emboli resulting from atrial fibrillation, mural thrombus after a myocardial infarction, carotid artery disease).

A2: What are the relevant points to elicit from the history?

It is important to know whether the patient has any symptoms suggestive of an alternative underlying condition, such as palpitations (atrial fibrillation) or previous chest pain (mural thrombus). Headaches and pruritus are typical of PRV, and one should ask directly if the patient has experienced amarousis fugax.

A3: What are the possible clinical signs?

One should examine to ascertain if the patient has an irregular tachycardia (atrial fibrillation), carotid bruits or cardiac murmurs. The spleen is typically enlarged in PRV, and there may be plethoric facies and excoriations caused by itching and scratching.

A4: What additional investigations are indicated?

Polycythaemia is classified as true (real increase in red cell mass) and false (reduction in plasma volume). True polycythaemia is further subclassified as primary (PRV) or secondary to some other pathology within the patient, such as hypoxic lung or cardiac disease or renal cell carcinoma. In patients with suspected polycythaemia, if the haematocrit is below 0.60 in males or below 0.56 in females, the diagnosis of true polycythaemia will need to be confirmed by blood volume studies (directly measuring red cell mass and plasma volume). In equivocal cases, oxygen saturation, a chest radiograph and abdominal ultrasonography should also be performed to rule out pulmonary, cardiac and renal causes of polycythaemia.

In PRV, 95 per cent of patients have a mutation of the *JAK2* gene. It is thought that around 5 per cent of patients with PRV do not have the *JAK2* mutation, but a high uric acid or high vitamin B12 level, along with a low erythropoietin level, with or without splenomegaly, is very suggestive of primary polycythaemia.

This patient also requires an electrocardiogram (ECG), carotid Doppler ultrasonography, an echocardiogram or computed tomography (CT) of the head, depending on his symptoms and clinical signs.

A5: What is the treatment?

The patient requires urgent hospital intervention to begin red cell venesection. As the platelet count is so high, hydroxycarbamide or the platelet-lowering agent anagrelide should be commenced to reduce the platelet count to normal levels along with antiplatelet therapy (aspirin or clopidogrel).

A6: What is the long-term outcome?

Long-term management includes regular venesection to keep the haematocrit below 0.45, antiplatelet therapy (aspirin or clopidogrel) and 'mild' chemotherapy (e.g. hydroxycarbamide) to reduce the platelet count to normal levels. Specific inhibitors of *JAK2* are undergoing clinical trials. Overall survival for PRV is typically more than 10 years, but thrombosis, progression to acute myeloid leukaemia (up to 20 per cent of patients) and myelofibrosis (up to 15 per cent of patients) are life-threatening complications.

CASE 9.6 – **A 23-year-old man is brought into A&E having become acutely unwell while shopping.**

A1: What are the likely diagnosis and the possible differential diagnoses?

The clinical history is one of sudden collapse and shock following what appears to be a relatively short period of ill-health. The differential diagnosis includes acute blood loss, sepsis (including meningitis), pancreatitis, hypoglycaemia, cerebral pathology (fits, thrombosis, haemorrhage) and cardiac problems (infarction, arrhythmia). The patient's blood count shows that there is marrow failure, with inability to produce red cells, neutrophils and platelets. This can occur with many conditions, but the high WCC (presumably blasts) indicates that the patient has acute leukaemia. This is completely in keeping with the fairly rapid onset of his symptoms.

A2: What are the relevant points to elicit from the history?

This would need to be from a third party and would focus on features of anaemia (e.g. lethargy, palpitations, dyspnoea), low neutrophil count (infections) and low platelet count (nose bleeds and bruising). It would also be necessary to exclude other possibilities for his collapse (e.g. type 1 diabetes, heavy drinking, epilepsy).

A3: What are the possible clinical signs?

Clinically the patient is shocked – low blood pressure, tachycardia, tachypnoea. The high temperature is very suggestive of septic shock precipitated by neutropenia. The most common organisms are Gram-negative bacteria, but Gram-positive sepsis is also possible. There may be ecchymoses related to the low platelet count.

A4: What additional investigations are indicated?

The patient needs assessment of renal and liver function, calcium, urate, glucose and amylase, arterial blood gases, blood and urine culture, ECG and chest radiograph. Coagulation studies should be done to investigate the possibility of disseminated intravascular coagulopathy (DIC), possibly precipitated by a Gram-negative septicaemia. This diagnosis can be confirmed by measuring fibrinogen degradation products such as D-dimers. Cerebral imaging should be considered urgently to rule out or confirm intracerebral bleeding.

A5: What is the treatment?

The patient is shocked, and therefore raising the blood pressure to allow adequate organ perfusion is essential. Crystalloids are required, but correction of the abnormal coagulation with fresh frozen plasma or cryoprecipitate (which is a better source of fibrinogen than fresh frozen plasma) will also help.

Placement of a central venous line to measure central venous pressure and aid fluid replacement and a urinary catheter to assess urine output should be considered. If fluids alone do not adequately raise the blood pressure, inotropes should be instituted. If respiratory failure ensues, assisted ventilation will be required.

Platelet transfusions will raise the platelet count and reduce the risk of fatal haemorrhage. The immediate commencement of broad-spectrum antibiotics with activity against both Gram-negative and Gram-positive bacteria is critical if the patient is to survive.

Although the patient is very anaemic, this is not the source of shock. Red blood cell transfusions will raise the Hb and potentially aid oxygen delivery to the tissues, but this is potentially dangerous because the patient has a very, very high WCC, and a sudden increase in intravascular cells via transfusion has a very high risk of precipitating hyperleucostasis, which can be catastrophic. Correction of the anaemia can usually wait until the WCC has been reduced with chemotherapy. If a red cell transfusion is thought to be potentially of benefit, this should be given very slowly.

A6: What is the long-term outcome?

Septic shock associated with neutropenia has a very high mortality rate, but assuming the patient survives this immediate life-threatening complication, the cure rate for acute leukaemia ranges from 20 per cent to 80 per cent, depending on the particular prognostic type.

OSCE counselling case

OSCE COUNSELLING CASE 9.2 – **What advice would you give a GP who writes to you about a 37-year-old African Caribbean woman with mild fluctuating neutropenia (0.8–1.5×10^9/L; normal range 2.0–8.0×10^9/L) over the past 4 years?**

This woman has long-standing isolated but fluctuating neutropenia. The normal range quoted for most haemocytometers is usually based on an Anglo-Saxon white population and therefore may not be appropriate for all ethnic groups. African Caribbean individuals are well described as having lower neutrophil counts (as low as 0.5×10^9/L) but have no increased infective risk. For this patient, the neutrophil count may well be 'normal'. Other causes of isolated neutropenia should be considered, including autoimmune disorders (e.g. systemic lupus erythematosus, rheumatoid arthritis), drugs (angiotensin-converting enzyme [ACE] inhibitors), and familial and chronic benign neutropenia. Systemic problems of the bone marrow are highly unlikely (e.g. cancer – haematopoietic and non-haematopoietic, vitamin B12 and folate deficiency) because this condition has not deteriorated over 4 years. Cyclical neutropenia, a rare cause of neutropenia, is a possible differential diagnosis but, as the patient has no predisposition to infections, no further investigations are required.

Overall, the GP should be reassured, but regular monitoring every 12 months or so would be advisable until the diagnosis is clear.

HAEMOGLOBINOPATHIES

Questions

Clinical cases

For the case scenarios given, consider the following:

Q1: What are the likely diagnosis and the possible differential diagnoses?
Q2: What are the relevant points to elicit from the history?
Q3: What are the possible clinical signs?
Q4: What additional investigations are indicated?
Q5: What is the treatment?
Q6: What is the long-term outcome?

CASE 9.7 – **A 3-year-old girl is referred with failure to thrive.**

The patient is the first child born to Asian parents, who have recently moved to the UK. There was no family history of note. On examination the girl is pale and slightly icteric, with frontal skull bossing. Her pulse is 110/min and regular, with no obvious added heart sounds. On auscultation the chest is clear. Abdominal examination reveals distension with hepatomegaly 3 cm and splenomegaly 5 cm below the costal margins.

Investigations reveal the following:

- Hb 5.1 g/dL (normal range 11.5–16.5 g/dL)
- MCV 58 fL (normal range 80–100 fL)
- MCH 19 pg (normal range 27–33 pg)
- WCC 9.1×10^9/L (normal range 4–11.0×10^9/L)
- platelets 317×10^9/L (normal range 150–400×10^9/L)
- ferritin 12 ng/mL (normal range 6–81 ng/mL)
- folate 4.1 ng/L (normal range 2.1–20 ng/L)
- vitamin B12 273 ng/L (normal range 130–900 ng/L)
- iron 18 μmol/L (normal range 10–30 μmol/L)
- iron-binding capacity 60 μmol/L (normal range 40–75 μmol/L)
- sodium 142 mmol/L (normal range 135–145 mmol/L)
- potassium 4.8 mmol/L (normal range 3.4–5.0 mmol/L)
- urea 5.0 mmol/L (normal range 2.5–7.0 mmol/L)
- creatinine 79 μmol/L (normal range 50–100 μmol/L)
- total protein 71 g/dL (normal range 60–80 g/dL)
- albumin 33 g/dL (normal range 35–50 g/dL)
- bilirubin 38 μmol/L (normal range 1–22 μmol/L)
- AST 65 IU/L (normal range 19–48 IU/L)
- ALP 71 IU/L (normal range 30–115 IU/L)
- LDH 1584 U/L (normal range 200–500 U/L).

CASE 9.8 – **An 18-year-old African woman awoke with shortness of breath and bilateral chest pain.**

The woman is admitted through A&E. She was previously well, apart from a cough the previous day, but she awoke this morning with shortness of breath and bilateral chest pain. She says she had a similar episode 3 years earlier shortly after arriving in the UK from Nigeria. On examination she is very distressed and tachypnoeic. Her temperature is 39.7 °C. General examination is unremarkable, apart from the respiratory system and a chronic skin ulcer above the right medial malleolus. Her respiratory rate is 36/min, with reduced air entry and percussion note at the right midzone. There are widespread bilateral coarse crepitations.

Investigations reveal the following:

- Hb 6.8 g/dL (normal range 11.5–16.5 g/dL)
- MCV 84 fL (normal range 80–100 fL)
- MCH 29 pg (normal range 27–33 pg)
- WCC 17.1×10^9/L (normal range 4–11.0×10^9/L)
- platelets 619×10^9/L (normal range 150–400×10^9/L)
- ferritin 45 ng/mL (normal range 6–81 ng/mL)
- folate 6.2 ng/L (normal range 2.1–20 ng/L)
- vitamin B12 416 ng/L (normal range 130–900 ng/L)
- sodium 139 mmol/L (normal range 135–145 mmol/L)
- potassium 4.8 mmol/L (normal range 3.4–5.0 mmol/L)
- urea 11.2 mmol/L (normal range 2.5–7.0 mmol/L)
- creatinine 169 μmol/L (normal range 50–100 μmol/L)
- total protein 64 g/dL (normal range 60–80 g/dL)
- albumin 34 g/dL (normal range 35–50 g/dL)
- bilirubin 42 μmol/L (normal range 1–22 μmol/L)
- AST 58 IU/L (normal range 19–48 IU/L)
- ALP 71 IU/L (normal range 30–115 IU/L)
- LDH 1381 U/L (normal range 200–500 U/L)
- arterial blood gases:
  - pH 7.36 (normal range 7.35–7.45)
  - PO_2 6.9 kPa (normal range 11.3–14.0 kPa)
  - PCO_2 5.1 kPa (normal range 4.7–6.0 kPa)
- chest radiograph: widespread shadowing, especially at the right midzone.

OSCE counselling case

OSCE COUNSELLING CASE 9.3 – If two parents who are carriers of sickle-cell disease have three children, what is the chance of no child being a carrier or suffering from full-blown sickle-cell disease?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

The area of haemoglobinopathies is a test of your knowledge of ethnicity, hereditary diseases, erythropoiesis, paediatrics, and the hazards and benefits of blood transfusions. In keeping with most fatal hereditary conditions, haemoglobinopathies mostly have autosomal recessive inheritance but with variable penetrance. Different types of haemoglobinopathy occur in different areas of the world, but with globalization they are becoming a more common clinical problem in the UK. Management can be split into preventive, prophylactic and therapeutic.

Answers

Clinical cases

CASE 9.7 – **A 3-year-old girl is referred with failure to thrive.**

A1: What are the likely diagnosis and the possible differential diagnoses?

There are only four conditions that give rise to hypochromic (low MCH)/microcytic (low MCV) anaemia: iron deficiency, thalassaemia major, anaemia of chronic disease, and hereditary sideroblastic anaemia (usually X-linked recessive inheritance, i.e. affects boys). The normal ferritin, iron and iron-binding capacity rule out iron deficiency and anaemia of chronic disease. The raised bilirubin, AST and LDH indicate ineffective erythropoiesis or haemolysis, which is characteristic of thalassaemia major. Thalassaemic conditions are found in many different ethnic groups, including Mediterranean, Middle Eastern and Asian.

A2: What are the relevant points to elicit from the history?

Thalassaemia major is the result of the inability to produce either alpha- or beta-globin chains due to hereditary genetic defects in the respective genes. Thalassaemia major is the result of inheriting two genetic defects – one from each parent, i.e. autosomal recessive inheritance. Over 100 different genetic defects have been described. Very severely affected fetuses may not be viable, leading to stillbirth. You need to ask whether there is any family history of stillbirth or anaemia and whether the two parents are related, i.e. consanguineous.

A3: What are the possible clinical signs?

Children present with failure to thrive, pallor and shortness of breath (caused by anaemia), mild jaundice (resulting from ineffective erythropoiesis and haemolysis), abdominal distension (hepatomegaly and splenomegaly caused by extramedullary haematopoiesis, haemolysis and later iron overload) and bony enlargement (resulting from marrow hyperplasia – frontal bossing, maxillary and parietal bone enlargement).

A4: What additional investigations are indicated?

A blood film will reveal a severe hypochromic/microcytic anaemia with erythroblasts present in the peripheral blood, and with target cells and basophilic stippling. If there is inability to produce either alpha- or beta-globin chains, the developing erythroid cell will try to produce other types of Hb to compensate.

Haemoglobin electrophoresis will detect absent or reduced HbA and the presence of abnormal haemoglobins, e.g. HbF, HbH (β4), HbBarts (γ4) and HbA2. In some patients who are carriers of alpha-thalassaemia, Hb electrophoresis may be normal and more sophisticated tests such as globin chain synthesis may be required. As the underlying molecular changes are characterized, molecular genetic studies are being increasingly used for diagnostic purposes.

Having identified that a patient has or is a carrier of thalassaemia, it is necessary to screen family members. Any identified carriers should have genetic counselling to make them aware of the risks for any future children. Advice regarding antenatal screening or possible termination of future pregnancies needs to be given by counsellors experienced in this field.

A5: What is the treatment?

The mainstay of treatment for affected individuals is a red cell transfusion programme. This not only relieves symptoms but also prevents the bony overgrowths that occur.

If children are treated early, splenomegaly may not occur. If there is a delay in diagnosis or starting a transfusion programme, splenomegaly and hypersplenism may occur, which increases transfusion requirements. In this situation splenectomy may be performed but due to infective problems, this is usually deferred until after the age of 5 years. Immunization with pneumococcal, meningococcal C and *Haemophilus influenzae* vaccines and long-term prophylactic antibiotics is required by all patients after splenectomy.

Among the many risks of blood transfusion is iron overload, which occurs as a result of regular blood transfusions. Each unit of blood contains 250 mg iron, and regular monitoring of ferritin to detect early iron overload is required.

This iron accumulation damages normal tissues, including the liver, pituitary, heart, gonads and pancreas, and therefore treatment with the iron chelator desferrioxamine (subcutaneous) with or without deferiprone is required. Iron excretion by desferrioxamine is increased by vitamin C supplementation. Regular eye and hearing assessments are necessary for all patients on long-term desferrioxamine. Deferasirox is a relatively new drug replacing desferrioxamine as the first-choice iron chelator in many areas of the world. Monitoring of renal and hepatic function is required. If organ damage due to iron overload has occurred, hormone replacements (e.g. insulin) may be required.

As regular blood transfusions are the mainstay of therapy, immunization against hepatitis B is recommended.

The underlying problem is one of failure of the developing red cells to produce adequate Hb. Haematopoietic stem cell transplantation from a suitable allogeneic donor is hazardous, with many possible pitfalls (including death), but is potentially curative.

A6: What is the long-term outcome?

People who are carriers of thalassaemia have a normal life expectancy. Before iron chelation therapy became widespread, people with thalassaemia used to die by the age of 20–30 years. In theory, well-chelated patients should have a normal life expectancy, but in reality they often die prematurely. Stem cell transplantation is potentially curative, provided that patients do not succumb to transplantation complications.

CASE 9.8 – An 18-year-old African woman awoke with shortness of breath and bilateral chest pain.

A1: What are the likely diagnosis and the possible differential diagnoses?

This young African woman presents with respiratory failure and chest pain. The differential diagnosis includes pulmonary embolism, chest infection, asthma and sickle-cell crisis (chest syndrome). The clinical picture is not typical of asthma, and the anaemia and biochemical pictures of haemolysis are not explained by pulmonary embolism alone. The clinical examination and chest radiograph are highly suggestive of a chest infection, but this alone does not completely explain the clinical picture and blood results. Intractable skin ulceration over the malleoli is a common feature of sickle-cell disease. The patient's clinical presentation and investigations are highly suggestive of a sickle-cell crisis, probably precipitated by a chest infection.

Haemoglobin S (HbS) is insoluble and forms crystals when deoxygenated. This distorts the red blood cells, giving them their characteristic shape and blockage of the microcirculation, leading to ischaemia and infarction.

A2: What are the relevant points to elicit from the history?

Sickle-cell disease has a highly variable clinical course, with some patients having a virtually normal life and others succumbing in infancy to crises or infection. It is important to ascertain whether the patient is known to have sickle-cell disease or has had previous crises or if one of her parents or siblings is known to have sickle-cell disease or to be a sickle carrier. Precipitating factors known to lead to sickle crises, including hypoxia (altitude), surgery, trauma, cold, infections and dehydration, should be sought.

A3: What are the possible clinical signs?

Anaemia (pallor, tachycardia, tachypnoea) is universal as a result of chronic intravascular haemolysis. Acute sickle-cell crisis is caused by acute occlusion of the microcirculation, leading to tissue hypoxia and organ infarction on a background of intravascular red cell haemolysis. Clinical signs are highly variable, depending on the predominantly affected organ. Acute pain – bony (e.g. long bones, vertebrae, ribs) or abdominal (e.g. spleen, liver, gut infarction) – is very common. Splenomegaly is common in young children, but ultimately splenic infarction leading to hyposplenism supervenes. Cerebral vessel occlusion can manifest as hemiparesis, paraparesis, fits, loss of or reduced consciousness and blindness. The combination seen in this patient of fever, leucocytosis, dyspnoea, chest pain and pulmonary infiltrate is often referred to as 'acute chest syndrome'. The clinical and chest radiograph findings are non-specific and hence do not distinguish sickling within the chest from a chest infection.

Chronic sickle-cell disease leads to ischaemic necrosis of joints and secondary arthritic changes. High-output cardiac failure as a result of a combination of chronic anaemia, myocardial and pulmonary microinfarction often leads to premature death. Renal impairment caused by papillary necrosis and proliferative retinopathy is a late manifestation. Hepatomegaly is usually modest, but pigmented gallstones and biliary disease are common. Leg ulcers are a common typical feature.

A4: What additional investigations are indicated?

First you need to confirm the diagnosis of sickle-cell disease. This is most easily done by looking at the blood film. Blood film changes of hyposplenism (target cells, Howell–Jolly bodies, thrombocytosis) will also be seen. The presence of HbS can be confirmed with a Sickledex test and Hb electrophoresis.

A5: What is the treatment?

General measures to treat any underlying precipitating factor (e.g. analgesia, antibiotics, rehydration, oxygen therapy) are essential. The patient should be anticoagulated with heparin (unless contraindicated) because she has a very high risk of thrombosis.

Blood transfusion of red cells dilutes HbS, improving microvascular circulation and oxygen delivery; it also temporarily suppresses HbS production. Partial exchange transfusion is usual.

All patients with sickle-cell disease should take oral folic acid. Regular blood transfusions of red cells to keep the level of HbS below 30 per cent will effectively prevent crises occurring. As long-term blood transfusions are potentially very hazardous, this approach should probably be reserved for high-risk periods, such as before surgery or during pregnancy.

Hydroxyurea (hydroxycarbamide) increases production of HbF, which has a protective effect on sickling cells and reduces crises.

Patients with sickle-cell disease are hyposplenic and should therefore receive pneumococcal, meningococcal C and *H. influenzae* immunization and life-long penicillin. Allogeneic haematopoietic stem cell transplantation is potentially curative but carries a high risk. It may have a role in selected patients, such as children with strokes.

A6: What is the long-term outcome?

In the developing world many patients with sickle-cell disease die in childhood from crises or infection. With good medical care, many patients survive into middle age.

OSCE counselling case

OSCE COUNSELLING CASE 9.3 – If two parents who are carriers of sickle-cell disease have three children, what is the chance of no child being a carrier or suffering from full-blown sickle-cell disease?

As sickle-cell disease is an autosomal recessive condition, each parent must have one normal gene and one sickle gene. Thus, each individual child has a one in four chance of not being a carrier and not having sickle-cell disease. Thus, the chance of all three children not being carriers or having full-blown sickle-cell disease is $1/4 \times 1/4 \times 1/4 = 1$ in 64.

REVISION PANEL

- Iron deficiency occurs when iron intake/absorption does not balance iron loss, i.e. bleeding. A thorough history is essential to establish the aetiology of the iron deficiency and direct investigations.
- Macrocytic anaemia with neurological deficit is pernicious anaemia until proved otherwise.
- A raised globulin should always raise the possibility of underlying myeloma.
- Very high white counts are a medical emergency, and urgent assistance from a haematologist is essential.
- Polycythaemia is very common and needs to be properly investigated and the correct management instituted.
- Shock in the setting of marrow failure (neutropenia) should always be suspected to be due to sepsis and treated immediately with broad-spectrum antibiotics.
- Always remember that normal ranges may differ between different ethnic groups.
- Thalassaemia should be considered in any patient presenting with microcytic anaemia from one of the high thalassaemia prevalence areas of the world.
- Sickle-cell crisis is a medical emergency with a high rate of potential complications. Advice from a clinician experienced in looking after patients with sickle-cell disease should be sought.

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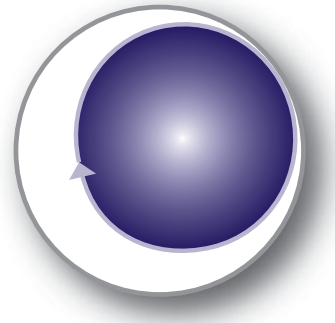

10 Oncology emergencies

Daniel Rea

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely diagnosis?
Q2: What aspects of the physical examination are most relevant?
Q3: What investigations would be performed?
Q4: How would the diagnosis be confirmed?
Q5: What would be the initial management?
Q6: What issues need to be addressed following acute management?

CASE 10.1 – A 66-year-old man complains of recent-onset bilateral leg weakness, polydipsia, constipation and difficulty passing urine.

A 66-year-old man has been sent to the accident and emergency (A&E) department with a 10-day history of progressive lower limb weakness. In addition, he complains of low thoracic back pain. He complains of frequency and difficulty passing urine, constipation and excessive thirst. He was diagnosed with early prostate cancer 2 years ago and is being treated with goserelin, a luteinizing hormone-releasing hormone (LHRH) agonist. In other respects, he is in good health. He lives alone in a second-floor flat.

CASE 10.2 – A 48-year-old woman develops fever 10 days after adjuvant chemotherapy for early breast cancer.

A 48-year-old woman presents to A&E while visiting a relative. She complains of feeling unwell and has a temperature of 38 °C. She underwent a mastectomy and reconstructive surgery 6 weeks earlier for a node-positive invasive breast cancer. Ten days ago she started her first cycle of a planned programme of chemotherapy at a hospital 200 miles away. She does not know what drugs she was given. She is normally fit and well with no other medical complaints. She has a respiratory rate of 24/min, her pulse is 120 beats/min and her blood pressure is 95/60 mmHg.

CASE 10.3 – A 59-year-old smoker has dyspnoea and arm and facial swelling.

A 59-year-old man presents to his general practitioner (GP) with a 1-week history of progressive facial swelling, swelling of both arms, and shortness of breath on climbing a flight of stairs. He has smoked 20 cigarettes a day for 40 years and works as a garage foreman. He is sent to A&E following a chest radiograph that shows a widened mediastinum and a right hilar mass. He had a previous chest radiograph 6 months earlier, which was normal apart from some patchy shadowing in the left midzone, which is no longer present.

OSCE counselling cases

OSCE COUNSELLING CASE 10.1 – **'How will I cope at home if complete recovery is not achieved?'**

The 66-year-old man with prostate cancer and leg weakness, described in Case 10.1, is now clinically stable and awaiting imaging investigations. He is aware of the likely cause of his symptoms and signs.

OSCE COUNSELLING CASE 10.2 – **'How long have I got to live?'**

The patient in Case 10.1 asks how long he has to live.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

- Cytotoxic chemotherapy involves the use of drugs with a narrow therapeutic index, so side effects are common and can be life-threatening.
- Prompt intervention usually results in complete resolution of acute toxicity, but late toxicities may be slow to resolve or irreversible.
- As acute toxicity is reversible, aggressive management of severe complications is appropriate, even in patients with advanced incurable malignancy.
- Short-term neutropenia is very common after cytotoxic chemotherapy of common solid malignancies, but it requires intervention only when accompanied by infection. When the risk of febrile neutropenia is high, primary or secondary prophylaxis with growth factors will reduce the risk of neutropenic complications.
- Acute complications of malignancy require prompt assessment and, where invasive intervention is appropriate, this should be introduced as soon as possible to relieve symptoms and limit the extent of damage and disability. Supportive care and symptom relief should be introduced immediately. Acute complications of malignant disease rarely resolve completely and often mark a transition into a new phase of the patient's illness. Careful assessment of the consequences of a new complication is required and may have implications for future prognosis, physical and psychological health. They usually indicate failure of current therapy and indicate a need to review this.

Answers

Clinical cases

CASE 10.1 – A 66-year-old man complains of recent-onset bilateral leg weakness, polydipsia, constipation and difficulty passing urine.

A1: What is the likely diagnosis?

A1: The likely diagnosis is spinal cord compression secondary to bone metastasis from prostate cancer that has become refractory to first-line endocrine therapy. This is complicated by hypercalcaemia as a result of widespread bone involvement.

A2: What aspects of the physical examination are most relevant?

- hydration status
- functional status (how well can the patient walk?)
- presence of spinal tenderness
- presence of a sensory level
- degree and extent of lower limb weakness, muscle tone and reflexes
- sacral sensation, anal tone and presence of clinically detectable bladder distension.

A3: What investigations would be performed?

- whole-spine magnetic resonance imaging (MRI)
- urea and electrolytes (U&Es)
- creatinine, calcium, albumin and prostate-specific antigen (PSA)
- full blood count (FBC) and international normalized ratio (INR).

A4: How would the diagnosis be confirmed?

Whole-spine MRI will identify the presence and level of spinal cord compression. Imaging of the whole spine will identify additional lesions that will affect decision-making and permit treatment planning. Corrected serum calcium will establish the presence of hypercalcaemia, which may be accompanied by biochemical evidence of dehydration and renal failure.

A5: What would be the initial management?

- high-dose dexamethasone
- intravenous (IV) rehydration, followed by IV bisphosphonate
- catheterization if in retention
- spinal decompression and stabilization as treatment of choice if technically achievable and multiple levels of compression excluded
- urgent radiotherapy to the sites of compression if surgery is contraindicated.

A6: What issues need to be addressed following acute management?

The prognosis after spinal cord compression is generally poor, with a median survival of 12 months. Functional status is superior for patients treated surgically, however. Postoperative radiation will be required, and second-line options for treatment for advanced prostate cancer should be considered, such as chemotherapy or second-line hormone therapy. Rehabilitation after treatment will depend on the degree of neurological recovery and may require extensive physiotherapy. Physiotherapy, occupational therapy and nursing assessment of the patient and his home environment will be required to facilitate discharge planning. Home adjustments or relocation may be needed. Ongoing monitoring of hypercalcaemia and maintenance bisphosphonates are needed. Long-term control may be achieved with oral bisphosphonates but, if unsuccessful, regular IV bisphosphonates are required.

CASE 10.2 – **A 48-year-old woman develops fever 10 days after adjuvant chemotherapy for early breast cancer.**

A1: What is the likely diagnosis?

This is very likely to be neutropenic sepsis. Virtually all cytotoxic drugs cause myelosuppression, and infection is a frequent complication of myelosuppression. Infection can progress rapidly and may be fatal if uncontrolled.

A2: What aspects of the physical examination are most relevant?

Examination should focus on assessment of the severity of presumed infection and the potential source of infection. Vital signs should be confirmed. Surgical wounds should be examined, including donor sites for reconstruction. Respiratory and abdominal examinations are important. Examination of the oral cavity and perineal area should be performed, noting ulceration and the presence of candidiasis. The peripheral circulation should be assessed and any evidence of widespread bleeding noted such as ecchymoses or petechiae.

A3: What investigations would be performed?

- FBC, including differential white blood cell count (WCC)
- arterial blood gases (performed after platelet count has confirmed this is safe)
- blood cultures, including separate cultures from indwelling lines
- U&Es and creatinine C-reactive protein (CRP)
- urine culture and swabs from any open wounds
- chest radiograph
- sputum culture if produced.

A4: How would the diagnosis be confirmed?

Neutropenia will be confirmed by blood count. Arbitrarily, neutropenia is defined as an absolute neutrophil count below 1.0×10^9/L. Associated thrombocytopenia may also be present; if detected, coagulation status should be assessed, including D-dimers, because disseminated intravascular coagulation can complicate severe sepsis.

A5: What would be the initial management?

Rapid IV fluids should be commenced initially using plasma expanders where hypotension is present. Broad-spectrum IV antibiotics should be administered using the regimen recommended by the local hospital neutropenic sepsis policy. Where a source of infection is suspected, such as a respiratory focus, secondary antibiotics should be added, again following the local protocol. An allergy history should be obtained and a recent antibiotic history noted, which may influence drug choice. Pulse oximetry

and blood gas evaluation may indicate the need for oxygen supplementation. The patient should be catheterized if she is not passing urine freely or if hypotension persists after fluid load. If hypotension does not respond adequately to fluid load, the patient should be managed in a high-dependency or intensive care environment. Inotropic support may be required to maintain adequate cardiac output. Severe metabolic acidosis may require correction, and artificial ventilation may be needed. The use of granulocyte colony-stimulating factors (G-CSFs) in established neutropenic sepsis is controversial but is commonly given to patients with severe sepsis and marked neutropenia. The requirement for IV antibiotics and length of inpatient stay is reduced. Patients with low-risk febrile neutropenia without sepsis and moderate neutropenia above 0.5×10^9/L can be discharged early, provided adequate support is available

A6: What issues need to be addressed following acute management?

Neutropenic sepsis in solid tumours (non-leukaemic) usually responds promptly to standard treatment, and most patients make a full uncomplicated recovery after the return of normal neutrophil function. Intravenous antibiotics are generally administered for at least 24 h after resolution of fever, with appropriate oral antibiotics thereafter until all signs of infection have resolved. If fever does not settle within 48 h, full clinical review should take place. Repeat cultures should be taken, microbiological advice sought and a change in antibiotics considered. The possibility of a viral or fungal infection should also be considered and treated if appropriate. The treating oncologist should be notified of the details of the episode and will need to take all the patient's circumstances into account when deciding appropriate modification of the treatment programme. Consideration of dose reduction or prophylaxis against future neutropenic sepsis is an appropriate strategy if further chemotherapy is used.

CASE 10.3 – **A 59-year-old smoker has dyspnoea and arm and facial swelling.**

A1: What is the likely diagnosis?

This is superior vena cava obstruction (SVCO) secondary to malignancy. The patient's smoking history and the rapid appearance of the radiological abnormality make the most likely diagnosis small cell lung cancer, but it is not possible to reliably exclude a non-small cell lung cancer or a high-grade lymphoma. The symptoms could be caused by venous thrombosis, although this does not explain the abnormal radiology. There may be associated thrombus.

A2: What aspects of the physical examination are most relevant?

Full examination is required but should focus particularly on the respiratory and circulatory systems. The presence of clubbing should be noted, and the chest and upper body should be examined for venous distension and diversion. The neck veins should be examined and the degree of facial swelling noted. Periorbital swelling may be present, and the patient's ability to close his eyes should be assessed. A paradoxical pulse and reduced-output state may indicate coexistent cardiac tamponade. Examination of the entire body for evidence of metastatic deposits is required. Lymph node masses and liver involvement may help with identification of source for histological confirmation and assist staging assessment.

A3: What investigations would be performed?

Computed tomography (CT) will define the mediastinal abnormality more accurately than chest radiograph and identify areas of external compression and associated thrombus. Computed tomography should include the abdomen to complete staging of the malignancy. Phlebography will establish patency of the superior vena cava and should be performed in conjunction with percutaneous stent insertion. Bronchoscopy should be performed to obtain a tissue diagnosis and indication of the presence of a primary bronchogenic neoplasm. Full blood count, INR, U&Es, creatinine, calcium and liver function tests

are useful ancillary investigations; low sodium could indicate syndrome of inappropriate antidiuretic hormone secretion (SIADH), which would favour a diagnosis of small cell lung cancer. High calcium would indicate a possible squamous cell carcinoma or bone involvement. Tumour markers are of modest value, a high carcinoembryonic antigen (CEA) level being indicative of a probable adenocarcinoma, and a high lactate dehydrogenase (LDH) possibly indicating a lymphoid malignancy.

A4: How would the diagnosis be confirmed?

Phlebography or CT will confirm the clinical diagnosis of SVCO, but both may be needed for complete evaluation. Histological diagnosis of the type of malignancy can usually be obtained at bronchoscopy, but if no malignancy is seen CT-guided biopsy or mediastinoscopy may be required to sample areas of suspected malignancy. An accurate tissue diagnosis is increasingly important, as treatment is increasingly tailored towards tumour type. Molecular markers are used in assessing the potential benefit of targeted therapies. The most important reason for a tissue diagnosis in this case is to identify or rule out a potentially curable condition such as high-grade lymphoma.

A5: What would be the initial management?

Radiologically guided stent placement provides the optimal means to palliate SVCO, resulting in rapid relief of symptoms. Anticoagulation should commence after stent placement. High-dose corticosteroids may provide temporary relief of symptoms but could make interpretation of lymphoma histology more difficult and should therefore be avoided if possible until a tissue diagnosis has been obtained. The underlying disease should be treated correctly. A bulky high-grade lymphoma causing SVCO should be treated initially with chemotherapy, which may be curative. A small cell lung cancer has a high response rate to chemotherapy, and localized disease will respond well to radiotherapy, but treatment is non-curative. Non-small cell lung cancer presenting with SVCO is very unlikely to be amenable to surgical resection but can be usefully palliated by either chemotherapy or radiotherapy.

A6: What issues need to be addressed following acute management?

Assuming that this patient does indeed have small cell lung cancer, stenting should successfully relieve the obstruction and he will start to respond to chemotherapy. The long-term outlook is bleak, however, with a median survival of around 12 months. The patient may need psychological support and help adjusting to his fatal prognosis. He may need to retire on ill-health grounds and require help accessing appropriate financial support. Irrespective of his physical requirements, he and his family or close friends should be seen by a lung cancer support nurse or specialist palliative care nurse (Macmillan Nurse), who can help explore all of the above issues and help him access appropriate support as and when required. Close communication between hospital and community-based care is essential for the optimal future management of this patient. If an alternative diagnosis such as adenocarcinoma of the bronchus is reached, then the options for additional palliative treatment with biological agents such as epidermal growth factor receptor (EGFR) antagonists will need to be assessed by mutational analysis of the EGFR gene.

OSCE counselling cases

OSCE COUNSELLING CASE 10.1 – 'How will I cope at home if complete recovery is not achieved?'

The reality is that complete recovery after spinal cord compression is unusual unless diagnosed very early, when minimal cord damage has taken place. In the case described, it is very difficult to predict the outcome. The patient is likely to be shocked and frightened by the diagnosis and needs time to adjust to the change in circumstances. It is reasonable to suggest that detailed discussion be deferred until the extent of residual deficit is known, so there can be a realistic assessment of what the patient will be able to do and how independent he will be. In discussing treatment options, the patient can expect to have the best- and worst-case scenarios described and an indication of how likely any of the possible outcomes are. Rather than guess at these, it is entirely appropriate to request specialist assistance at this stage.

OSCE COUNSELLING CASE 10.2 – 'How long have I got to live?'

All doctors encountering patients with terminal malignant disease will be asked this question. The atmosphere and environment in which this issue is discussed are important. An explanation that the answer is complicated and will take time is acceptable, provided that you return soon; where possible, anticipating the question that is going to be asked will allow you to control the circumstances.

You need to establish that the patient is ready to discuss this question and that you are sure that he wishes to hear an answer to the question. The patient may be expressing a whole series of anxieties about the terminal illness and not really wish to be confronted with a direct answer in weeks or months. Ensure that the patient has the appropriate support from relatives or friends. If this is not possible, an additional member of staff who knows the patient well should be present and willing to stay with him or her after you leave. It is important to find time to talk about the question and the patient's reaction to your answers.

You should explain that estimating prognosis is inaccurate on an individual basis, with wide variations between patients. Ask the patient to tell you what he thinks the prognosis may be; you can then guide him forwards or backwards in his estimate. Avoid being too specific by providing a median survival figure; giving a sensible range is a better way to illustrate the likely prognosis. You will need to gauge how the patient is reacting during the conversation, taking things more slowly when he displays unease. Avoid becoming a source of unrealistic expectations, but always try to conclude the discussion on an optimistic aspect of the consultation.

REVISION PANEL

- Spinal cord compression from metastases may present with difficulty walking and 'off legs'. If in doubt, an urgent MRI should be performed and treatment commenced with dexamethasone.
- Neutropenic sepsis should be considered in any febrile patient receiving cytotoxic therapy. Virtually all cytotoxic drugs cause myelosuppression, and infection is a frequent complication of myelosuppression. Infection can progress rapidly and may be fatal if uncontrolled.
- Neutropenia will be confirmed by blood count. Arbitrarily, neutropenia is defined as an absolute neutrophil count below 1.0×10^9/L. Thrombocytopenia and anaemia may also be present and must be treated accordingly.
- Superior vena cava obstruction is an emergency and should be considered in a smoker with progressive facial swelling, swelling of both arms and shortness of breath. A CT scan of the chest will establish the diagnosis.

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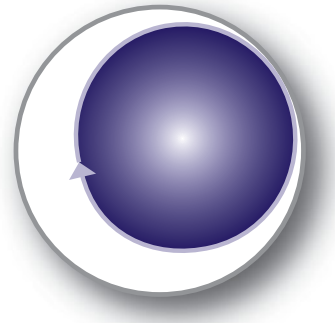


11 Neurology

Stuart Weatherby

DISORDERS OF CONSCIOUSNESS

CEREBROVASCULAR DISEASE

DISEASES OF PERIPHERAL NERVES

HEADACHE

CENTRAL NERVOUS SYSTEM DEMYELINATION

DISORDERS OF CRANIAL NERVES

MOVEMENT DISORDERS

MISCELLANEOUS NEUROLOGICAL DISORDERS

DISORDERS OF CONSCIOUSNESS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What are the issues that need to be discussed with a patient newly diagnosed with epilepsy?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.1 – A 58-year-old previously well man suffers an episode of loss of consciousness just after leaving the golf club bar with his friends.

The patient smells of urine, seems a bit dazed, has a mild headache and feels achy but otherwise is normal. He cannot recall anything about the incident. He is a smoker.

CASE 11.2 – A 24-year-old woman who is known to have epilepsy started fitting after a family argument. An ambulance was called.

The ambulance team tell you that when they arrived at the hospital the patient had been fitting for 30 min. She is still fitting when she arrives in hospital and appears non-responsive. Her body is thrashing violently on the bed. Her eyes are screwed tightly shut. Her oxygen saturation is 99 per cent air. Her pupils react to light and her plantar responses are down-going. The rest of the examination is normal.

CASE 11.3 – A 21-year-old woman presents with a history of an episode of loss of consciousness 3 months ago.

The patient is otherwise well and plays hockey for the university's first team. Her friends witnessed her loss of consciousness and have come to the clinic with her. The event occurred while she was socializing in a hot and busy pub. After standing for 25 min waiting to be served at the crowded bar, she felt light-headed and became very pale and sweaty, her vision darkened and she crumpled down on to the floor. She was unrousable for a few seconds but then came round quickly, with no confusion. While she was unrousable, her limbs were observed to jerk two or three times. A medical student who was in the pub told her that she had had an epileptic 'fit'. Examination is normal and no postural blood pressure drop is noted.

OSCE counselling case

OSCE COUNSELLING CASE 11.1 – **'Will the epilepsy have any future implications for me?'**

A 22-year-old woman is admitted to hospital following a witnessed epileptic seizure. What are the issues that need to be discussed with a patient newly diagnosed with epilepsy?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

OVERVIEW OF EPILEPTIC SEIZURE TYPES

The classification of epileptic seizures can seem confusing, because multiple terms are used. Seizure type can be described on the basis of the clinical phenotype or on the basis of the underlying aetiology. The following simplified classification permits an understanding of the relevance of various terminologies. There are two main types: generalized and focal (see www.ilae-epilepsy.org/ctf/over_frame.html for more details).

- *Focal seizures:* only part of the brain (the focus) is affected. Consciousness is not lost, although it may be impaired. Partial seizures are sometimes called 'localization-related seizures', because an underlying structural abnormality is implied.
- *Generalized seizures:* the 'whole brain' is affected, and the key clinical feature is loss of consciousness. A generalized seizure may involve the whole brain at onset (primary generalized seizure – the whole brain has a predisposition to seizure) or may start as a focal seizure that then spreads to involve the whole brain (secondary generalized seizure).

In most adults, epilepsy is of a focal nature, with or without secondary generalization. Structural lesions should be excluded (space-occupying lesions and cerebrovascular disease are more common in elderly people; minor structural lesions, including scarring, focal areas of atrophy and cryptogenic foci, are more common in younger adults).

Initial onset of primary generalized seizures is rare outside of childhood and young adulthood. Although paediatric and rare epilepsy syndromes are outside the scope of this text, it is useful to briefly discuss juvenile myoclonic epilepsy. This is primary generalized epilepsy that usually starts in childhood or adolescence. It is associated with brief episodes of myoclonus (brief generalized single body jerks). Juvenile myoclonic epilepsy requires life-long treatment.

The generalized seizures can be subdivided on phenotypic grounds rather than on the basis of underlying aetiology:

- *convulsive tonic–clonic (generalized convulsions)* – loss of consciousness and tonic and clonic phases of muscular contractions
- *absence type (absence seizures)* with sudden immediate and short-lived loss of consciousness and no loss of postural tone
- *other generalized seizure types* – e.g. myoclonic (this may be brief generalized single body jerks, often throwing the individual to the ground) and atonic (sudden loss of postural tone with collapse to the ground – 'drop attack').

The focal seizures can also be subdivided on phenotypic grounds:

- focal motor seizures
- focal sensory seizures
- secondary generalized seizures.

MANAGEMENT OF PROLONGED SEIZURES AND STATUS EPILEPTICUS

Secure airway, give oxygen, assess cardiac and respiratory function, and give intravenous (IV) benzodiazepine. Carers in the community may be able to terminate serial seizures by giving rectal diazepam or lorazepam. In the hospital setting, IV lorazepam 4 mg (or diazepam 10 mg) is more appropriate and should be given again after 10 minutes if there is no response. If there is a history of alcohol abuse, IV thiamine should be administered. If there is any suspicion of hypoglycaemia, 50 mL 25% glucose should be given intravenously. (Note that glucose given alone in a patient with alcohol problems can precipitate Wernicke's encephalopathy.)

If fitting persists, the patient should receive phenytoin 18 mg/kg IV at a rate not exceeding 50 mg/min, followed by maintenance doses of about 100 mg every 6–8 h. An alternative is fosphenytoin, a phenytoin pro-drug prescribed in terms of phenytoin equivalent. If fitting persists after 30 min, the patient should be transferred promptly to intensive care for more aggressive treatment to control seizures (e.g. with phenobarbital). It is crucial to diagnose and treat the underlying cause of the seizures and to recognize any associated injuries or complications (e.g. aspiration pneumonia).

Answers

Clinical cases

CASE 11.1 – A 58-year-old previously well man suffers an episode of loss of consciousness just after leaving the golf club bar with his friends.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are generalized seizure and syncope. In this situation there is very little history on which to base a diagnosis, but it is a commonly occurring scenario. The differential diagnosis essentially breaks down into causes of seizure and causes of syncope. Causes for transient loss of consciousness include the following:

- epilepsy
- cardiac:
  - arrhythmia
  - decreased cardiac output from mechanical causes, e.g. outflow obstruction
- hypovolaemia
- hypotension:
  - vasovagal attack
  - drugs
  - dysautonomia
- vascular:
  - carotid sinus syncope
  - carotid disease
- metabolic:
  - hypoglycaemia
  - anaemia
  - anoxia
- multifactorial:
  - vasovagal
  - cardiac syncope
  - cough syncope
  - micturition syncope.

A2: What issues in the given history support or refute a particular diagnosis?

The fact that the patient smells of urine, seems a bit dazed, has a mild headache, feels achy, and cannot recall anything about the incident is most consistent with a generalized convulsive seizure.

Seizures may be classified as generalized (consciousness lost) or partial (consciousness not lost). There is also a variant of partial seizures (complex-partial) in which consciousness is impaired. Epilepsy subtypes are briefly reviewed in 'Key concepts' above.

A3: What additional features would you seek to support a particular diagnosis?

The diagnosis of causes of loss of consciousness is fundamentally a clinical issue and based primarily on an accurate history. Insufficient history may be one reason that the misdiagnosis rate for epilepsy is

so high (up to 26 per cent in one population-based study, the most common conditions mistaken for epilepsy being syncope and non-epileptic seizures). A corroborative history is essential.

Although the patient says he cannot remember anything about the incident, he should be questioned closely to try to find out how he felt just before he lost consciousness. Did the event truly begin abruptly (consistent with a seizure), or did he feel strange or have *déjà vu* or *jamais vu* symptoms beforehand? (These symptoms are suggestive of a complex-partial seizure that may have then become generalized.) Did he develop a shaking in one side that progressed before he lost consciousness? (These symptoms suggest a partial motor seizure that became generalized.) Alcohol is known to provoke seizures and, as the patient had the event after leaving the golf club bar, he may have been drinking alcohol. Medical problems such as hypoglycaemia in diabetes mellitus can also provoke seizures. A comprehensive past medical and drug history should be obtained. As the patient is a smoker, it is important to question him for constitutional symptoms such as weight loss and cough with haemoptysis.

Witnesses should be interviewed (with the patient's permission) to get a description of the events.

- *What were the circumstances?* In generalized seizures, the event occurs abruptly, frequently without warning, and is not related to posture. The patient often appears normal before the event. In syncope, the patient often feels light-headed beforehand. Some types of syncope are related to circumstances, e.g. standing suddenly (postural hypotension), coughing (cough syncope), urination (micturition syncope – generally in men), in association with palpitations (syncope related to arrhythmia) or anxiety (e.g. in vasovagal syncope).
- *What did the patient look like?* Generalized seizures are usually of a tonic–clonic type and the patient tends to fall stiffly (tonic) and then start a coarse generalized limb shaking (clonic). This tends to go on for around 30 s, during which the patient is unresponsive to all stimuli. If examined during this period, the pupils are unreactive to light and the plantar responses are up-going. The patient may bite his tongue and be incontinent of urine. When the patient regains consciousness, he is often confused (postictal confusion) with aching muscles and a headache. In generalized seizures, the patient may be cyanosed or look normal. It is common for oxygen saturations to be low during a prolonged generalized tonic–clonic epileptic seizure. Often convulsive seizures of this type occur singly or in groups of two or three. Prolonged series of such seizures without regaining consciousness in between is called convulsive status epilepticus and requires urgent treatment. In syncope, the patient often appears pale shortly before and during the event. The period of loss of consciousness tends to be very brief (seconds). There is no confusion afterwards.

A4: What clinical examination would you perform, and why?

- Look in the patient's mouth for evidence of tongue biting (this can occur during a generalized seizure).
- A common cause for seizures in this age group is cerebrovascular disease. Evidence of ischaemic heart disease should be sought. Postural hypotension, arrhythmia and cardiac murmurs can also be associated with syncopal events.
- Neurological examination should concentrate on looking for lateralizing signs. These may occur as a result of a focal cerebral lesion, e.g. from a stroke or a space-occupying lesion. Fundoscopy, if it identifies papilloedema, suggests the presence of raised intracranial pressure from a space-occupying lesion.
- The patient smokes, so the possibility of a cerebral metastasis from a bronchogenic carcinoma should be considered.
- If there is a history of alcohol excess, it is important to assess for signs of chronic liver disease.

A5: What investigations would be most helpful, and why?

- *BM stick* – allows rapid measurement of glucose

- *electrocardiogram (ECG)* – should be done in all patients because epilepsy and cardiac causes of loss of consciousness can be difficult to distinguish; if arrhythmias are suspected, a 24 h ECG is helpful
- *full blood count (FBC)* – anaemia and infection can provoke seizures
- *urea and electrolytes (U&Es) and calcium* – hyponatraemia and hypocalcaemia in particular can provoke seizures
- *blood glucose* – hypoglycaemia can provoke seizures
- *brain imaging* – computed tomography (CT) of the brain will exclude a space-occupying lesion and may identify evidence of cerebrovascular disease, and it is often used for rapid assessment; magnetic resonance imaging (MRI) of the brain is better at identifying small structural lesions and is the brain imaging modality recommended by many authorities.

Electroencephalography (EEG) should be performed in all patients to support the diagnosis of epilepsy in patients with a suitable history and to help with seizure classification and localization. It is important to note that a 'normal' EEG does not exclude epilepsy, and a 'non-specifically abnormal' EEG does not necessarily imply an underlying significant neurological problem. Diagnosis of epilepsy is based primarily on a clear history. One reason for the high rate of misdiagnosis in epilepsy may be inappropriate interpretation of the EEG result. A single resting EEG shows abnormalities in only 50 per cent of patients with epilepsy. Sensitivity increases if the EEG is done within 24 h of a seizure, repeated or performed after sleep deprivation. Most useful of all is if the EEG can be performed during a seizure with video monitoring of the patient (video-telemetry). Conversely, normal phenomena, artefacts and non-specific abnormalities, occurring in about 20 per cent of the general population, are open to misinterpretation and may yield false-positive results. Correct analysis of the EEG is dependent on the context in which it is performed. If an EEG is requested as a screening tool for a patient with, for example, 'funny turns', it may yield minor abnormalities and cause more diagnostic uncertainty than it solves.

A6: What treatment options are appropriate?

This patient is likely to have suffered a secondary generalized seizure, but a diagnosis of epilepsy cannot be made on the basis of a single seizure. Infection, drugs and metabolic problems can provoke seizures. Anti-epileptic drugs (AEDs) are therefore not usually started after a first seizure unless the risk of recurrence is thought to be high. Epilepsy may be viewed as a chronic neurological condition characterized by recurrent unprovoked seizures. The nature of the seizures depends on which brain structures are affected.

Anti-epileptic drugs are usually started after the second seizure. Current indications and side-effect profiles for the various AEDs are readily available in the British National Formulary. The principles of treatment are addressed and commonly used first-line monotherapy agents are discussed in brief.

A treatment should be effective, with minimal side effects for the patient. At present there is no clear consensus as to where the balance between efficacy and side effects lies. In circumstances where there is no urgency to start treatment, the decision should ideally be made jointly by the patient and a neurologist. Potentially acceptable side effects will differ from patient to patient; there are particular issues when prescribing for women, because drug interactions with the oral contraceptive pill, safety in pregnancy and breastfeeding need to be taken into account. The aim of treatment is to control seizures with a single agent (monotherapy), although a small proportion of patients may eventually require more than one AED.

There are now a large number of AEDs (including phenytoin, sodium valproate, carbamazepine, lamotrigine, levetiracetam, topiramate, oxcarbazepine, tiagabine and phenobarbital, to name but a few). Some are licensed for use only as adjuncts (i.e. as an add-on treatment in patients with difficult-to-treat epilepsy) and should not be initially used as monotherapy.

At present, commonly prescribed first-line monotherapy AEDs in patients who do not require urgent treatment include sodium valproate, lamotrigine and carbamazepine. Lamotrigine and sodium valproate are accepted as suitable for primary generalized seizures, partial/secondary generalized seizures, and epileptic seizures of uncertain nature. Carbamazepine is not generally used for primary generalized seizures because it may worsen this seizure type significantly.

CASE 11.2 – **A 24-year-old woman who is known to have epilepsy started fitting after a family argument. An ambulance was called.**

A1: What is the likely differential diagnosis?

Non-epileptic seizure disorder is overwhelmingly likely in this scenario. Before making this diagnosis, however, it is important to be confident that the other important diagnosis of prolonged generalized tonic–clonic seizure (status epilepticus) has been excluded. Status epilepticus is defined as continuous epileptic seizures for more than 30 min or recurrent seizures over 30 min with failure to regain consciousness in between events. Untreated, status epilepticus carries a high mortality; it occurs in 3–7 per cent of patients with epilepsy.

A2: What issues in the given history support or refute a particular diagnosis?

A2: Onset during a stressful event can be suggestive of a psychogenic factor. Epileptic seizures can be triggered by stressful events, however, so this feature is rather non-specific. The fact that the patient is known to have epilepsy does not support either an epileptic or a non-epileptic aetiology. A significant number of patients (about 30 per cent) have mixed epileptic and non-epileptic seizure disorders.

What additional features would you seek to support a particular diagnosis?

This case demonstrates the importance of making a diagnosis before starting potentially dangerous treatments. Non-epileptic seizure disorder is considered to have a psychogenic basis. Non-epileptic attacks are found to be most common in women aged 20–50 years. Factors that may play a part in their onset often include a personal or family history of psychiatric disorder or depression, previous significant life events such as bereavement, or a history of physical, sexual or emotional abuse.

A4: What clinical examination would you perform, and why?

The fact that the patient's eyes are tightly shut suggests a volitional component to the muscle activity. This would not be expected to occur in status epilepticus. Wild thrashing, hip thrusting, normal pupillary responses, normal oxygen saturations and normal plantar responses are suggestive of non-epileptic seizures. The patient may respond to deep pain stimuli during the seizure. In status epilepticus, the patient is completely unresponsive.

A5: What investigations would be most helpful, and why?

An EEG should be done. Although it seems rather self-evident, it is important to emphasize that non-epileptic seizures are *not* epileptic seizures. Correct identification of non-epileptic seizures is particularly important to prevent inappropriate transfer to intensive care for epilepsy management. An EEG performed during the seizure will be normal in a non-epileptic seizure but would be expected to show epileptiform discharges during generalized status epilepticus. Serum prolactin is often elevated during and shortly after a prolonged generalized tonic–clonic seizure. It is not generally significantly elevated by a non-epileptic seizure. It should be remembered, however, that prolactin levels can also be increased by drugs (e.g. phenothiazines). This can occasionally cause diagnostic confusion.

A6: What treatment options are appropriate?

Patients with non-epileptic seizure disorder require a psychotherapeutic approach to help control their condition. The fits self-terminate. Status epilepticus is a potential differential diagnosis in this situation; the management of status epilepticus is outlined in 'Key concepts' above.

CASE 11.3 – **A 21-year-old woman presents with a history of an episode of loss of consciousness 3 months ago.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are syncope (simple faint – vasovagal syncope), cardiac arrhythmias, hypoglycaemia, hyperventilation, drug-related or -provoked, and epilepsy. This history is highly suggestive of syncope and is most likely to be a vasovagal event.

A2: What issues in the given history support or refute a particular diagnosis?

The symptoms related to posture, and the fact that the patient became pale and felt light-headed before losing consciousness (i.e. a relatively long premonitory period), suggest impairment of cerebral blood flow. The facts that the patient crumpled to the floor rather than falling stiffly, and that loss of consciousness was very short-lived and with rapid recovery, are also highly suggestive of a syncopal event.

The circumstances of the events (a hot, crowded situation) are highly suggestive of vasovagal syncope. The fact that the patient is otherwise very active would suggest that a primary cardiac arrhythmogenic or structural lesion is less likely (although it does not entirely exclude it).

A few short-lived and transient limb-jerking movements are compatible with a syncopal event (and are *not* diagnostic of epilepsy), although longer-lasting jerking movements of the limbs are more suspicious of epileptic seizures.

A3: What additional features would you seek to support a particular diagnosis?

Is there is a past or family history of epilepsy or heart problems? Did the patient have palpitations before the event (more suggestive of an arrhythmia)? Was there any incontinence or tongue biting with the episode of loss of consciousness? This is common with epileptic seizures but not in syncope.

Remember that a patient may not volunteer aspects of a history that are potentially embarrassing, and direct questioning may be needed to elicit this information.

A4: What clinical examination would you perform, and why?

One would not usually expect to find any abnormalities in the general or neurological examination. During examination, however, particular attention should be paid to excluding abnormalities in the cardiac system (e.g. arrhythmias, heart murmurs). A postural blood pressure drop may sometimes be found.

A5: What investigations would be most helpful, and why?

An ECG would help to further discount the (unlikely) possibility of a primary cardiac/arrhythmogenic cause. Otherwise, no other investigations are necessary at present.

Importantly, an EEG is not indicated; if performed, it may complicate matters – a substantial proportion of 'normal' EEGs may show minor alterations in wave morphology that can confuse the unwary.

If the patient has further events, further investigation with a 24 h ECG may identify disorders of heart rhythm. If an arrhythmogenic cause is strongly suspected and the 24 h ECG is normal, a cardiac 'memo' can be helpful. If a structural cause is strongly suspected, an echocardiogram can identify evidence of outflow obstruction. Tilt-table testing is sometimes helpful in patients with severe and frequent episodes of syncope if cardiac abnormalities have been excluded.

A6: What treatment options are appropriate?

This patient requires reassurance that the episode was a faint rather than an epileptic seizure. She should try to avoid precipitating activities.

OSCE counselling case

OSCE COUNSELLING CASE 11.1 – 'Will the epilepsy have any future implications for me?'

Epilepsy is a long-term diagnosis. Issues surrounding AED choice, seizure triggers (fatigue, alcohol and other drugs, stress, occasionally photosensitivity), specific issues for women, driving regulations, safety in the home, and the cognitive effects of epilepsy and AEDs must be discussed with the patient. It is important to document in the notes that this has been done, for medicolegal reasons. A useful checklist is available from the Scottish Intercollegiate Guidelines (www.sign.ac.uk). Comprehensive guidelines are also available from the National Institute for Health and Clinical Excellence (www.nice.org.uk).

The following issues need to be discussed.

- Explain what epilepsy is.
- Discuss the side effects of the various AED options.
- Discuss triggers to seizures, e.g. lack of sleep, infections, drugs, poor compliance with AED medication.
- Discuss sudden unexplained death in epilepsy (SUDEP). There are around 500 cases of SUDEP in the UK every year, which is more than the annual number of cases of cot deaths. The causes are not clear, but SUDEP appears to be more frequent in people with poor seizure control and who are non-compliant with treatment. All patients with epilepsy should be informed about SUDEP, but it is important to do this at an appropriate time and not necessarily at the time of diagnosis.

The following issues should also be discussed.

Issues for women

Women taking one of the enzyme-inducing anticonvulsants (including carbamazepine, phenytoin and topiramate) may need to take a high-dose oral contraceptive because the low dose is likely to be less effective.

The risk that children of parents with epilepsy will themselves develop epilepsy is only about 5 per cent, unless the parent has a clearly hereditary form of the disorder. Patients should be managed in an obstetric clinic with access to a physician specializing in epilepsy. Use of the long-established AEDS during pregnancy appears to be associated with an approximate two- or threefold increase in the risk of major congenital malformations in women with epilepsy. The risk of malformation appears to be dose-related, and a higher rate is seen in women receiving two or more drugs. The risks appear to be greatest with sodium valproate. Risks may be minimized by taking folic acid supplements, so it is important for a patient to try to plan pregnancy in advance (or to take 5 mg folic acid per day if there is a possibility of conception). Pre-pregnancy and post-delivery vitamin K is also recommended to prevent haemorrhagic disease of the newborn. No pharmaceutical company guarantees that their product is safe during pregnancy. Patients should generally continue treatment in pregnancy, as the risks of stopping (e.g. injury during a fit, fetal hypoxia in prolonged generalized seizures) are generally greater than the risks of continuing.

Lifestyle

Consider employment and relationship issues, and inform the patient about driving issues. The doctor has a legal obligation to explain to the patient who has had an epileptic seizure that he or she must inform the Driver and Vehicle Licensing Agency (DVLA) and must not drive until the medical panel of the DVLA has considered the case. The patient is under a legal obligation to inform the DVLA.

The following apply if the patient holds a group 1 licence (normal car licence). After an unprovoked single seizure, the stipulation of the DVLA is that the patient must not drive until he or she has been fit-free for 6 months. If the patient has had more than one seizure, the stipulation is that a period of

12 months of seizure freedom is required before returning to driving. DVLA guidelines on episodes of loss of consciousness are occasionally updated and vary depending on the type of licence, whether a seizure was provoked, and in episodes of 'unexplained' loss of consciousness (e.g. when the patient presents alone with no recall about the event) whether there is a high or low risk of recurrence. The DVLA website shows the current recommendations for driving after many types of illness (www.dft.gov.uk/dvla/medical/ataglance.aspx).

No driving restrictions are currently required for a simple faint for a normal driving licence (group 1). If the faints are recurrent, then the three 'Ps' should apply on each occasion – an identifiable provocation, a prodrome and a postural element.

After syncope with a high risk of recurrence, if the cause is identified and treated, the DVLA usually allows a patient to drive 4 weeks later. If the cause is not identified, the stipulation is usually 6 months off driving (assuming there are no further events).

Stopping AED after 2 years of seizure freedom

Some 70–80 per cent of fits will stop with a single AED. After a period of seizure freedom, it is appropriate to discuss the pros and cons of stopping treatment because the epilepsy may have remitted. After being fit-free after 2 years of monotherapy, the probability of remaining seizure-free in the following 2 years is approximately 80 per cent if the AED is continued and about 55–60 per cent if the AED is discontinued. It is important to note that some primary epilepsy syndromes such as juvenile myoclonic epilepsy will not remit, and the patient will require life-long treatment.

CEREBROVASCULAR DISEASE

Questions

Clinical case

For the case scenario given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.4 – A previously well 39-year-old man attends the accident and emergency (A&E) department with a left-sided headache, neck pain and slight word-finding difficulty after a mild whiplash injury 2 h earlier.

He says his right arm 'doesn't feel right'. His wife has noticed a slight drooping of his eyelid on the left.

Answers

Clinical case

CASE 11.4 – **A previously well 39-year-old man attends A&E with a left-sided headache, neck pain and slight word-finding difficulty after a mild whiplash injury 2 h earlier.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are dissection of the left carotid artery, migraine with aura, left-sided intracerebral haemorrhage, and cerebrovascular disease causing a left-sided stroke in the middle cerebral artery territory. The most likely cause is a dissection of the left carotid artery.

A2: What issues in the given history support or refute a particular diagnosis?

Carotid artery dissection is a significant cause of stroke in patients younger than 40 years. Dissections are usually subadventitial (between the media and adventitia or within the media), creating a false lumen that can cause stenosis, occlusion or pseudo-aneurysm of the vessel. Simultaneously, the dissection may cause the formation of a thrombus, from which fragments embolize. Strokes resulting from carotid dissection may thus have a haemodynamic or embolic origin. In this case, a major clue to the cause of this patient's stroke is that he has a painful drooping left eyelid, which suggests the possibility of Horner's syndrome. Horner's syndrome is caused by damage to the sympathetic supply to the eye. The sympathetic fibres travel with the carotid artery, and carotid dissection may damage these fibres. Horner's syndrome consists of ptosis, miosis, enophthalmos and sometimes loss of sweating on one half of the face. It is important to consider a carotid dissection in any case of painful Horner's syndrome.

As in this patient, carotid artery dissections have non-specific presenting symptoms such as neurological deficits and headache. They often occur at a relatively young age and in previously healthy individuals, either spontaneously or after various degrees of trauma.

Neurologists manage stroke in all age groups. This patient is very young to have significant cerebrovascular disease. The other causes mentioned would not generally be expected to cause Horner's syndrome, but they remain possibilities. Each aura symptom in migraine usually lasts only 20 minutes.

A3: What additional features would you seek to support a particular diagnosis?

If the patient does not have a previous or family history of migraine, this reduces the possibility of migrainous aetiology. Is there a history suggestive of a connective tissue disorder such as Marfan syndrome (a heritable condition that affects the connective tissue characteristics, including tall stature, lax joints, lens dislocation and cardiovascular abnormalities) or Ehlers–Danlos syndrome (heritable disorders of connective tissue, characterized by skin extensibility, joint hypermobility and tissue fragility caused by a defect in collagen)? These connective tissue disorders can predispose to arterial dissections.

A4: What clinical examination would you perform, and why?

Signs of an upper motor neuron pattern sensorimotor deficit in the right arm, and signs of Horner's syndrome should be found. It is important to search for evidence of a head injury and, given the history of neck pain, to exclude evidence of spinal cord damage (bilateral limb weakness and sensory loss).

A5: What investigations would be most helpful, and why?

Computed tomography of the brain will in most circumstances be adequate to demonstrate ischaemic damage in the middle cerebral artery distribution, although MRI is more sensitive. Ultrasonography of carotid arteries is fast, convenient, non-invasive and highly sensitive, and may identify a dissection. Invasive contrast arteriography is more accurate but carries a greater risk. Non-invasive alternatives include CT and magnetic resonance angiography (MRA). Electrocardiography and echocardiography may also be performed to rule out a cardiac source of cerebral emboli in many cases of 'young stroke'.

A6: What treatment options are appropriate?

Formal anticoagulation for a period of months is usually favoured, although the evidence base for this is relatively poor. In practice, the choice between anticoagulation agents and aspirin is made depending on various circumstances (e.g. severity of stroke, length of time since dissection).

DISEASES OF PERIPHERAL NERVES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.5 – A 29-year-old man presents with a 10-day history of progressive ascending leg weakness and numbness.

He suffered a 'stomach bug' while on holiday in Spain about 3 weeks ago. He was previously well.

CASE 11.6 – A 65-year-old man with type 2 diabetes (requiring insulin for the past 5 years) presents with a progressive ascending symmetrical numbness and burning.

The symmetrical numbness and burning discomfort have involved his feet (and more recently his ankles) over the past 8 years.

CASE 11.7 – A pregnant 35-year-old woman presents with a 4-month history of tingling in her left hand.

This is worse at night and often wakes her. She finds that hanging her left arm down outside the bed or shaking the left hand may help. She was previously well.

Answers

Clinical cases

CASE 11.5 – **A 29-year-old man presents with a 10-day history of progressive ascending leg weakness and numbness.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are Guillain–Barré syndrome (acute inflammatory demyelinating polyneuropathy [AIDP]), botulism, diphtheria and acute intermittent porphyria.

A2: What issues in the given history support or refute a particular diagnosis?

The story of ascending numbness and weakness about 10 days after an acute infection is typical of Guillain–Barré syndrome, which is an acute peripheral neuropathy causing weakness, paraesthesia and hyporeflexia. Progression generally stops 5 weeks after onset, and maximal weakness typically occurs at 2 weeks. The weakness is almost always symmetrical. Around 60 per cent of patients have a gastrointestinal or respiratory infection 1–3 weeks before onset. Mortality of the disease is in the range 5–10 per cent; the condition does not tend to recur. Cranial nerves may be involved in 45–75 per cent of cases and may be the dominant clinical feature, e.g. the Miller Fisher syndrome (a variant with ophthalmoplegia, ataxia and areflexia). A process similar to Guillain–Barré syndrome (chronic inflammatory demyelinating polyneuropathy [CIDP]) may occur over a period of months.

Botulism is often a food-borne disease, caused by the bacterium *Clostridium botulinum*, but wound botulism is increasingly recognized in people who inject drugs. Although there can be an incubation period, the symptom progression is very rapid. Early oropharyngeal symptoms, ciliary paralysis (fixed pupils) and normal sensation distinguish botulism from Guillain–Barré syndrome.

Diphtheria is an acute infectious disease caused by *Corynebacterium diphtheriae*. There is often a high fever and a tonsillar/pharyngeal membrane. The condition is now rare due to immunization programmes.

Acute intermittent porphyria, an autosomal dominant metabolic problem with increased production and excretion of porphobilinogen, can also cause a rapidly advancing symmetrical peripheral neuropathy. It is rare, however, and there are often accompanying features of abdominal pain.

A3: What additional features would you seek to support a particular diagnosis?

The neuropathy may progress to involve the respiratory muscles, and the patient may reach a critical state without any obvious prior clinical deterioration. The patient should be questioned about whether he has shortness of breath, particularly when lying flat (respiratory muscle weakness is more apparent in this position).

A4: What clinical examination would you perform, and why?

Guillain–Barré syndrome is an acute peripheral neuropathy. Examination should reveal a symmetrical global weakness of the legs and a reduction in sensation to all modalities in a stocking distribution. Reflexes become diminished and then absent as the disease progresses.

An important part of the clinical examination is to assess respiratory function. Forced vital capacity (FVC) measurements are essential; FVC is the volume of air expelled by a forced maximal expiration from a position of full inspiration. A peak expiratory flow rate, as used in assessing patients with asthma, is *not* appropriate and should not be used.

A5: What investigations would be most helpful, and why?

- *FVC:* as the natural history of the condition is that it will continue to deteriorate over 5 weeks, regular FVC measurements are essential to detect incipient hypoventilatory respiratory failure.
- *Lumbar puncture:* an elevated cerebrospinal fluid (CSF) protein would be expected but may remain normal in 10 per cent of patients. It may take 1–2 weeks after the onset of weakness for the elevation in CSF protein to become apparent. The CSF white cells should remain normal; if they are significantly elevated (e.g. >50), an associated human immunodeficiency virus (HIV) infection should be considered.
- *Neurophysiology – nerve conduction studies:* these may be normal in the first 2–3 weeks but are then likely to demonstrate evidence of demyelination, with conduction block, slowed distal latencies and decreased motor conduction velocities.
- *Blood tests, U&Es, antibody tests, vitamin B12 and folate, serological studies for infection (e.g.* Mycoplasma*,* Campylobacter*):* blood investigations may identify low sodium (e.g. from syndrome of inappropriate antidiuretic hormone secretion [SIADH]). Vitamin B12 deficiency would not really be expected to cause such a rapidly progressive neuropathy, but it is possible and is a treatable cause of neuropathy; if the lumbar puncture was normal, it should be considered further.

A6: What treatment options are appropriate?

Intravenous immunoglobulin (IVIG) and plasma exchange therapy are comparable in terms of efficacy. Most patients generally receive IVIG because it is easier to administer and may shorten recovery time by 50 per cent. As the patient is likely to be relatively immobile, prophylaxis with low-molecular-weight (LMW) heparin should be considered.

Effective management involves monitoring the patient closely to look for complications, in particular progressive respiratory failure, cardiac arrhythmias and autonomic instability. It is important to note that that a chronic form of Guillain–Barré syndrome (CIDP) exists, characterized by a progressive or relapsing demyelinating polyneuropathy over 3 months. The findings on investigation are generally very similar to those of Guillain–Barré syndrome, although patients with CIPD may also respond to corticosteroids.

CASE 11.6 – **A 65-year-old man with type 2 diabetes (requiring insulin for the past 5 years) presents with a progressive ascending symmetrical numbness and burning.**

A1: What is the likely differential diagnosis?

The likely diagnosis is chronic sensory peripheral neuropathy caused by diabetes mellitus.

A2: What issues in the given history support or refute a particular diagnosis?

The patient has had diabetes mellitus for long enough to develop complications. The slow progression, in a symmetrical fashion, affecting a stocking distribution, is typical of a peripheral neuropathy. The burning discomfort is consistent with neurogenic pain.

A3: What additional features would you seek to support a particular diagnosis?

Although the likely cause is a chronic peripheral neuropathy caused by diabetes mellitus, one should take care before making such assumptions. The problem could be multifactorial. Other causes of a peripheral neuropathy should be excluded.

A history of chronic excess alcohol intake, vitamin B12 and folate deficiency, thyroid disease, renal failure, autoimmune diseases (which may cause a vasculitic neuropathy) or paraproteinaemia (e.g. multiple myeloma) should be sought.

A4: What clinical examination would you perform, and why?

Examination should reveal a stocking sensory loss with loss of ankle jerk reflexes. Often dorsal column sensation (vibration sense, joint position sense, light touch) is preferentially affected. Look for other complications of diabetes mellitus (e.g. retinopathy, cerebrovascular disease, ischaemic heart disease, peripheral vascular disease, renal failure).

A5: What investigations would be most helpful, and why?

The following blood tests should be done:

- glucose
- glycated haemoglobin (HbA1c)
- urea and electrolytes
- vitamin B12 and folate
- thyroid function tests
- immunoglobulins and electrophoresis.

The blood tests are to identify other causes of a peripheral neuropathy and also to assess longer-term diabetic control (HbA1c).

Neurophysiological studies of nerve conduction are often useful in classifying whether the neuropathy is predominantly demyelinating (loss of the myelin insulation around the nerves, causing slow conduction velocity) or axonal (thinning of the nerve fibres, causing small-amplitude responses). Demyelinating peripheral neuropathies are more frequently the result of acquired causes and may be aggressive, but they are more often treatable. A cause should be identifiable in almost all cases. Axonal neuropathies are generally more indolent and slowly progressive.

In this case, the cause is likely to be a diabetic peripheral neuropathy. In many cases of slowly progressive axonal peripheral neuropathy, however, investigations do not always reveal an identifiable cause. The neuropathy is then termed an idiopathic axonal peripheral neuropathy.

A6: What treatment options are appropriate?

Treatment is symptomatic treatment of the pain with drugs such as amitriptyline and gabapentin. Treatment of the cause, in this case optimizing diabetic control, will slow progression of the neuropathy.

CASE 11.7 – A pregnant 35-year-old woman presents with a 4-month history of tingling in her left hand.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are left carpal tunnel syndrome, left ulnar neuropathy and left cervical root lesions.

The main sensory supply to the hand is from median and ulnar nerves (and a minimal contribution in the anatomical snuffbox from the radial nerve). Carpal tunnel syndrome is a compressive problem affecting the median nerve.

A2: What issues in the given history support or refute a particular diagnosis?

The most likely diagnosis is carpal tunnel syndrome. Carpal tunnel syndrome is more common in conditions where the carpal tunnel becomes narrowed, such as during pregnancy, trauma, rheumatoid arthritis and hypothyroidism. Worsening of symptoms at night and relief on shaking the affected hand are typical of carpal tunnel syndrome. The sensory disturbance in median/ulnar lesions affects only the hand. The sensory disturbance associated with cervical root lesions is more extensive and extends above the hand. It should be emphasized that cervical root lesions in patients of this age group are very uncommon (although they occur with greater frequency in elderly people).

A3: What additional features would you seek to support a particular diagnosis?

In carpal tunnel syndrome, although there may be weakness in the median nerve muscles, it is the sensory symptoms that predominate. An ulnar neuropathy typically causes a more pronounced functional deficit than median nerve compression.

A4: What clinical examination would you perform, and why?

In carpal tunnel syndrome, the sensory symptoms are confined to the anterior aspect of the lateral three and a half fingers. Thenar atrophy may be noted. Weakness of thumb abduction is a useful clinical sign for the motor component of carpal tunnel syndrome. Hyperflexion of the wrist for 60 s may elicit paraesthesia (Phalen's sign). Tapping the volar wrist over the median nerve (Tinel's sign) may produce paraesthesia in the median distribution of the hand.

Complete ulnar nerve paralysis causes a claw hand. Wasting of the small hand muscles results in hyperextension of the fingers at the metacarpophalangeal joints and flexion at the interphalangeal joints. The sensory disturbance of ulnar neuropathy affects the medial one and a half fingers.

Cervical C6, C7 or C8 root damage can cause sensory loss in the hand, although this will extend into the forearm. Muscle weakness will be in the affected myotome and the relevant reflex arcs may be affected.

A5: What investigations would be most helpful, and why?

Nerve conduction/electromyography (EMG) studies are helpful in confirming the clinical diagnosis.

A6: What treatment options are appropriate?

For carpal tunnel syndrome, reduction of pressure on the median nerve will provide relief. In this case, fluid retention and oedema are likely to reduce after pregnancy and the symptoms may then remit. Placing the hand in a splint may give symptomatic benefit. Injecting the carpal tunnel with corticosteroid could provide relief. Often surgical release of the carpal tunnel is necessary.

For ulnar nerve palsy, surgical release at the site of compression may be needed.

For cervical root lesions, surgical decompression at the site of the cervical root lesion may be needed. As mentioned earlier, cervical root lesions in this age group are very uncommon.

HEADACHE

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.8 – A 40-year-old woman attends A&E with her worst-ever headache.

The headache started suddenly in the occipital area 5 h ago and was associated with nausea and vomiting and some photophobia. Her neck became stiff after around 2 h.

CASE 11.9 – A 25-year-old woman presents to A&E with a severe gradual-onset headache.

The headache is right-sided, throbbing and periorbital, and there is associated nausea. The patient has had similar episodic headaches over the past 5 years; they generally last 10 h before settling.

CASE 11.10 – A 70-year-old woman presents with sharp shooting pains in the region of the left cheek.

The pains last a few seconds and occur several times a day. She finds that yawning or touching the left cheek provokes attacks of the pain.

CASE 11.11 – A 70-year-old woman presents with a gradual-onset diffuse headache, which is more severe in the left temporal region.

The patient comments that wearing her spectacles has become uncomfortable, and combing her hair exacerbates the pain.

CASE 11.12 – **A 22-year-old woman presents with a 2-week history of headache of gradual onset.**

The headache is generalized, worse in the morning and exacerbated by coughing and straining. There is associated nausea. She started the combined oral contraceptive pill 6 weeks ago.

CASE 11.13 – **A 40-year-old man who was previously well presents with a 6-day history of gradual-onset worsening headache, lethargy, myalgia and fever, and by the sixth day altered behaviour.**

The patient is brought to hospital after his wife called an ambulance because he had a generalized seizure.

Answers

Clinical cases

CASE 11.8 – **A 40-year-old woman attends A&E with her worst-ever headache.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are subarachnoid haemorrhage, thunderclap headache, bacterial meningitis, viral meningitis, cerebral venous sinus thrombosis and migraine.

A2: What issues in the given history support or refute a particular diagnosis?

The history is typical of subarachnoid haemorrhage. This classically presents with sudden-onset, worst-ever headache with nausea, vomiting, photophobia and neck stiffness (although this can take a few hours to develop). The textbook description of subarachnoid haemorrhage is of a sudden-onset, worst-ever headache similar to a blow to the back of the head. If a patient presents in this way, subarachnoid haemorrhage should be at the top of the differential diagnosis. In practice, patients do not always follow the textbook description. A useful operational definition is of sudden-onset, first or worst headache, usually occipital and maximal within moments, which may develop over minutes and lasts at least 1 h. Subarachnoid haemorrhage may occur outside these parameters but is rare.

A thunderclap headache may present in exactly the same manner as a subarachnoid haemorrhage, but does not tend to last longer than an hour.

A3: What additional features would you seek to support a particular diagnosis?

The temperature may be mildly elevated by subarachnoid haemorrhage or cerebral venous sinus thrombosis. Bacterial and viral meningitis may cause a high fever. Thunderclap headache is not associated with a fever.

Approximately 1 per cent of all headaches seen in A&E are subarachnoid haemorrhage. The most common differential diagnosis for acute headache admitted to hospital is migraine. The symptoms of migraine tend to evolve, however, and the headache is not usually of sudden onset. The headache is often frontal and may be unilateral. Thunderclap headaches may be recurrent. A history of previous normal investigations for a recurrent headache of this type may preclude the need to exclude subarachnoid haemorrhage on each occasion.

Sudden-onset headache can also occur in other conditions such as cerebral venous sinus thrombosis (although this mode of presentation is rare), which tends to be more common in females. Bacterial meningitis may very rarely present in this fashion, although the patient usually has a more gradual-onset headache and may have a purpuric rash. Viral meningitis is unlikely because the patient often has a prodromal illness and a sudden-onset headache would be exceptional.

A4: What clinical examination would you perform, and why?

If the patient has had a subarachnoid haemorrhage, she may have focal neurological signs that give a clue as to the cause of the bleed – e.g. a nerve III palsy suggests a posterior communicating artery aneurysm. If there is elevated intracerebral pressure, fundoscopy may reveal papilloedema. In bacterial meningitis a purpuric rash may be identified and the patient may also have signs of septicaemia.

Patients with subarachnoid haemorrhage, bacterial meningitis, cerebral venous sinus thrombosis or migraine may have focal neurological abnormalities. Viral meningitis and thunderclap headache are not associated with focal neurological deficits.

A5: What investigations would be most helpful, and why?

Full blood count will show elevated white cells in a bacterial (neutrophilia) or viral (lymphocytosis) meningitis. It will be normal in migraine, thunderclap headache and cerebral venous sinus thrombosis. The FBC would be expected to be normal in subarachnoid haemorrhage.

Uncontrasted CT of the brain will show the presence of blood in about 98 per cent of cases of subarachnoid haemorrhage when done within 12 h.

Lumbar puncture should be carried out after 12 h in patients where the CT brain scan does not show blood. Lumbar puncture is 100 per cent accurate for the presence or absence of subarachnoid haemorrhage if carried out appropriately within 12 h to 2 weeks of symptom onset. It will also identify elevated white cells (as occurs in meningitis). The accurate diagnosis of a subarachnoid haemorrhage is dependent on identifying blood breakdown products in the CSF, rather than the identification of red blood cells (as red cells in the CSF can be due to a subarachnoid haemorrhage or a 'traumatic tap'). Blood within the CSF is broken down into bilirubin and is measurable after 12 h. In a subarachnoid haemorrhage, bilirubin will be identified in the CSF when performed after 12 h, whereas bilirubin breakdown products are not identified in a 'traumatic tap'.

A6: What treatment options are appropriate?

If investigations reveal subarachnoid haemorrhage, calcium antagonists (e.g. nimodipine) should be given. These reduce the mortality and morbidity from cerebral artery vasospasm provoked by the presence of subarachnoid blood and need to be given to all patients. Non-invasive or invasive angiography should be performed to identify the presence of an aneurysm, which can then be ablated by neuroradiological or neurosurgical techniques.

If investigations reveal an elevated CSF pressure but are otherwise normal, MRI of the brain with venogram sequences will identify or exclude the presence of a cerebral venous sinus thrombosis. The more typical presentation and management of cerebral venous sinus thrombosis are addressed in Case 11.12.

If investigations are normal, the differential diagnosis lies between thunderclap headache and migraine. A thunderclap headache is of sudden onset, whereas migraine headaches are generally of more gradual onset (it is good practice in this situation to retake the initial history). Migraine lasts longer than a thunderclap headache, and features of nausea, vomiting, photophobia and phonophobia are often more pronounced than in thunderclap headache. Furthermore, migraine may be associated with focal neurological symptoms and signs.

Although the history would be unusual for meningitis, it is appropriate to briefly discuss this important condition here. Patients in whom bacterial meningitis is suspected generally have a gradual-onset headache, rash, neck stiffness, nausea, vomiting, photophobia and confusion (although not necessarily all of them). A purpuric rash indicates a more generalized sepsis. In bacterial meningitis, the lumbar puncture results typically show raised protein, low glucose and raised white cells (neutrophils). If the lumbar puncture has been performed after the patient has been on antibiotics (i.e. partly treated bacterial meningitis), the white cells are often lymphocytes. In viral meningitis, the findings are normal (or very slightly raised) protein, normal glucose and raised white cells (lymphocytes). In tuberculous meningitis, the findings are raised protein, low glucose and raised white cells (lymphocytes).

In suspected bacterial meningitis, it is important to start appropriate antibiotics on an empirical basis as soon as possible (i.e. before doing a lumbar puncture). Instituting antibiotic therapy 1–2 h before lumbar puncture will not significantly decrease the diagnostic sensitivity if the culture of the CSF is done together with testing for bacterial antigens and with blood cultures. In most patients, initial empirical therapy with a broad-spectrum cephalosporin (cefotaxime or ceftriaxone), supplemented with ampicillin in young infants and older adults, is appropriate. In patients with suspected bacterial meningitis, it is

currently considered appropriate to start corticosteroids at the same time as initiating antibiotics, and to continue steroids for the first 4 days. Most regions have their own local policies, and these should be consulted because the situation regarding antimicrobial treatment may be subject to variation. Bacterial meningitis should be notified to public health physicians, who will contact trace and give prophylactic antibiotics as necessary. In patients who are immunocompromised, patients in whom tuberculous meningitis is suspected, and patients with a recent foreign travel history, other treatment regimens are necessary.

CASE 11.9 – **A 25-year-old woman presents to A&E with a severe gradual-onset headache.**

A1: What is the likely differential diagnosis?

The likely diagnosis is migraine.

A2: What issues in the given history support or refute a particular diagnosis?

Episodic gradual-onset severe headaches in young women are almost always migraine.

A3: What additional features would you seek to support a particular diagnosis?

The patient should be questioned for other features of migraine. Some patients find that various foodstuffs precipitate their headaches (e.g. cheese, chocolate, red wine, citrus fruit, crisps). There may be a hormonal component to the symptoms, and the headaches may be worse around the time of menstrual periods. Some hours before the onset of headache, patients may suffer premonitory symptoms, such as hunger or anxiety. An aura may precede the headache. Often there is a family history of migraine.

A4: What clinical examination would you perform, and why?

Examination is normal.

A5: What investigations would be most helpful, and why?

The diagnosis of migraine is based on history. No investigations are necessary. Migraine is the most common primary headache, affecting 10–20 per cent of the population of the USA. It occurs more commonly in women. The International Headache Society (www.i-h-s.org) has classified all headache types. There are two main types of migraine: migraine with aura and migraine without aura. The cardinal feature of migraine aura is that it evolves slowly; most aura symptoms develop over 5–20 min and usually last less than 60 min. The headache generally follows soon after the aura. Auras vary in type and complexity. Visual auras are the most common and include scotomata (blind spots in the visual field), fortification spectra and geometric visual patterns. Progressive sensory disturbance is the second most common migraine aura. The typical migraine headache is of gradual onset, throbbing and unilateral, although it may be bilateral in a substantial minority of patients. Nausea, vomiting, photophobia and phonophobia are often accompanying features.

A6: What treatment options are appropriate?

Many patients respond to simple analgesics, especially non-steroidal anti-inflammatory drugs, which are often given with an antiemetic such as metoclopramide. Diclofenac and domperidone suppositories may also be helpful. If these measures do not work, the triptan class of anti-migraine drugs (selective serotonin agonists) may be used. These drugs significantly reduce the severity and duration of the migraine headache, but they are not effective if given during the aura. They should be taken at the onset of the headache. Several guidelines are available for the diagnosis and management of migraine.

The guidelines of the British Association for the Study of Headache are available from www.bash.org.uk. In cases of frequent migraine, prophylactic agents such as beta-blockers or amitriptyline are often considered.

The combined oral contraceptive pill is currently contraindicated in women with migraine with aura, as a result of concerns about increased stroke risk.

Patients with frequent migraines sometimes respond by taking frequent doses of analgesics. This can lead to increased chronicity of the headache and a rebound medication overuse headache. Codeine and other opiates are particularly problematic in this respect.

CASE 11.10 – **A 70-year-old woman presents with sharp shooting pains in the region of the left cheek.**

A1: What is the likely differential diagnosis?

The likely differential diagnosis is trigeminal neuralgia.

A2: What issues in the given history support or refute a particular diagnosis?

Trigeminal neuralgia tends to occur in people aged over 60 years and is more common in women. It is characterized by brief paroxysms of pain localized in the maxillary or mandibular divisions of the trigeminal nerve.

A3: What additional features would you seek to support a particular diagnosis?

Attacks may be triggered by yawning or touching the area of skin innervated by the mandibular branch of the trigeminal nerve. It is important to note that involvement of the ophthalmic branch is very rare.

A4: What clinical examination would you perform, and why?

Examination is usually normal but may reveal altered sensation in the area of skin innervated by the mandibular branch of the trigeminal nerve.

A5: What investigations would be most helpful, and why?

Magnetic resonance imaging is generally used to exclude a vascular or other compressive lesion of the relevant divisions of the trigeminal nerve.

A6: What treatment options are appropriate?

Medical treatments include carbamazepine, gabapentin and amitriptyline.

If the pain is refractory to medical treatments, neurosurgical procedures including microvascular decompression (to separate the trigeminal nerve from a compressing blood vessel) and percutaneous glycerol rhizolysis (injecting glycerol to damage the trigeminal fibres causing the pain) may be considered.

CASE 11.11 – **A 70-year-old woman presents with a gradual-onset diffuse headache, which is more severe in the left temporal region.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are temporal arteritis and a space-occupying lesion.

A2: What issues in the given history support or refute a particular diagnosis?

In a patient of this age, it is always worth bearing in mind the possibility of a space-occupying lesion. This history is, however, typical of temporal arteritis.

Temporal arteritis is more common in people aged over 70 years, especially in women. It is a medium-/large-vessel vasculitis. Affected vessels are infiltrated by lymphocytes, plasma cells and multinucleated giant cells, often in a patchy fashion. Temporal arteritis is closely linked to polymyalgia rheumatica (a clinical syndrome characterized by severe aching and stiffness in the neck, shoulder girdle and pelvic girdle). Temporal pain and tenderness are characteristic, and the patient may complain of pain when wearing spectacles and combing her hair.

A3: What additional features would you seek to support a particular diagnosis?

The patient may have constitutional symptoms such as malaise, lethargy, weight loss and night sweats. She may notice increasing discomfort in the jaw when talking or chewing (jaw claudication).

The inflammatory process in the blood vessels may occur throughout various areas of the body and cause ischaemia. Visual loss, stroke, angina and arterial aneurysms may all be associated.

A4: What clinical examination would you perform, and why?

There is likely to be tenderness over the temporal arteries, which may have diminished or absent pulses.

A5: What investigations would be most helpful, and why?

An erythrocyte sedimentation rate (ESR) is usually (but not always) elevated and gives additional support to the clinical diagnosis. Abnormal liver function tests may occur, and the FBC may show an anaemia, leucocytosis or thrombocytosis. If the patient has typical symptoms, brain imaging is not necessary.

As this condition occurs in elderly people, and the headache phenotype can be rather variable, CT of the brain may be helpful to exclude a space-occupying lesion if there is clinical uncertainty over the diagnosis. Furthermore, a raised ESR can be associated with other conditions (e.g. myeloma, infections, cancers). In cases of diagnostic uncertainty, these conditions may need to be excluded.

Definitive diagnosis is achieved by temporal artery biopsy to identify the inflammatory lesions described above. The inflammation tends to be patchy and may not always appear in a single biopsy.

A6: What treatment options are appropriate?

Corticosteroids should be started immediately after clinical diagnosis. It is not necessary to perform a temporal artery biopsy first, because the inflammatory changes generally persist for 2 weeks. Treatment is usually with high-dose prednisolone orally, although if vision is threatened high-dose IV methylprednisolone infusions may be used initially. The response to treatment is typically rapid, within 48 h. In most cases it is usual to start the patient on 60 mg prednisolone and to slowly wean the dose down over several months once the symptoms are under control. If the ESR was initially raised, it can be used to guide treatment. When a patient gets to a dose of around 10 mg prednisolone, the dose reduction process is much slower (e.g. 1 mg/month). Often a dose threshold is found, below which the symptoms return, and the patient may therefore require long-term corticosteroids. If the patient is placed on long-term steroids, it is necessary to consider monitoring of bone density using a dual-energy X-ray absorptiometry (DEXA) scan and instituting ‘bone protection’ with drugs such as bisphosphonates to reduce the likelihood of steroid-induced osteoporosis.

CASE 11.12 – **A 22-year-old woman presents with a 2-week history of headache of gradual onset.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are cerebral venous sinus thrombosis, idiopathic intracranial hypertension and brain tumour.

A2: What issues in the given history support or refute a particular diagnosis?

This history is typical of both cerebral venous sinus thrombosis and idiopathic intracranial hypertension. The phenotype of the headache is of raised pressure (headache worse in the morning and exacerbated by coughing and straining), and other causes of raised pressure (e.g. brain tumour) are possible and need to be excluded. Prothrombotic states (e.g. combined oral contraceptive pill) predispose to cerebral venous sinus thrombosis. Cerebral venous sinus thrombosis and idiopathic intracranial hypertension are more common in women.

A3: What additional features would you seek to support a particular diagnosis?

Ask for symptoms of lateralizing weakness or sensory disturbance. This suggests underlying structural lesions and would be consistent with a brain tumour or possibly cerebral venous sinus thrombosis. Idiopathic intracranial hypertension does not cause limb weakness. Disturbance of visual function (particularly enlargement of the blind spots) may occur in both idiopathic intracranial hypertension and cerebral venous sinus thrombosis. Impairment of consciousness can occur in brain tumours with oedema, and in cerebral venous sinus thrombosis; it does not occur in idiopathic intracranial hypertension.

A4: What clinical examination would you perform, and why?

Patients with idiopathic intracranial hypertension are almost always female and overweight. Examination of visual function is important. Visual fields may be affected in both conditions (enlarged blind spots and constricted visual fields). Fundoscopy may reveal papilloedema. General neurological examination may reveal lateralizing signs.

A5: What investigations would be most helpful, and why?

Although CT of the brain is useful to exclude a tumour, the most appropriate imaging investigation is MRI of the brain with venogram sequences. This is more sensitive in identifying a cerebral venous sinus thrombosis. Recent evidence suggests that D-dimers are often elevated in patients with acute and subacute cerebral venous sinus thrombosis, but their measurement is not sensitive enough to confirm or exclude the condition definitively. It is important to monitor vision carefully, because visual loss can occur rapidly in both cerebral venous sinus thrombosis and idiopathic intracranial hypertension. An early sign is development of enlargement of the blind spots, which can be detected by clinical examination of the visual fields (but much more sensitively by formal charting of the visual fields).

If imaging studies are normal, then the likely diagnosis (if the patient is overweight and has papilloedema) is idiopathic intracranial hypertension. A lumbar puncture with CSF measurement will confirm the diagnosis by identifying raised intracranial pressure (pressure >25 cmH_2O).

A6: What treatment options are appropriate?

If investigations identify a brain tumour, oncological and neurosurgical opinions should be sought.

If investigations identify cerebral venous sinus thrombosis, the generally accepted treatment is formal anticoagulation, initially with heparin and then with warfarin for 3–6 months. Medications associated with hypercoagulable states, such as the combined oral contraceptive pill, should be discontinued.

If investigations identify idiopathic intracranial hypertension, it is important to stop any medication that may precipitate the condition (e.g. combined oral contraceptive pill, tetracycline antibiotics). Idiopathic intracranial hypertension occurs almost exclusively in people who are overweight; weight loss is the mainstay of treatment. Medications such as carbonic anhydrase inhibitors (e.g. acetazolamide) and diuretics (e.g. furosemide) are also used to reduce the CSF pressure.

It is important to realize that progressive visual field loss in idiopathic intracranial hypertension and cerebral venous sinus thrombosis is often asymptomatic. By the time the patient notices an impairment of visual acuity (a late-stage symptom in raised intracranial pressure), a significant degree of permanent visual loss may already have occurred. Regular monitoring of visual fields, both clinically and with formal perimetry, as part of the assessment of optic nerve function, together with visual acuity, colour vision and fundoscopy, is vital. Idiopathic intracranial hypertension is a more chronic condition than cerebral venous sinus thrombosis and requires longer-term monitoring of visual function.

If a patient with either of these two conditions develops progressive visual loss that does not respond to medication, neurosurgical procedures to protect optic nerve function should be considered (CSF diversion such as lumboperitoneal shunt, or optic nerve sheath fenestration). Although lumbar puncture can acutely reduce CSF pressure, the effect is transient. Repeated lumbar punctures do not help with longer-term management.

CASE 11.13 – **A 40-year-old man who was previously well presents with a 6-day history of gradual-onset worsening headache, lethargy, myalgia and fever, and by the sixth day altered behaviour.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are encephalitis, brain abscess and brain tumour.

A2: What issues in the given history support or refute a particular diagnosis?

A brain tumour or abscess could present in this fashion. The prodrome of a viral-type illness is suggestive of encephalitis, however, as is the progressive evolution of symptoms. The altered behaviour and subsequent fit suggest involvement of the substance of the brain, as occurs in encephalitis. In meningitis, behaviour change does not occur unless there is more extensive involvement (meningoencephalitis) or the patient has systemic infection.

A3: What additional features would you seek to support a particular diagnosis?

A history of close contacts with infectious diseases, travel abroad, tick or insect bites, or predisposition would increase the probability of an infectious cause.

A4: What clinical examination would you perform, and why?

Lateralizing neurological signs suggest a structural lesion within the brain but will not distinguish a cause. Similarly, papilloedema will suggest raised intracranial pressure but may occur in all of the above causes. If the patient has a metastatic brain tumour, general examination may reveal evidence of the primary tumour. Fever, however, is not generally a feature of a brain tumour.

A5: What investigations would be most helpful, and why?

Computed tomography of the brain will essentially exclude an intracerebral mass lesion and may be done rapidly (it can be useful particularly if the patient is confused), but the imaging modality of choice is MRI. This will better identify the nature of a space-occupying lesion and is much more sensitive at picking up the changes that occur in encephalitis. Herpes simplex virus encephalitis is the most common

and treatable encephalitis in the UK, and abnormalities are frequently noted in the temporal lobes on MRI.

An EEG is helpful if further consideration is being given to a potential diagnosis of encephalitis. It will generally be abnormal, showing increased slow-wave activity and possibly epileptiform discharges. In herpes simplex virus encephalitis, characteristic EEG changes of lateralized periodic complexes at regular intervals of 2–3 s are seen.

A lumbar puncture is not generally helpful in investigating brain tumours. It is contraindicated in brain abscesses. If imaging excludes a mass lesion and significant oedema, a lumbar puncture can be helpful to investigate encephalitis. In herpes simplex virus encephalitis, the CSF is often under increased pressure with raised white cells (lymphocytes), elevated protein and modestly reduced glucose (i.e. the lumbar puncture results may be similar to those in tuberculous or fungal meningitis). Polymerase chain reaction of the CSF is likely to detect the presence of herpes simplex virus 1 or 2. General blood investigations (including FBC and U&Es) should be performed in all patients – SIADH occurs reasonably frequently in encephalitis.

A6: What treatment options are appropriate?

In this patient, the mostly likely diagnosis is encephalitis. The aetiology of encephalitis is usually infectious and is most commonly the result of herpes simplex virus 1 or 2, although varicella zoster virus, Epstein–Barr virus, cytomegalovirus, measles, mumps, rubella, tick-borne disease and rickettsiae may also cause encephalitis. Outside the UK, other infective agents such as West Nile virus and Japanese B virus should be considered. In the immunocompromised patient, fungal and parasitic agents should be considered. With the exception of herpes simplex virus and varicella zoster virus encephalitis, the viral forms of encephalitis are not currently treatable. Symptomatic treatment is necessary in all patients. The antiviral agent aciclovir given IV for 10–14 days reduces both mortality and morbidity in herpes simplex virus and varicella zoster virus encephalitis. Aciclovir is given in all patients because clinically it is not possible to distinguish between the various forms of encephalitis. If there is significant cerebral oedema, treatment with the osmotic diuretic mannitol or corticosteroids needs to be considered (e.g. dexamethasone). If therapy is started early, the survival rate is over 90 per cent, although neuropsychiatric sequelae are common. If seizures are present, anticonvulsants should be started and continued for some months once the condition has resolved.

In practice antibiotics (as used for empirical bacterial meningitis therapy) are often started on admission (because bacterial meningitis is sometimes initially considered). If the investigations suggest a brain tumour, the imaging characteristics may suggest that this is either primary or secondary (i.e. metastatic). Further investigation to identify the site of the primary tumour and liaison with neurosurgeons and oncologists are indicated. If investigations suggest a brain abscess, investigation as to the source and whether there are predisposing factors (e.g. immunodeficiency) must be carried out. Liaison with neurosurgical colleagues is necessary because drainage and excision are often used. Non-surgical management (e.g. with a prolonged course of brain-penetrating antibiotics) is usually reserved for patients with an abscess in a difficult site for surgery.

CENTRAL NERVOUS SYSTEM DEMYELINATION

Questions

Clinical case

For the case scenario given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.14 – **A 35-year-old white woman presents with a 3-day history of progressive numbness below the umbilicus, with mild weakness of the lower limbs and urinary frequency.**

Five years previously the patient had a subacute episode of uncomfortable visual loss in the right eye with full recovery over a week.

Answers

Clinical case

CASE 11.14 – **A 35-year-old white woman presents with a 3-day history of progressive numbness below the umbilicus, with mild weakness of the lower limbs and urinary frequency.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are inflammation of the spinal cord (transverse myelitis) and spinal cord compression.

A2: What issues in the given history support or refute a particular diagnosis?

The most likely cause is inflammation of the spinal cord (transverse myelitis). The symptoms of lower limb weakness, a sensory level at the umbilicus and urinary dysfunction localize the problem to the thoracic cord. In patients of this age group, the gradual-onset history is suggestive of transverse myelitis, although a gradual onset may also occur in certain causes of spinal cord compression (e.g. tumour, epidural abscess). The previous history of visual disturbance suggests a previous inflammatory lesion in the optic nerve (optic neuritis) and that this event is also the result of central nervous system (CNS) inflammation (transverse myelitis). (A spinal cord infarction would be of sudden onset but would cause the same examination findings.)

A3: What additional features would you seek to support a particular diagnosis?

A preceding viral illness is suggestive of an inflammatory cause. Back pain is often a feature of spinal cord compression (trauma, tumour, epidural abscess), although mild back discomfort can occur in transverse myelitis. In cases of spinal cord compression caused by epidural abscess, the patient may be systemically unwell with a fever.

A4: What clinical examination would you perform, and why?

First, it is important to localize the lesion. In a thoracic spinal cord lesion, the patient should have increased tone in the legs, a pyramidal pattern of weakness and a sensory level on the trunk. Lower limb reflexes will be brisk and plantar responses up-going. A fever may occur in an epidural abscess. Mild pyrexia is compatible with a transverse myelitis.

Vertebral tenderness occurs in an epidural abscess and may occur in spinal cord tumour. Although the patient has made a full symptomatic recovery from her previous visual problem, examination may reveal impaired colour vision and a pale optic disc in the affected eye (both signs of optic nerve damage).

A5: What investigations would be most helpful, and why?

The subacute progressive onset after a viral infection in a previously well young woman is typical of transverse myelitis. Spinal cord compression, e.g. from a tumour, can present in a similar manner but is rare. Compression from an intervertebral disc would be unlikely in patients of this age group, and compression from an epidural abscess or spinal abscess is often (but not exclusively) associated with fever and localized spinal tenderness. Transverse myelitis is inflammation of the spinal cord. It may occur in isolation or in the setting of another illness. It may be associated with infections (viral or bacterial, e.g. *Mycoplasma pneumoniae*, *Borrelia* spp., syphilis, tuberculosis), autoimmune disease (e.g. systemic

lupus erythematosus, Sjögren's syndrome, sarcoidosis). Occasionally vitamin B12 deficiency can produce a spinal cord syndrome that may mimic transverse myelitis. In the western world, transverse myelitis in patients of this age group is most frequently associated with multiple sclerosis (MS). It is likely that this patient has MS because she has had a previous event consistent with inflammation in another part of the CNS (the optic nerves).

Magnetic resonance imaging at this level will help to distinguish between an inflammatory and a compressive lesion in the thoracic spinal cord. It is important, however, to image the whole spinal cord because occasionally lesions higher up can produce a similar clinical picture. Imaging of the brain and cervical spine is necessary because MS causes a characteristic pattern of inflammation in the brain, and inflammatory changes may also be identified within the cervical spine.

A lumbar puncture may be helpful to look for further evidence of CNS inflammation. Oligoclonal bands unique to the CSF are consistent with the underlying cause of the symptoms being MS. Visual-evoked potentials examine the integrity of the visual pathways by showing the patient a flashing chessboard pattern on a monitor and attaching electrical 'pick-ups' over the visual cortices. These may also provide paraclinical evidence of more widespread inflammatory problems within the CNS (as found in MS).

Multiple sclerosis is an idiopathic autoimmune inflammatory disease of the CNS characterized by inflammation and demyelination of the white matter in the brain and spinal cord. It is the most common neurological disease to affect young adults. The aetiology is uncertain, although both genetic and environmental factors are known to be important. In common with various autoimmune diseases, the condition occurs more frequently in women. Onset is usually between the ages of 30 and 40 years. Typically, patients initially suffer relapsing episodes of neurological dysfunction, with full or partial remissions (relapsing–remitting MS). The relapses may be provoked by infection.

After about 10 years, patients tend to slowly become more disabled, even between relapses (secondary progressive phase MS).

Common forms of neurological disturbance in MS include transverse myelitis, optic neuritis (a subacute, usually unilateral visual loss, with pain on eye movement and a relative afferent pupillary defect, i.e. the pupil of the affected eye does not respond to light but the consensual reflex is maintained – there is usually a full clinical recovery), and brainstem or cerebellar disturbances.

A definite diagnosis of MS is given when a patient has had at least two attacks of demyelination (hence 'multiple') at two different sites in the CNS at different time points. Visual evoked potentials may provide paraclinical evidence of demyelination within the clinically unaffected visual system and provide some evidence of lesions disseminated in the site. Magnetic resonance imaging provides similar information and is more useful. Multiple sclerosis produces high-signal inflammatory lesions in the brain in a periventricular distribution, and inflammatory changes may also be found in the cervical spinal cord. Other autoimmune or connective tissue disorders may cause changes in the brain and spinal cord that can be identified on MRI, but the periventricular pattern is fairly specific to MS.

If a patient presents with an episode of transverse myelitis without a significant past history, he or she has a 'clinically isolated syndrome'. It is uncertain whether this could be a one-off event, or the first symptom of MS. The presence of periventricular lesions on brain MRI, or oligoclonal bands in the CSF, is highly suggestive that the patient will have further neurological events affecting the CNS and thus be diagnosed with MS.

A6: What treatment options are appropriate?

Intravenous corticosteroids, usually given as 1 g prednisolone IV every day for 3 days, are the treatment of choice for all relapses in MS. Corticosteroids speed up the rate of recovery but do not modulate the disease process itself. If there are frequent and problematic relapses, disease-modifying therapies (interferon beta or copolymer) can reduce the relapse rate. Emerging data are showing encouraging results for a large number of immunomodulatory treatments (e.g. fingolimod, natalizumab, alemtuzumab), some of which may influence the rate of disability progression.

DISORDERS OF CRANIAL NERVES

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.15 – A 35-year-old man who has recently had a viral infection presents with a 48-h history of progressive-onset drooping of the left side of his face.

He has noticed his sense of taste is worse and noises seem louder.

CASE 11.16 – A 55-year-old man with diabetes presents with a 4-day history of progressive painful right periorbital pain, drooping of the right eyelid and double vision.

When he lifted his eyelid he noted that his right eye seemed to be deviated 'down and out' and he is unable to move it.

Answers

Clinical cases

CASE 11.15 – A 35-year-old man who has recently had a viral infection presents with a 48-h history of progressive-onset drooping of the left side of his face.

A1: What is the likely differential diagnosis?

The most likely diagnosis is Bell's palsy – an acute inflammatory lower motor neuron lesion of the facial nerve. This may be associated with a viral infection and may occur in all age groups and in both sexes. Maximum facial paralysis generally occurs in 48 h and in almost all cases within 5 days.

The facial nerve runs through the parotid gland, and so parotid tumours may cause a facial nerve palsy. In this situation, the onset may be more insidious.

There are a number of other causes of lower motor neuron facial palsies: Guillain–Barré syndrome, myasthenia gravis, sarcoidosis (a multisystem granulomatous inflammatory disease) and Lyme disease (caused by the tick *Borrelia burgdorferi*) can cause lower motor facial paralysis but are rare and usually bilateral. Moreover, one would expect additional signs and symptoms.

A2: What issues in the given history support or refute a particular diagnosis?

Bell's palsy may be associated with a viral infection, particularly herpes simplex virus. It is important to remember that the facial nerve runs through the parotid gland, and parotid tumours may cause facial nerve palsy; in this case, however, the onset would be expected to be insidious.

Hyperacusis (painful sensitivity to noise) occurs because of involvement of a branch of the facial nerve supplying the stapedius muscle, which acts to damp the ossicular chain. Taste sensation to the anterior two-thirds of the tongue is affected because the trigeminal nerve fibres that run in the chorda tympani nerve and supply the tongue join and travel with the facial nerve.

An upper motor neuron facial weakness is unlikely with this history, partly because other associated symptoms of sensory motor disturbance would be expected.

A3: What additional features would you seek to support a particular diagnosis?

Bell's palsy affects only the facial nerve, and more extensive symptoms would therefore be unlikely. In cases of parotid tumour, the patient may have noted swelling of the cheek.

A4: What clinical examination would you perform, and why?

Examination should confirm features of a left lower motor neuron facial lesion, such as left-sided facial weakness, difficulty in closing the left eye and an inability to furrow the left side of the forehead.

The forehead is bilaterally innervated by the facial nerve. In an upper motor neuron lesion causing unilateral facial paralysis, the forehead is therefore spared.

It is important to examine the patient for signs of a viral herpes zoster skin rash in the external auditory canal and mucous membranes of the oropharynx; this combination of Bell's palsy and herpes zoster is termed Ramsay Hunt syndrome.

A5: What investigations would be most helpful, and why?

Bell's palsy is a clinical diagnosis. In practice, if examination reveals only a lower motor neuron facial nerve palsy, then no other investigations are needed at this stage.

A6: What treatment options are appropriate?

If the eyelid does not close properly, the cornea can be damaged. The eye must be protected (e.g. taped shut), particularly during sleep.

Around 80 per cent of patients with Bell's palsy recover within a month. Early recovery of some motor function in the first 5 days is a favourable prognostic sign. A short course of oral corticosteroids combined with an antiviral agent is associated with improved recovery. If the patient does not recover it is worth reconsidering the cause. Ultrasonography of the parotid gland will identify a tumour causing compression of the facial nerve. Brain imaging will help identify tumours that invade the temporal bone and can cause facial palsy. A lumbar puncture will help in identifying evidence of Lyme disease and other infective agents.

CASE 11.16 – A 55-year-old man with diabetes presents with a 4-day history of progressive painful right periorbital pain, drooping of the right eyelid and double vision.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are compressive right nerve III palsy and infarction of the right nerve III.

A2: What issues in the given history support or refute a particular diagnosis?

The hallmarks of a nerve III palsy are unilateral ptosis and ophthalmoplegia, the eye being deviated down and out.

A3: What additional features would you seek to support a particular diagnosis?

If the cause of nerve III palsy is compression, the pupil of the affected eye will be fixed and dilated (pupil-involving nerve III palsy). If the cause of nerve III palsy is infarction of the nerve, the pupil of the affected eye is unaffected (pupil-sparing nerve III palsy). Enlargement of the pupil is a sign of compression because the pupilloconstrictor fibres are located peripherally in the nerve. Infarction of nerve III characteristically involves the central portion of the nerve but spares the peripheral fibres.

Pain may be a feature of both compression and infarction of cranial nerve III. Nerve III infarction is common in people with diabetes and hypertension. It is important, however, not to assume that this patient has a nerve III infarct just because he has a vascular risk factor.

A4: What clinical examination would you perform, and why?

Pupillary examination is important to help distinguish between a compressive nerve III palsy and a vascular cause, for the reasons outlined above. In a nerve III palsy, the ptosis is often quite profound. The eye should be deviated down and out.

As a rule of thumb, all cases of painful pupil involving nerve III palsies suggest a compressive cause.

A5: What investigations would be most helpful, and why?

If the patient has a painful pupil-involving nerve III palsy, an urgent CT scan of the brain and a CT angiogram are needed.

The acute onset of a painful pupil-involving nerve III palsy suggests a rapidly expanding lesion such as an aneurysm, most commonly of the posterior communicating artery. It is vital not to miss this. There is a significant risk of the aneurysm bursting and causing a subarachnoid haemorrhage. Computed tomography and CT angiography are likely to identify an aneurysm. If an aneurysm is identified, it is important to liaise with neurosurgical and neuroradiological colleagues to consider clipping the aneurysm or endovascular ablation.

If no aneurysm is identified, other causes of compressive nerve III palsy should be considered, such as tumours, carcinomatous lesions of the skull base or cavernous sinus, inflammatory lesions of the nerve or orbit, and giant cell arteritis. These are often accompanied by other symptoms or signs, however. An ESR and MRI of the brain (with contrast or with venogram sequences) are helpful in identifying these other causes.

In a pupil-sparing nerve III palsy, imaging may show evidence of cardiovascular disease and vascular risk factors should be explored.

MOVEMENT DISORDERS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.17 – A 60-year-old woman attends with gradual-onset very slowly progressive tremor in both hands over 10 years.

The tremor is not present at rest. The patient finds it difficult to drink or to use cutlery. She comments that her grandfather, mother and brother had or have similar symptoms. She finds that a small tot of whisky helps ease the tremor.

CASE 11.18 – A 25-year-old man with 'psychiatric problems' presents with a progressive 2-year history of 'movement problems' (at rest and on intention) and slurring of speech.

The patient's cousin died in his teens of a 'liver problem'.

Answers

Clinical cases

CASE 11.17 – **A 60-year-old woman attends with gradual-onset very slowly progressive tremor in both hands over 10 years.**

A1: What is the likely differential diagnosis?

The likely diagnosis is benign essential tremor.

A2: What issues in the given history support or refute a particular diagnosis?

Benign essential tremor is familial in 50 per cent of cases (autosomal dominant), and there may be a striking improvement with alcohol. It tends to affect both hands. It is slowly progressive.

A3: What additional features would you seek to support a particular diagnosis?

The tremor is characteristically coarse, affects the upper limbs distally, and is exacerbated by sustained postures. Cerebellar tremor is different because it is particularly evoked when attempting fine coordinated movements.

A4: What clinical examination would you perform, and why?

Other than the coarse symmetrical tremor, more prominent when the patient holds her hands outstretched, no other abnormalities are identified.

A5: What investigations would be most helpful, and why?

Benign essential tremor is a clinical diagnosis, and investigations are not generally necessary. Occasionally, in the early stages, benign essential tremor can be confused with Parkinson's disease.

A6: What treatment options are appropriate?

Propranolol or primidone may be appropriate. Not all patients require treatment, however, and often the treatment response is poor.

CASE 11.18 – **A 25-year-old man with 'psychiatric problems' presents with a progressive 2-year history of 'movement problems' (at rest and on intention) and slurring of speech.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are an organic movement disorder (Wilson's disease), a drug-related movement disorder and a psychogenic movement disorder.

A2: What issues in the given history support or refute a particular diagnosis?

Progressive onset tremor in a patient with a psychiatric problem may be a drug-related tremor caused by antipsychotic medication. It is possible that the patient has a dyskinesia from antipsychotic medication

(which can also cause parkinsonian-type symptoms). An alternative is that he has a psychogenic movement disorder.

In any young patient with a movement disorder, it is important to consider and exclude the diagnosis of Wilson's disease. Wilson's disease is an autosomal recessive inherited condition caused by mutation in the ATP7B gene on chromosome 13q. The gene is expressed predominantly in liver, kidney and placenta and, to a lesser extent, in heart, brain, lung, muscle and pancreas; the result is an excess of tissue copper deposition. Liver disease is the most common presenting problem in children. Neurological features are a more common mode of presentation in adults. About 35–50 per cent of patients present with neurological or psychiatric symptoms. The condition is important because it is treatable. If left untreated, however, it is fatal. As this young man has a psychiatric history and a family history of liver disease, it is highly likely that the diagnosis is Wilson's disease.

A3: What additional features would you seek to support a particular diagnosis?

It is important to find out the patient's psychiatric medication and doses. Antipsychotics can cause dyskinesia. Even if the patient is on high doses of antipsychotic medication, Wilson's disease must be excluded.

A4: What clinical examination would you perform, and why?

Typical findings in Wilson's disease are irregular random brief abrupt movements of the arms (chorea). A brown crescentic deposit in the periphery of the iris, known as the Kayser–Fleischer ring, is often found, particularly in patients with significant neurological involvement; this is a granular deposit of copper. If the patient has brown eyes, the deposit may not be easy to visualize. Signs of liver disease may also be present.

A5: What investigations would be most helpful, and why?

The following investigations may be helpful:

- slit-lamp microscope examination to identify the Kayser–Fleischer ring
- low serum copper level
- low serum caeruloplasmin level
- increased 24 h urinary copper level
- MRI of the brain often shows changes in the basal ganglia.

A6: What treatment options are appropriate?

Copper-chelating agents such as penicillamine are appropriate, with monitoring of serum copper to guide treatment.

MISCELLANEOUS NEUROLOGICAL DISORDERS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support or refute a particular diagnosis?
Q3: What additional features would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 11.19 – A 30-year-old woman presents with a 3-month history of feeling generally lethargic, intermittent drooping of her left eye and intermittent double vision.

The patient feels her muscles are generally weaker. These symptoms are worse towards the end of the day. She has also noticed that her voice is weaker, again worse at the end of the day.

CASE 11.20 – A previously well 50-year-old man presents with a 5-month history of progressive weakness in his upper and lower limbs.

The symptoms initially affected the patient's hands, the right more than the left. He comments that the muscles in his hands have got 'thinner' and he has noticed some 'flickering' of the muscles in his arms. There are no sensory symptoms.

CASE 11.21 – A 50-year-old man presents with a 12-month history of gradual-onset tremor in his right hand.

The tremor is present at rest, and the patient feels that it is aggravated by stress. His handwriting is deteriorating and getting smaller, and he feels that his movements are generally slower. Otherwise his health is good.

OSCE counselling case

OSCE COUNSELLING CASE 11.2 – **'Will I be able to look after myself in 6 months?'**

A 35-year-old woman is told she has multiple sclerosis and is concerned that she will not be able to look after herself.

Answers

Clinical cases

CASE 11.19 – A 30-year-old woman presents with a 3-month history of feeling generally lethargic, intermittent drooping of her left eye and intermittent double vision.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are myasthenia gravis and Lambert–Eaton myasthenic syndrome (LEMS).

A2: What issues in the given history support or refute a particular diagnosis?

The history is typical of myasthenia gravis, caused by antibodies against acetylcholine (ACh) nicotinic postsynaptic receptors at the neuromuscular junction. Myasthenia gravis has a bimodal age distribution and predominantly affects young adults aged 20–30 years and people over the age of 50 years. Myasthenia gravis is characterized by fluctuating weakness worsened by exertion. Weakness increases during the day and improves with rest. The hallmark of the history and examination is significant fatiguing of the muscles with use.

It can be difficult in practice to distinguish LEMS from myasthenia gravis. Both conditions present with increasing weakness after exertion, and there are also some clinical differences. It is rare for LEMS to present with double vision or dysphagia. In LEMS, the muscles of the trunk, shoulder and pelvic girdle are most frequently involved. It is caused by an autoimmune attack directed against the voltage-gated calcium channels on the presynaptic motor nerve terminal. Fifty per cent of LEMS cases are associated with an underlying neoplasm, particularly small cell carcinoma of the lung.

In this clinical case, the patient is young. LEMS tends to affect people in older age groups, and occurrence at the age of 30 years would be very unusual.

A3: What additional features would you seek to support a particular diagnosis?

The patient should be questioned to determine whether she has fatiguing weakness in other muscle groups. In around 25 per cent of patients, myasthenia gravis is confined to the eye muscles, and the clinical features are therefore limited to ptosis and diplopia (ocular myasthenia). The disorder may spread to other areas (generalized myasthenia) over years, however. In generalized myasthenia, the weakness tends to involve predominantly ocular, facial and bulbar muscles (weakness of speech and swallowing) and axial muscles (especially weakness of head flexion).

A history of drug use should be sought. A number of drugs, including aminoglycosides, tetracyclines, penicillamine, beta-blockers, lithium and corticosteroids, can worsen myasthenic symptoms and may therefore provoke symptom onset.

Myasthenia gravis can be associated with autoimmune diseases, and symptoms of thyroid dysfunction should be sought.

A4: What clinical examination would you perform, and why?

On examination the patient has a mild ptosis of the left eye. Eye movements appear normal, but after you have finished testing them the patient complains that the double vision seems to be starting again. There is mild proximal muscle weakness. Sensory and reflex examinations are normal.

If the diagnosis of myasthenia gravis is suspected, it is important to actively assess the patient for fatiguability of muscle power. This is an add-on to the general neurological examination and so will be found only if it is specifically considered. One method is to continually or repeatedly test power in a particular muscle group (e.g. up-gaze of the eyes to demonstrate a fatiguable ptosis). Sensory examination and deep tendon reflexes are normal. In LEMS, reflexes are often depressed. It is very important to remember that respiratory muscle weakness may occur, and FVC measurements should be made. Testing for signs of thyroid disease or an enlarged thymus should be carried out.

A5: What investigations would be most helpful, and why?

Anti-ACh receptor antibodies are present in around 85 per cent of patients with generalized myasthenia gravis and 50 per cent of patients with pure ocular myasthenia gravis. Thyroid abnormalities are associated in about 4 per cent of patients. Computed tomography of the chest is needed because a proportion of patients with myasthenia gravis have a thymoma. Anti-smooth muscle antibodies are present in about 84 per cent of patients with thymoma under 40 years of age.

Edrophonium is a short-acting acetylcholinesterase inhibitor. It potentiates neuromuscular transmission by reducing breakdown of ACh at the neuromuscular junction. A positive edrophonium test shows a significant improvement in muscle power after administration. The test is usually carried out in a double-blind fashion. The test is not used frequently nowadays because of concerns about cardiac side effects. A therapeutic trial of pyridostigmine may provide the same information.

In myasthenia gravis, neurophysiological studies show a decremental response to repetitive stimulation. As fatiguability of respiratory muscles may result in hypoventilatory failure, FVC measurements may be needed to monitor respiratory function.

In LEMS, anti-voltage-gated calcium channel antibodies can be identified with a blood test. Neurophysiological tests often show a marked and progressive increment in the amplitude of response (often termed 'incremental response').

A6: What treatment options are appropriate?

Pyridostigmine is a longer-acting acetylcholinesterase inhibitor and is helpful for symptomatic control in myasthenia gravis. It may be sufficient in patients with mild ocular symptoms only. Patients with generalized myasthenia gravis also need disease-modifying therapy. Immunosuppression with corticosteroids followed by steroid-sparing agents (e.g. azathioprine) is the standard oral medication of choice. As a short-term dip in myasthenic control may occur when steroids are started, it is common practice to start treatment in hospital and to increase the steroid doses very slowly. Intravenous Ig or plasma exchange can be useful in producing improvement more rapidly. If the patient is found to have a thymoma, it should be surgically removed. In young patients with thymic hyperplasia and high anti-ACh receptor antibodies, thymectomy appears to induce remission in a proportion of patients (although there is no comprehensive evidence base for this).

An underlying malignancy requires treatment. For LEMS, treatment with 3,4-diaminopyridine may be effective. Plasma exchange and IVIG are also helpful.

CASE 11.20 – A previously well 50-year-old man presents with a 5-month history of progressive weakness in his upper and lower limbs.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are motor neuron disease (MND), progressive cervical myeloradiculopathy (progressive compression of the cervical cord and cervical nerve roots), multifocal motor neuropathy and myasthenia gravis.

A2: What issues in the given history support or refute a particular diagnosis?

The most likely diagnosis in this case is MND. Motor neuron disease is a progressive degenerative disorder of motor neurons. As the motor neuron pathway starts within the CNS (in the Betz cells) and travels peripherally, the clinical features of MND may be predominantly upper motor neuron or lower motor neuron, or both. Motor neuron disease usually starts in the fourth to seventh decades of life. It is universally fatal, with a mean disease duration of 3 years. It begins insidiously with weakness (which may be asymmetrical), muscle atrophy or fasciculations in one or more limbs. As the disease progresses, the weakness becomes more symmetrical. It is likely that the 'thinning' of the muscles described by the patient represents atrophy and that the flickering is fasciculations. There are no abnormalities of sensation in MND. No loss of anal sphincter tone occurs, because smooth muscles are not involved.

A3: What additional features would you seek to support a particular diagnosis?

The most common form of MND involves a combination of upper and lower motor neuron features. Lower motor neuron signs include atrophy and fasciculations, while upper motor neuron (corticospinal tract) signs include up-going plantar response, spasticity and brisk tendon reflexes. More rarely, the disease predominantly affects the motor nuclei of the lower brainstem and causes weakness of the muscles of the jaw, tongue and pharynx (termed 'progressive bulbar palsy'). If lower motor neuron features predominate, the appearances may be similar to myasthenia gravis or LEMS (helpful distinguishing features include the fact that eye signs are common in myasthenia gravis but do not occur in MND, and wasting and fasciculations do not occur in myasthenia gravis or LEMS). If the features are of a dominant lower motor neuron problem of the limbs, a rare form of motor peripheral neuropathy called multifocal motor neuropathy is a possible differential diagnosis (helpful distinguishing features include the fact that in multifocal motor neuropathy there is often little wasting of the muscles). High cervical cord compression (involving exiting nerve roots, i.e. cervical myeloradiculopathy) can mimic the more typical cases of MND where there are mixed upper and lower motor neuron signs. With a spinal cord lesion, however, sphincter function is often affected, whereas sphincter function is preserved in MND.

A4: What clinical examination would you perform, and why?

Examination normally shows mixed upper and lower motor neuron features.

A5: What investigations would be most helpful, and why?

Serum creatine phosphokinase is often elevated in MND, but this is non-specific. Magnetic resonance imaging of the cervical spine excludes a cervical cord lesion. In MND, neurophysiological studies show denervation in the muscle groups of at least three different segments of the body (because MND is a diffuse process) and no sensory abnormalities. In multifocal motor neuropathy, neurophysiological studies identify conduction block. The neurophysiological features of myasthenia gravis and LEMS are discussed in Case 11.19.

A6: What treatment options are appropriate?

Treatment is symptomatic support, although symptomatic treatments for complications (cramps, spasticity, drooling, dysphagia, ventilatory failure) are the mainstay of managing this disease. As the disease progresses, speech and swallowing may become so weak that vocal communication and oral feeding are impossible. A communication board may help the patient with communication, and a percutaneous gastrostomy feeding tube may be necessary to maintain adequate nutrition.

Ventilatory failure as a result of progressive muscle weakness develops in the later stages of the disease. Nocturnal hypoventilation may cause early-morning headache and lethargy. Non-invasive respiratory support (e.g. nocturnal ventilatory support using a tight-fitting mask) can help alleviate these symptoms.

The use of invasive ventilation (e.g. ventilation via tracheostomy) is a complex issue. It will prolong life but may well prolong suffering. It may also result in an altered mode of death (e.g. pneumonia). To try to accommodate the patient's wishes, it is important to discuss these issues at an appropriate, but relatively early, stage in the disease.

Riluzole is a disease-modifying therapy with a modest effect. It results in a modest decrease in risk of tracheostomy or death by about 20 per cent over 12 months of treatment. It does not cause symptomatic improvement, however, and does not prevent death. Side effects such as fatigue, nausea and worsening liver function may necessitate discontinuing treatment.

CASE 11.21 – **A 50-year-old man presents with a 12-month history of gradual-onset tremor in his right hand.**

A1: What is the likely differential diagnosis?

The likely differential diagnosis is Parkinson's disease.

A2: What issues in the given history support or refute a particular diagnosis?

Although other conditions (e.g. benign essential tremor, vascular parkinsonism, 'Parkinson plus' syndromes) can cause diagnostic confusion, this history is particularly suggestive of Parkinson's disease.

A3: What additional features would you seek to support a particular diagnosis?

The cardinal features of Parkinson's disease are tremor, bradykinesia and rigidity. Patients are often noted to have an 'expressionless' face, and their handwriting becomes smaller (micrographia). They have poor arm swing and may have stooped posture (particularly later in the disease course). Frequent falls, shuffling gait, difficulty in initiating movements and 'freezing up' occur later in the disease course.

Some patients with cerebrovascular disease may have a parkinsonian appearance. This tends to manifest in a slow, stiff, rigid-type gait, and tremor is not a major feature.

A4: What clinical examination would you perform, and why?

The tremor is 'pill rolling' (imagine rolling a pill between the index finger and thumb), which occurs at rest and *not* by intention. This is an important difference from cerebellar tremor, which is typically brought out by testing limb coordination (e.g. when attempting to touch the tip of the examiner's moving finger).

The tone will appear generally increased (rigidity), and movements (especially rapid alternating movements) will be slower (bradykinesia).

A5: What investigations would be most helpful, and why?

In typical cases the diagnosis is made on clinical grounds alone.

A6: What treatment options are appropriate?

Treatment is symptomatic and does not alter the disease course. If the patient does not have functional limitation, treatment can be deferred. In this particular case, the patient appears to be limited and it would be appropriate to begin treatment.

There is an argument for trying to delay drug treatment in Parkinson's disease for as long as possible. The earlier treatment is started, the earlier the patient starts to develop difficult side effects such as unwanted movements (dyskinesias). These issues should be discussed with the patient. The gold standard, most efficacious treatment is L-dopa, which must be combined with a peripheral decarboxylase inhibitor to minimize peripheral side effects such as nausea and vomiting. There is evidence, however, that treatment with L-dopa may be associated with an earlier onset of limiting dyskinesia, relative to the

newer, but less efficacious dopamine agonists that boost in vivo dopamine production. Currently it is usual practice to delay the use of L-dopa and to begin treatment with a dopamine agonist. Treatment response in the early years of the disease is very good. L-Dopa is added in when the effects of the dopamine agonists are no longer sufficient.

Dopamine is known to play a part in the reward system of the brain. It is increasingly recognized that dopaminergic drugs, including dopamine agonists, may produce significant behavioural side effects. Patients may become hypomanic or hypersexualized or indulge in compulsive behaviours such as compulsive gambling, eating disorders or punding (repetition of complex behavioural patterns such as collecting). Rasagaline, a relatively new monoamine oxidase inhibitor type B, is increasingly used as early monotherapy in Parkinson's disease, in part because of this syndrome.

In later disease, the disease itself and the effects of treatment become more unpredictable. Higher doses of medication may be required to control symptoms, but these may cause limiting dyskinesias. Catechol-O-methyltransferase inhibitors are used as treatment adjuncts, e.g. to prolong the duration of action or minimize the dose of L-dopa. Apomorphine given subcutaneously is used in the late stage, when patients are poorly responsive to oral treatment; this reduces the duration of the 'off' periods when patients are unable to move. Neurosurgery (deep brain stimulation) may benefit carefully selected patients who have symptoms that cannot be controlled with medication.

OSCE counselling case

OSCE COUNSELLING CASE 11.2 – **'Will I be able to look after myself in 6 months?'**

The patient must be informed by a senior doctor and given time to ask any questions that they may have. The patient should have family members with them if they wish. Offering a follow-up consultation soon afterwards is useful to address any issues that the patient later thinks of. Specialist nurses play a particularly valuable role in this follow-up.

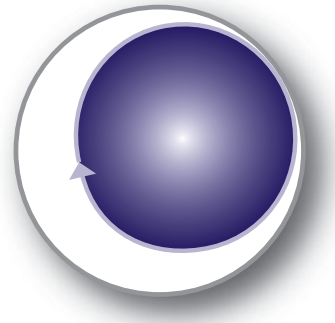
It should be explained that patients with MS have a tendency to inflammation within the brain and spinal cord, and that they may therefore experience episodes (termed 'relapses') of weakness, sensory problems or visual disturbance.

Patients are often very frightened that they may quickly become disabled. At diagnosis, it is important to try to help the patient be positive about the condition. It can be helpful to explain that a significant proportion of patients do not suffer significant fixed deficit for many years, and that there is even a category of 'benign' MS. It is also helpful to explain that there are effective symptomatic treatments for MS. In addition, if a relapse causes a significant functional deficit, corticosteroid pulses speed recovery. If there are frequent and problematic relapses, disease-modifying therapies can reduce the relapse rate, and some may influence the progression of disability.

It should be explained that the cause of MS is unknown but that there is a genetic susceptibility and infections can trigger relapses. Pregnancy is not a problem in MS, and in fact there is often a slight improvement during pregnancy. The risk of MS occurring in the children of patients with MS is about 3–5 per cent. The patient should be offered the contact details of the MS Society, which can offer support and advice. As MS is a chronic neurological disease, all patients receive regular follow-up. Many regions also have specialist nurse support for this condition.

REVISION PANEL

- Seizures may be classified as generalized (consciousness lost) or partial (consciousness not lost).
- Epilepsy is a long-term diagnosis. Issues surrounding AED choice, seizure triggers (fatigue, alcohol and other drugs, stress, occasionally photosensitivity), specific issues for women, driving regulations, safety in the home, and the cognitive effects of epilepsy and AEDs must be discussed with the patient.
- Carotid artery dissection is a significant cause of stroke in patients under the age of 40 years.
- Ascending numbness and weakness about 10 days after an acute infection is typical of Guillain–Barré syndrome, which is an acute peripheral neuropathy causing weakness, paraesthesia and hyporeflexia.
- A chronic peripheral neuropathy may be caused by diabetes mellitus, chronic excess alcohol intake, vitamin B12 and folate deficiency, thyroid disease, renal failure, autoimmune diseases (which may cause a vasculitic neuropathy) and paraproteinaemia (e.g. multiple myeloma).
- Carpal tunnel syndrome is common in conditions where the carpal tunnel becomes narrowed, such as in pregnancy, trauma, rheumatoid arthritis and hypothyroidism. Worsening of symptoms at night, and relief on shaking the affected hand, are typical of carpal tunnel syndrome. It is an example of an isolated mononeuropathy.
- Symptoms of a subarachnoid haemorrhage are a sudden-onset worst-ever headache, similar to a blow to the back of the head. There may be focal neurological signs that give a clue as to the cause of the bleed – e.g. a nerve III palsy suggests a posterior communicating artery aneurysm.
- Other causes of headaches include bacterial meningitis, viral meningitis, cerebral venous sinus thrombosis, benign intracranial hypertension, giant cell arteritis and migraine.
- Trigeminal neuralgia tends to occur in people aged over 60 years and is more common in women. It is characterized by brief paroxysms of pain localized in the maxillary or mandibular divisions of the trigeminal nerve.
- Symptoms of lower limb weakness, a sensory level at the umbilicus and urinary dysfunction of gradual onset are suggestive of a transverse myelitis, although a gradual onset may also occur in certain causes of spinal cord compression (e.g. tumour, epidural abscess).
- Multiple sclerosis is an idiopathic autoimmune inflammatory disease of the CNS characterized by inflammation and demyelination of the white matter in the brain and spinal cord.
- Bell's palsy is an acute inflammatory lower motor neuron lesion of the facial nerve. Other causes of lower motor neuron facial palsies include Guillain–Barré syndrome, myasthenia gravis, sarcoidosis and Lyme disease.
- Wilson's disease may result in irregular random brief abrupt movements of the arms (chorea). A brown crescentic deposit in the periphery of the iris, known as the Kayser–Fleischer ring, is often found, particularly in patients with significant neurological involvement.
- Parkinson's disease is associated with the triad of tremor, bradykinesia and rigidity.



12 Infectious diseases

Chris Ellis

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely diagnosis or differential diagnosis?
Q2: What investigations should be performed?
Q3: What would be the initial management?
Q4: What is the prognosis?

CASE 12.1 – A 26-year-old man presents with fever, headache and confusion.

A 26-year-old executive presents with a 1-week history of headache and 2 days of confusion. He has a temperature of 39 °C. He returned 3 weeks previously from a 2-week safari in Kenya. Full blood count (FBC) and biochemical profile are normal; computed tomography (CT) shows no abnormality.

CASE 12.2 – A 30-year-old woman presents with prolonged fever of unknown origin.

A 30-year-old woman is referred with a 6-month history of fever in the evenings, often accompanied by a faint erythematous rash with aches and pain, some of which clearly arise from the joints. She has not lost weight. She has already been investigated extensively, with a normal chest radiograph and abdominal CT. Rheumatoid antibodies and antinuclear antibodies (ANA) are both negative. On examination you find a faint macular rash, a temperature of 39 °C, a 3 cm smooth liver enlargement and 1 cm glands in both axillae. Cardiovascular examination is unremarkable. Blood cultures have yielded no growth.

CASE 12.3 – A 30-year-old woman has fainted and has fever and a rash.

The patient was well until 48 hours before presentation. Her illness began with nausea and vomiting, and later she felt feverish. On the morning of admission she got up,and then felt faint and briefly lost consciousness. On admission her temperature is 39 °C, her pulse is 110/min, and her blood pressure is 100/60 mmHg supine. There is a diffuse erythematous rash on her face and trunk, which blanches on pressure. She is menstruating.

CASE 12.4 – A 30-year-old man presents with productive cough, feverishness and weight loss.

A 30-year-old Somali man who has lived in the UK for 2 years presents with 1 month of productive cough, feverishness and weight loss. On examination, he is thin but otherwise no abnormality is detected. A chest radiograph shows patchy consolidation of the right upper zone. There is no significant past medical history.

CASE 12.5 – **A 36-year-old woman presents with fever, headache and a rash.**

A 36-year-old female university lecturer presents with 3 days of fever, headache and a rash that she describes as 'a return of her suntan'. Four weeks earlier she returned from a 2-week holiday in Kenya. She is on no medication. She has several 1 cm diameter glands in her neck, pharyngitis and a maculopapular rash on her trunk. Her temperature is 38 °C.

CASE 12.6 – **A 22-year-old man presents with persistent diarrhoea and weight loss.**

A 22-year-old male medical student presents 6 weeks after returning from his elective period in Nepal. While there, he had two episodes of watery diarrhoea and took a single dose of ciprofloxacin on each occasion; his symptoms settled within 48 h. He was well on return but developed watery diarrhoea 1 week later, which has persisted; he now reports five or six motions a day, with some abdominal distension and excessive flatus. He has lost 6 kg in the past 2 weeks.

OSCE counselling cases

OSCE COUNSELLING CASE 12.1 – **'I am a 26-year-old builder. Last year I fell off a ladder and had to have my spleen removed. Someone in the pub told me I can die of septicaemia. Was he right, and what can I do about it?'**

OSCE COUNSELLING CASE 12.2 – **'I am a gay man who has one regular partner, but occasionally I have sex with new male acquaintances. Although I try to remember to "play safe", I don't think I have always succeeded. I am fully fit and, as far as I know, none of my partners is HIV positive. Would you advise me to be tested?'**

OSCE COUNSELLING CASE 12.3 – **'I am a 24-year-old mother of a 6-month-old baby girl. My widowed mother was recently in hospital for a hip replacement, and her wound was infected with methicillin-resistant *Staphylococcus aureus* (MRSA). I love my mother but don't want her in my home as she could infect my baby. In any case, shouldn't she have been kept in hospital?'**

Key concepts

The following are definitions of sepsis, often referred to in the literature as systemic inflammatory response syndrome (SIRS).

- Sepsis: two or more of:
  - temperature >38 °C or <36 °C
  - pulse >90/min
  - respiratory rate >20/min
  - white blood cell count (WBC) >12 000 or <4000.
- Severe sepsis: sepsis with one or more of:
  - hypotension
  - confusion
  - oliguria
  - hypoxia
  - acidosis
  - disseminated intravascular coagulation (DIC).
- Septic shock: severe sepsis with hypotension despite fluid resuscitation.

Answers

Clinical cases

CASE 12.1 – A 26-year-old man presents with fever, headache and confusion.

A1: What is the likely diagnosis or differential diagnosis?

Headache, fever and confusion suggest encephalitis, but this man is at risk of falciparum malaria, which can produce a picture identical to encephalitis (so-called cerebral malaria). The differential diagnosis therefore includes two conditions for which early treatment can be literally vital – herpes simplex encephalitis and falciparum malaria.

A2: What investigations should be performed?

A haematological sample should be sent immediately to look for malarial parasites, which will usually be seen as rings within erythrocytes. It is crucial that the request be made specifically, because automated cell counters do not detect malarial parasites. The normal CT excludes cerebral swelling, and so it is safe to perform a lumbar puncture; the cerebrospinal fluid (CSF) may contain lymphocytes and erythrocytes in keeping with a primary encephalitis.

A3: What would be the initial management?

It would be prudent to cover both of the treatable life-threatening possible diagnoses, unless the blood film conclusively confirms falciparum malaria. Malaria should be covered by intravenous (IV) quinine (consult the current British National Formulary for details, and confer with the regional infectious diseases department), and IV aciclovir will cover herpes encephalitis.

A4: What is the prognosis?

The prognosis of severe malaria is good, provided the patient survives the first few days, but during that period the full sepsis syndrome may be encountered, with acute renal failure, disseminated intravascular coagulation (DIC) and adult respiratory distress syndrome (ARDS).

About a third of patients with herpes encephalitis die, a third survive with varying degrees of permanent brain damage, and a third eventually make a virtually complete recovery. Early treatment is crucial to a good outcome, but even patients who are treated very promptly may have permanent brain damage.

CASE 12.2 – A 30-year-old woman presents with prolonged fever of unknown origin.

A1: What is the likely diagnosis or differential diagnosis?

This is adult systemic Still's disease. Patients who have been pyrexial for several weeks usually turn out to have occult infection, occult neoplasm (lymphoma or non-obstructing cancers, e.g. renal) or a connective tissue disorder. This story is typical of systemic Still's disease in young adults.

A2: What investigations should be performed?

First-line investigations for pyrexia of unknown origin are FBC and biochemical profile, blood culture, midstream urine, and chest radiograph (with malarial parasites requested specifically and urgently if

the patient has been in a malarial area in the preceding 3 months). If these are unhelpful, proceed to ANA and imaging of the abdomen (ultrasonography is usually available first, but CT is necessary if ultrasonography is inconclusive and no other diagnosis has emerged).

Adult Still's disease is underrecognized, partly because there is no specific test. It has some definite features, however:

- daily fever (typically early evening)
- arthralgia/arthritis
- negative rheumatoid factor and negative ANA
- two of: leucocytosis; rash-transient erythema, often with fever; serositis (e.g. pleural effusion); hepatomegaly; splenomegaly; generalized lymphadenopathy.

A3: What would be the initial management?

A trial of corticosteroids should be the initial management. Clinicians are often reluctant to give steroids to patients for fear of lighting up occult infection. In practice, this is almost never a problem. Prolonged steroid therapy can, indeed, lead to activity of dormant tuberculosis (TB), but it makes little difference to most bacterial infections. Furthermore, the response in conditions such as Still's disease is usually rapid and decisive so that, if the patient is not apyrexial and dramatically improved within 3 days, the therapy should be reconsidered.

A4: What is the prognosis?

The prognosis is usually good. It may take several months before the patient can be weaned off steroids entirely, and relapses are common for about 5 years after the first episode, after which they usually cease. A minority of patients develop an established connective tissue disorder such as a rheumatoid disorder.

CASE 12.3 – **A 30-year-old woman has fainted and has fever and a rash.**

A1: What is the likely diagnosis or differential diagnosis?

There is enough evidence to justify treating this woman for presumed septic shock. A possible focus of infection could be the genital tract; a tampon should be sought and, if present, removed. Toxic shock syndrome (TSS) is a specific form of septic shock caused by toxins liberated by staphylococci, which may colonize the vagina and multiply on tampons or cause soft tissue infection such as cellulitis.

A2: What investigations should be performed?

Any patient with sepsis should be examined carefully for a focus, including careful inspection for evidence of skin or soft tissue infection, and evidence of focal infection in the thorax, abdomen and pelvis. Blood cultures must be taken. A chest radiograph is mandatory because pneumonia may not be apparent clinically. When appropriate, the vagina should be examined and a tampon or intrauterine contraceptive device (IUCD) removed and cultured.

Sepsis is a clinical diagnosis based on a constellation of abnormalities (see 'Key concepts' above). A positive blood culture (bacteraemia) supports it, and in this case isolation of a toxin-producing *S. aureus* from a tampon would confirm TSS. The critical practical point is, however, that immediate management will not be affected by what the laboratory may report later.

A3: What would be the initial management?

Initial management includes IV fluids, which should be given as rapidly as possible, and high-dose IV broad-spectrum antibiotics to ensure specific cover for any likely focus. In this case, standard broad-spectrum cover should be augmented by a potent anti-staphylococcal agent such as flucloxacillin. When pneumonia is suggested clinically or radiologically, treatment should be augmented with cover for

atypical pathogens (e.g. a macrolide such as clarithromycin or a quinolone). When appropriate, the focus of infection (tampon, IUCD; aspirate or drain fluctuant areas in soft tissue infection) should be removed.

A4: What is the prognosis?

The prognosis depends very much on the promptness and thoroughness of immediate intervention. Complete recovery is the aim, but the more the initial intervention is delayed, the more likely is progression to a full sepsis syndrome, with circulatory collapse, acute renal failure, ARDS and DIC.

CASE 12.4 – **A 30-year-old man presents with productive cough, feverishness and weight loss.**

A1: What is the likely diagnosis or differential diagnosis?

Pulmonary TB is overwhelmingly the most likely diagnosis. Acute bacterial pneumonias typically progress more rapidly. The absence of a previous history makes bronchiectasis unlikely.

A2: What investigations should be performed?

Sputum should be sent for TB microscopy and culture. If TB is confirmed, the patient should be tested for human immunodeficiency virus (HIV) after appropriate counselling.

A3: What would be the initial management?

It is common practice for patients with this presentation to receive an antibacterial appropriate for community-acquired pneumonia (e.g. amoxicillin plus a quinolone or a macrolide such as clarithromycin), pending confirmation of the diagnosis of TB. There is an argument for avoiding quinolones in this context because they have anti-tuberculous activity and it is important to avoid promoting resistance to agents that may be needed in the future to treat TB. Once the diagnosis is confirmed, the patient should be treated with a combination of rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months, reducing to rifampicin and isoniazid for a further 4 months. He will need careful supervision to ensure compliance and recovery. If he is smear-positive (acid-fast bacilli seen on Ziehl–Neelsen staining), he will be highly infectious and will remain so until 2 weeks after the start of treatment. Consider isolating him in hospital for this period.

The patient should be officially notified to the consultant in communicable disease control, who will arrange for screening of household contacts and, if appropriate, of acquaintances and colleagues.

A4: What is the prognosis?

The prognosis is good. Over 95 per cent of compliant patients with the drug-sensitive strain of TB are cured at the end of the conventional 6-month course of treatment, with a relapse rate of no more than 2 per cent. Most relapses occur within 1 year of stopping treatment. If the patient is HIV-positive, treatment should still cease at 6 months, but the relapse rate will be higher.

CASE 12.5 – **A 36-year-old woman presents with fever, headache and a rash.**

A1: What is the likely diagnosis or differential diagnosis?

Falciparum malaria must be considered in any patient with a fever within 3 months of return from an endemic area. It would not cause lymphadenopathy or a rash. This could be a non-specific viral infection, glandular fever (primary Epstein–Barr virus infection) or a primary HIV illness.

A2: What investigations should be performed?

A blood sample asking for malaria parasites and a glandular fever screen should be done.

After discussion, the patient agrees to testing for HIV infection, having admitted to unprotected sex during her holiday. Her HIV test is positive. (Modern HIV serology tests for both antigen and antibody, but if the diagnosis is likely, a negative test should still be repeated 1 week later.)

Primary HIV infection presents as a glandular fever-like illness, often with a rash, and is one of the HIV presentations most likely to present to accident and emergency (A&E) departments in patients in whom the underlying diagnosis is not yet established. Other front-door presentations include *Pneumocystis carinii* pneumonia (typically 3–4 weeks of dry cough, with more recent shortness of breath on effort or fever), oral candidiasis and generalized lymphadenopathy.

A3: What would be the initial management?

The patient should be referred for specialist HIV care and started on antiretroviral treatment when the CD4 lymphocyte count has fallen to about 250.

A4: What is the prognosis?

Provided the patient is established on antiretroviral therapy at an appropriate stage, the prognosis appears good, with most patients who started modern treatment when it was introduced in 1996 enjoying a good quality of disease-free life 9 years later.

CASE 12.6 – **A 22-year-old man presents with persistent diarrhoea and weight loss.**

A1: What is the likely diagnosis or differential diagnosis?

Giardiasis (infection with the protozoon *Giardia lamblia*) is the most likely cause of these symptoms. The most common cause of transient travellers' diarrhoea is probably enterotoxigenic strains of *Escherichia coli*, which causes hypersecretions from the small intestine. This has a short incubation period of 1–2 days and rarely causes diarrhoea lasting more than a week.

Giardia lamblia multiplies more slowly than bacteria, and symptoms commonly start a few days after the traveller has returned from where he or she acquired it. Watery diarrhoea is usual for the first 2–3 weeks, but malabsorption may then develop, with more bulky stools and flatulence from the fermentation of undigested sugars.

A2: What investigations should be performed?

Stool should be sent for culture and microscopy, but a negative result does not exclude giardiasis and a therapeutic trial of an anti-giardial agent such as tinidazole is good practice.

A3: What would be the initial management?

Initial management is a single dose of tinidazole, repeated after 1 week.

A4: What is the prognosis?

The prognosis is excellent. Symptoms of giardiasis improve decisively within a few days of starting appropriate treatment. If there is no improvement, small bowel endoscopy should be performed and a biopsy taken. This may reveal less common parasites such as cyclospora or the flat mucosa indicative of coeliac disease.

OSCE counselling cases

OSCE COUNSELLING CASE 12.1 – **'I am a 26-year-old builder. Last year I fell off a ladder and had to have my spleen removed. Someone in the pub told me I can die of septicaemia. Was he right, and what can I do about it?'**

The spleen protects very specifically against capsulated bacteria. Pneumococci are by far the biggest threat, with fulminating pneumococcal septicaemia being about 1000 times more frequent in splenectomized patients than in the intact population. The risk appears to be less in individuals who are splenectomized after traumatic rupture than in those whose spleen was removed electively. Consensus advice is to offer pneumococcal vaccine and life-long prophylactic penicillin to all splenectomized patients.

OSCE COUNSELLING CASE 12.2 – **'I am a gay man who has one regular partner, but occasionally I have sex with new male acquaintances. Although I try to remember to "play safe", I don't think I have always succeeded. I am fully fit and, as far as I know, none of my partners is HIV positive. Would you advise me to be tested?'**

The advantage of people at high risk of HIV knowing their status clearly outweighs any disadvantages. For this individual, the main advantage is that if he tests positive, he can have his virus load and CD4 lymphocyte count monitored so that antiretroviral therapy can be started as soon as it is clear that his infection has entered a stage when acquired immunodeficiency syndrome (AIDS) is inevitable, but before significant attrition of the CD4 lymphocytes. The aim is for the CD4 population to be stabilized at a level above that likely to be associated with life-threatening opportunistic infections such as *P. carinii* pneumonia. He should be offered same-day testing to minimize anxious waiting. He should be seen with the result, not informed of it over the phone. The importance of safe sex must be reinforced, whatever the result of the test.

OSCE COUNSELLING CASE 12.3 – **'I am a 24-year-old mother of a 6-month-old baby girl. My widowed mother was recently in hospital for a hip replacement, and her wound was infected with MRSA. I love my mother but don't want her in my home as she could infect my baby. In any case, shouldn't she have been kept in hospital?'**

Methicillin-resistant *S. aureus* rarely causes clinically significant infection in healthy individuals, including healthy babies. Significant infection in hospital is largely confined to elderly or debilitated people. There

is no reason why colonized patients should not go home, if they are fit enough to manage. If they are admitted to hospital, they may have the depressing experience of being nursed in a side room, because there is some evidence that this reduces the likelihood of transmission to others. Common sites for colonization are the nostrils and wounds. If there is no evidence of an inflammatory response, there is no imperative to treat the patient; if wounds are inflamed, the choice of antibiotic should be guided by sensitivity testing, although there may be no alternative to IV agents such as vancomycin. Colonization can be treated with topical antiseptics in an attempt to eliminate MRSA if readmission to hospital is likely to be necessary within 1 year.

REVISION PANEL

- Consider sepsis if two or more of the following are present: temperature >38 °C or <36 °C; pulse >90/min; respiratory rate >20/min; white blood cell count >12 000 or <4000.
- Always consider falciparum malaria in a traveller returning from an endemic area. Failure to treat results in acute renal failure, DIC and ARDS.
- Patients who have been pyrexial for several weeks usually turn out to have occult infection, occult neoplasm (lymphoma or non-obstructing cancers, e.g. renal), a connective tissue disorder or rarely Still's disease.
- Toxic shock syndrome is a specific form of septic shock caused by toxins liberated by staphylococci, which may colonize the vagina and multiply on tampons or cause soft tissue infection such as cellulitis.
- Consider pulmonary TB in any person with a chronic productive cough, weight loss and night sweats.
- Primary HIV infection may present as a glandular fever-like illness, often with a rash in patients in whom the underlying diagnosis is not yet established. Other front-door presentations include *P. carinii* pneumonia (typically 3–4 weeks of dry cough, with more recent shortness of breath on effort or fever), oral candidiasis and generalized lymphadenopathy.
- Offer pneumococcal vaccine and life-long prophylactic penicillin to splenectomized patients.

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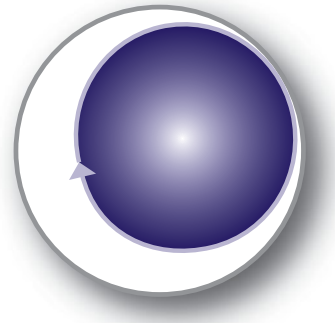


13 Dermatology

Nevianna Tomson

MALIGNANT MELANOMA

NON-MELANOMA SKIN CANCER

ECZEMA

MALIGNANT MELANOMA

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 13.1 – A 40-year-old woman presents with a brown mark on her leg.

A 40-year-old woman presents with a 3-month history of a gradually enlarging brown mark over her left shin. It has bled spontaneously on two occasions and appears to have become darker over the past few weeks.

CASE 13.2 – An 80-year-old woman attends the accident and emergency (A&E) department after a fall at home. She comments that the 'age spot' on her forehead has become 'more noticeable'.

An 80-year-old woman attends A&E after a fall at home. The attending casualty officer incidentally notices a dark brown and black-coloured mark over her forehead. It is entirely asymptomatic and has been present for many years. The patient comments that it has become more noticeable over the past few months.

CASE 13.3 – A 62-year-old man presents with a brown mark under his thumbnail.

A 62-year-old African Caribbean man presents to his general practitioner (GP) having developed a dark-brown longitudinal streak under his right thumbnail. It has appeared in the past 2 months and is asymptomatic.

OSCE counselling cases

OSCE COUNSELLING CASE 13.1 – 'My mother died of melanoma. Is there anything I should do?'

A 20-year-old woman has come to see you concerned about her risk of developing malignant melanoma. She tells you that her mother died aged 35 years from metastatic malignant melanoma, and her maternal aunt has recently been diagnosed at the age of 50 years with melanoma. Does the woman have an increased risk of developing melanoma? What can she do to minimize her risk of melanoma in the future?

OSCE COUNSELLING CASE 13.2 – 'What happens now that I have been diagnosed with malignant melanoma?'

A 49-year-old man has recently had a suspicious mole excised from his back. The histology has confirmed this to be a malignant melanoma. He attends the dermatology clinic and is told the diagnosis. What is the next step in his management?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Malignant melanoma is an invasive malignant tumour of melanocytes that usually develops in skin that was previously normal, but may arise in a pre-existing mole. The leg is the most common site in women and the back in men, although malignant melanoma can affect any site of the body. Acral lentiginous melanoma is the most common melanoma in oriental and black patients but is rare in white patients. It occurs on palmar and plantar skin and under the nails. Mucosal melanoma may occur in the oral cavity, around the anus or on the genitalia but is rare.

The main diagnostic feature of malignant melanoma is the history of change in a pigmented lesion. The Glasgow Seven-Point Check List and the American ABCDE System have been devised to help with diagnosing malignant melanoma. The Glasgow system lists three major features – change in size, irregularity in colour and irregularity of outline – and four minor features – diameter >6 mm, inflammation, bleeding, itching or change in sensation.

Excision biopsy of the mole is suggested in the presence of one major feature. The presence of minor features adds to the suspicion of melanoma. In the UK, the American ABCDE system is mainly used:

- A: asymmetry of the shape of the lesion
- B: irregularity of the border
- C: variation in colour
- D: diameter of the lesion (increase in diameter)
- E: elevation (mole becomes raised or nodular).

A malignant melanoma usually looks different from the patient's other moles.

Answers

Clinical cases

CASE 13.1 – **A 40-year-old woman presents with a brown mark on her leg.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are malignant melanoma, benign mole, seborrhoeic wart, dermatofibroma, freckle, solar lentigo and pigmented basal cell carcinoma (BCC).

A2: What issues in the given history support the diagnosis?

The patient gives a clear history of a pigmented lesion that is changing in size and colour. Both of these features suggest malignant melanoma. Melanomas may appear black or have irregular pigmentation with shades of white, red, blue, brown or black. Associated symptoms such as itching or bleeding can also signify that a melanoma is developing but are less important than change in size, shape and colour.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important to establish how the lesion began. Was there a pre-existing mole? If so, when did it start to change? Determine how the lesion has changed. Is it simply a change in diameter, or has its outline become more irregular? Benign moles usually have a symmetrical even outline, whereas malignant melanomas tend to have an irregular edge with one area advancing more than the rest of the lesion. Finally, determine whether there is any family history of skin cancer, in particular malignant melanoma.

A4: What clinical examination would you perform, and why?

Examine the lesion in detail. Remember ABCDE. A dermatoscope may be used to examine the lesion more closely and in trained hands improves diagnostic accuracy. If a malignant melanoma is suspected, a general examination to look for secondary metastases is mandatory, paying particular attention to any cervical, axillary or inguinal lymphadenopathy and examining for hepatomegaly.

A5: What investigations would be most helpful, and why?

The only way to confirm a melanoma is to excise the lesion and send it for histological analysis. This will determine the Breslow thickness of the melanoma (a measurement, in millimetres, of how deeply tumour cells are invading from the epidermis of the skin into the dermis). The Breslow thickness is related directly to prognosis and will determine whether further tests need to be done. The TNM cancer grading system is used to determine the stage of the melanoma (0–IV) using the Breslow thickness to determine the tumour stage (T), the number of involved lymph nodes to determine the lymph node staging (N), and the presence and number of distant metastases (M). In general, melanomas greater than 2 mm in Breslow thickness are in stage IIB and above; it is recommended that these patients have further investigations, including full blood count (FBC), liver function tests (LFTs), lactate dehydrogenase (LDH), and a computed tomography (CT) scan of the chest, abdomen and pelvis to look for metastases. Patients with tumours that are over 1 mm in Breslow thickness are usually offered a sentinel lymph node

biopsy, a new technique that is used to identify the lymph node that drains tissue fluid from the area of the melanoma. The node is then removed to see whether it contains cancer cells.

A6: What treatment options are appropriate?

Surgical excision is the only definitive treatment for malignant melanoma. Initially the mole is removed with a 2 mm margin of normal skin and analysed for Breslow depth. National Cancer Guidelines recommend a second re-excision of the scar to prevent local recurrence of the melanoma. If the melanoma is of Breslow thickness less than 1 mm, then a 1 cm re-excision is recommended. For lesions of Breslow thickness over 1 mm, a re-excision of 2–3 cm may be recommended. Chemotherapy may be used to palliatively treat metastatic disease, but this is often as part of clinical trials.

CASE 13.2 – An 80-year-old woman attends A&E after a fall at home. She comments that the 'age spot' on her forehead has become 'more noticeable'.

A1: What is the likely differential diagnosis?

The likely differential diagnoses are lentigo maligna, lentigo maligna melanoma, solar lentigo, simple or senile lentigo, malignant melanoma, seborrhoeic keratosis and café-au-lait spot.

A2: What issues in the given history support the diagnosis?

Lentigo maligna is an in situ malignant melanoma. It can closely resemble other pigmented lesions, such as simple or solar lentigos and flat seborrhoeic keratosis. It appears as a flat pigmented lesion with colours that may vary from light tan to dark brown or black. It gradually enlarges but is otherwise asymptomatic. Its margin is usually irregular. It becomes thickened and nodular as it invades through the basement membrane and is then known as lentigo maligna melanoma.

A3: What additional features in the history would you seek to support a particular diagnosis?

Lentigo maligna typically occurs over sun-exposed areas. Most patients give a history of significant sunlight exposure throughout their lives. Ask the patient whether the lesion is more noticeable because it has enlarged or developed an irregular border or colour.

A4: What clinical examination would you perform, and why?

Examine the lesion in detail for irregularity in border and colour, and measure its size. In particular, note any nodularity that may suggest progression to lentigo maligna melanoma. Examine the patient for lymphadenopathy.

A5: What investigations would be most helpful, and why?

Magnification of the lesion by dermoscopy can be useful in trying to distinguish lentigo maligna from simple lentigo and early seborrhoeic keratosis. Incisional or excisional biopsy of the lesion is necessary, however, to confirm the diagnosis of lentigo maligna and distinguish it from lentigo maligna melanoma.

A6: What treatment options are appropriate?

Ideally, lentigo maligna should be excised surgically. It usually occurs in elderly people, however, and is often quite sizeable at presentation. Dermatologists sometimes prefer to observe these lesions and monitor with serial photographs or perform an incisional biopsy to sample a large part of the lesion.

Excision can be undertaken, especially if the lesion becomes thickened and is suspected to have developed into lentigo maligna melanoma. Early lentigo maligna can also be treated with radiotherapy.

CASE 13.3 – **A 62-year-old man presents with a brown mark under his thumbnail.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are subungual melanoma, trauma, linear melanonychia (straight, longitudinal, brown/black, evenly pigmented line – common in the nails of black people but very rarely in white people), and fungal nail infection.

A2: What issues in the given history support the diagnosis?

In the absence of a history of trauma, a subungual melanoma must be considered as the most likely diagnosis.

A3: What additional features in the history would you seek to support a particular diagnosis?

Ask the patient whether he recalls any trauma to the nail. Are any of the other nails affected in a similar way?

A4: What clinical examination would you perform, and why?

Examine the nail carefully. In subungual melanoma, the pigment under the nail is deep and often irregular. Deep red/purple colours or pinpoint russet areas suggest haemorrhage from trauma. Look out for Hutchinson's sign – a flat pigmented irregular patch of skin over the nail fold, highly diagnostic of subungual melanoma. The nail may also be deformed and may split as the melanoma underneath thickens. The patient must be examined for metastatic spread.

A5: What investigations would be most helpful, and why?

A nail biopsy is the only way to confirm or refute the diagnosis.

A6: What treatment options are appropriate?

The melanoma is surgically excised, which frequently necessitates amputation of the digit.

OSCE counselling cases

OSCE COUNSELLING CASE 13.1 – 'My mother died of melanoma. Is there anything I should do?'

The incidence of melanoma is rapidly increasing. In the UK, it has been estimated that the lifetime risk of developing malignant melanoma is 1 in 91 for men and 1 in 77 for women. Ultraviolet (UV) light is considered to be the most important factor. Intense and infrequent exposure once or twice a year appears to carry a greater risk than chronic continuous sunlight exposure. Fair-skinned people, people with red hair, blue eyes and poor tanning capacity, and people who burn frequently when exposed to sunlight have the greatest risk of developing melanoma.

Most malignant melanomas occur sporadically, but 2–10 per cent of patients diagnosed with malignant melanoma give a positive family history of melanoma in one or more first-degree relatives. This may be a result of inheritance of specific melanoma susceptibility genes or grouping of other known risk factors, such as similar skin type, sun exposure and the number of pigmented naevi in family members.

Prevention of melanoma is extremely important. Patients must be educated on the dangers of UV radiation and sunburn, and the importance of using photoprotection, including clothing, to cover sun-exposed areas and high-factor sunscreens. Patients should also be educated on the features of malignancy to look out for, in order to help with early detection and treatment of malignant melanoma in the future.

OSCE COUNSELLING CASE 13.2 – 'What happens now that I have been diagnosed with malignant melanoma?'

The patient may need to have the following, depending on the Breslow depth of the melanoma:

- full clinical examination to look for metastases
- investigations to look for metastatic spread of the melanoma – FBC, LFTs, LDH and CT scan of the chest, abdomen and pelvis
- patients with tumours over 1 mm in Breslow thickness are usually offered a sentinel lymph node biopsy
- further excision of the scar with a 1–3 cm margin to minimize the risk of local recurrence in the future
- follow-up for up to 5 years to exclude local recurrence or metastatic spread; at each visit the patient should have the scar examined and a general examination to look for cervical, axillary and inguinal lymphadenopathy and hepatomegaly. The patient should be taught how to self-examine the scar and how to look for lymphadenopathy.

NON-MELANOMA SKIN CANCER

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 13.4 – **A 70-year-old man presents with an ulcer on his scalp.**

A 70-year-old man presents with an ulcer over the vertex of his scalp. He has been losing his hair since the age of 30 years and noticed the sore appearing 6 months ago. It has increased in size and bleeds on minimal trauma.

CASE 13.5 – **A 48-year-old man presents with a lump on his cheek that is getting bigger.**

A 48-year-old man who works as a landscape gardener presents to his GP, having noticed a small lump appearing over his right cheek about a year ago. It has been slowly increasing in size but is otherwise asymptomatic.

CASE 13.6 – **An 82-year-old woman presents with two red patches on her shin.**

An 82-year-old woman has come to see you with two red scaly patches over her right shin. She is not sure how long they have been present because they are not giving her any symptoms. Two years ago she had some solar keratoses over her forehead that were treated with cryotherapy.

OSCE counselling case

OSCE COUNSELLING CASE 13.3 – **'What can I do to reduce my risk of more skin cancers in the future?'**

A 42-year-old woman has recently had two nodular BCCs excised from her face. She attends for a routine follow-up visit.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Actinic keratoses (solar keratoses) are areas of chronic sun-induced skin damage occurring on exposed sites (face, balding scalp, ears, dorsum of hands). They are usually multiple and appear as rough red scaly lesions. Small lesions are more easily felt than visualized. They are considered premalignant and have the potential to progress to squamous cell carcinoma (SCC). A variety of treatments are available, the most commonly used being cryotherapy, 5-fluorouracil (5FU) cream, diclofenac gel and curettage.

Bowen's disease is another name for intraepidermal squamous cell carcinoma (in situ SCC). It occurs predominantly in elderly people over sun-exposed sites (usually over the lower legs). Lesions present as a red plaque with a variable amount of scale and enlarge slowly over time. They are typically asymptomatic but may itch, ulcerate or bleed. Often they are misdiagnosed as eczema or psoriasis. In a fifth of patients, multiple lesions occur. Progression to invasive SCC has been reported in about 5 per cent of patients. Treatment of Bowen's disease is with cryotherapy, 5FU cream, diclofenac gel, photodynamic therapy or surgical excision/curettage.

Basal cell carcinoma (rodent ulcer) is the most common skin cancer. It originates from the basal cells of the lower epidermis and is locally destructive but rarely metastasizes. It is common on the head and neck and over the back and chest. It presents as an asymptomatic nodule that slowly enlarges and may occasionally bleed. It is often diagnosed incidentally. Ideally, it should be surgically removed by excision, but a superficial BCC or multiple BCCs may be removed by curettage and cautery. Superficial BCCs may be medically treated with 5FU cream, imiquimod cream, photodynamic therapy or cryotherapy. Occasionally, radiotherapy may be used.

Squamous cell carcinoma is a malignant tumour that arises from keratinocytes and has the potential to metastasize. It presents on sun-exposed sites (face, ears, balding scalp, dorsum of hands, forearms, lower legs) as a tender lump or ulcer that enlarges quite rapidly and fails to heal. Surgical excision is the treatment of choice, but radiotherapy may also be used.

Answers

Clinical cases

CASE 13.4 – **A 70-year-old man presents with an ulcer on his scalp.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are SCC, solar keratosis, Bowen's disease, ulcerated BCC, keratoacanthoma and viral wart.

A2: What issues in the given history support the diagnosis?

A non-healing ulcer over a sun-exposed area raises the possibility of an SCC. Patients may report that the lesion crusts over or bleeds when traumatized (e.g. on combing hair) or spontaneously.

A3: What additional features in the history would you seek to support a particular diagnosis?

Ultraviolet irradiation is the most common cause, so it is important to ask about previous sun exposure. Has the patient worked outdoors or lived abroad? Has he received psoralen and ultraviolet A (PUVA) treatment or used sunbeds in the past? Ask about X-ray irradiation, used in the past to treat tinea capitis, eczema and psoriasis, which may have been a predisposing factor. Squamous cell carcinomas are also well known to arise in scars, such as those from previous burns. Immunosuppressants also predispose to non-melanoma skin cancers, and SCCs are common in recipients of organ transplants. Also enquire about any family history of skin cancer.

A4: What clinical examination would you perform, and why?

Examine the ulcer and measure its size. The rest of the skin must also be examined for other sun-induced cutaneous premalignant and malignant conditions, such as solar keratosis, Bowen's disease and BCC. Look also for any clinical signs of metastasis, paying particular attention to the regional lymph nodes.

A5: What investigations would be most helpful, and why?

The lesion must be biopsied or excised to confirm the diagnosis histologically.

A6: What treatment options are appropriate?

The treatment of choice is surgical excision with a 4 mm margin of normal skin excised with the tumour. Radiotherapy is also very effective and typically used for patients who refuse surgery, patients with non-resectable tumours, and where tumour margins are ill-defined. Patients are followed up to look for clinical signs of recurrence.

CASE 9.5 – **A 48-year-old man presents with a lump on his cheek that is getting bigger.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are BCC, epidermoid cyst, sebaceous hyperplasia, intradermal naevus, seborrhoeic keratosis, viral wart, SCC and keratoacanthoma.

A2: What issues in the given history support the diagnosis?

A BCC must be considered when there is a history of a slowly enlarging lump over a sun-exposed site. It generally starts as an asymptomatic papule that becomes nodular and ulcerates centrally.

A3: What additional features in the history would you seek to support a particular diagnosis?

Ask the patient about exposure to UV light, X-ray irradiation and use of immunosuppressant medication, as you would when an SCC is suspected.

A4: What clinical examination would you perform, and why?

Examine the lesion and measure its diameter. The lesion classically appears as a pearly papule or nodule with telangiectasia and a raised rolled edge (nodular BCC). Basal cell carcinomas are usually subdivided into types:

- *superficial BCC* – flat red patches usually over the trunk; a rolled, pearly, telangiectatic border may be visible
- *nodular/cystic BCC* – as described above
- *multifocal BCC* – these start as nodules that expand, with areas of apparent regression between them; there are fine strands of tumour connecting the nodules, however
- *morphoeic BCC* – elevated smooth firm plaque that is often misdiagnosed as a scar; may appear pearly with telangiectasia
- *pigmented BCC* – as for nodular BCC, but with pigmented margins; a pigmented BCC may be mistaken for malignant melanoma.

A5: What investigations would be most helpful, and why?

A diagnostic biopsy may be performed for histological confirmation of the type of BCC. Lesions that look classical for BCC, however, are best excised with a 4 mm margin of normal skin.

A6: What treatment options are appropriate?

Surgical treatment can be by excision with a 4 mm margin or curettage and cautery for small, multiple and superficial lesions. Cryotherapy is sometimes used for superficial or multiple lesions. Radiotherapy may be more appropriate in elderly people and in people who refuse surgery. Patients do not require follow-up if the BCC has been completely excised, but they are often followed up if the BCC is treated in another way as there is then a higher risk of recurrence.

CASE 13.6 – **An 82-year-old woman presents with two red patches on her shin.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are Bowen's disease, actinic keratosis, SCC, BCC, eczema, psoriasis and seborrhoeic keratosis.

A2: What issues in the given history support the diagnosis?

A red scaly patch on the lower leg of an elderly woman is typical of Bowen's disease. Most lesions are asymptomatic and go unnoticed by the patient.

A3: What additional features in the history would you seek to support a particular diagnosis?

Lesions of Bowen's disease show gradual radial growth. Ask the patient about symptoms such as bleeding or ulceration, which may occur as the lesion enlarges. Most lesions are caused by chronic UV light irradiation, so ask the patient about sun exposure.

A4: What clinical examination would you perform, and why?

Examine the lesions and record the diameter of each. Look for induration, erosion or ulceration of the plaques, which may suggest malignant transformation into SCC. Examine the rest of the skin for other premalignant or malignant lesions.

A5: What investigations would be most helpful, and why?

The diagnosis is usually made on clinical examination and can be confirmed by biopsy of the lesion.

A6: What treatment options are appropriate?

Cryotherapy with liquid nitrogen, topical 5FU cream or imiquimod cream is usually used and is very effective, although it may lead to ulceration, particularly when treating lesions on the lower limbs of elderly people. Curettage and cautery or occasionally excision can also be used. Photodynamic therapy is usually reserved for large or multiple lesions.

OSCE counselling case

OSCE COUNSELLING CASE 13.3 – **'What can I do to reduce my risk of more skin cancers in the future?'**

Prevention of skin cancer involves educating patients about the disease in order to change their behaviour and lifestyle. Advise the patient to limit her exposure to UV light by wearing suitable clothing to cover her trunk and limbs, and a wide-brimmed hat to protect her scalp, face and ears. She should avoid going outdoors during the middle of the day when the sun is at its strongest ('Between eleven and three, hide under a tree'). A sunscreen of sun protection factor 30 or above should be applied to any sun-exposed site. She should also be educated to examine her skin regularly for any new lesions so that any skin cancers can be detected early and treated.

ECZEMA

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 13.7 – An 18-year-old girl presents with painful weeping lesions over her face.

An 18-year-old girl attends A&E complaining of painful weeping lesions over her face. These started 2 days ago over her chin and have now spread to involve her entire face. She has had eczema since she was a baby, but it has not been active for the past 2 years. Last week she had a cold sore over her upper lip.

CASE 13.8 – A 24-year-old woman with sore red hands.

A 24-year-old hairdresser has developed painful red scaly lesions over the palmar aspect of both hands. She has noticed small blisters and weeping areas when it is very severe. While she was on maternity leave last year her hands improved, but since she has returned to work the condition has flared up again.

OSCE counselling cases

OSCE COUNSELLING CASE 13.4 – **'Which creams should I use for my baby's eczema?'**

A mother comes to see you with her 6-month-old baby. He developed eczema soon after birth, with red dry areas over his cheeks, limb flexures and abdomen, and dry scale (cradle cap) over his scalp. She has been prescribed lots of different creams by different GPs each time she takes him to the surgery and is not sure where to use each cream. Explain to her what general measures she can take to help improve the child's eczema, and explain where and how to use emollients and topical steroids.

OSCE COUNSELLING CASE 13.5 – **'I have been referred for patch testing. What does this involve?'**

A 42-year-old man has been referred to the contact dermatitis clinic for patch testing. He is a keen gardener and suspects the eczema over his hands results from contact with plants in the summer months. Explain to him what patch testing involves.

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

There are several different types of eczema.

- *Atopic eczema* is a chronic pruritic inflammatory disorder, mainly affecting children but sometimes persisting into adulthood. It is characterized by relapses and remissions. It is frequently associated with other atopic disorders such as asthma and hayfever.
- *Seborrhoeic eczema* is a chronic eczematous disorder with erythema and scaling distributed over the face (glabella, alae of the nose, eyebrows, sideburns, ears), scalp, flexures and upper trunk. It is typically associated with overgrowth of the yeast *Pityrosporum ovale* (also known as *Malassezia furfur*) and may be asymptomatic.
- *Discoid eczema* is characterized by coin-shaped raised erythematous lesions occurring over the trunk and limbs. It usually occurs in older people, but it can also present in young adults. Secondary infection with staphylococci is common.
- *Pompholyx eczema* is characterized by pruritic vesicular eruptions over the palms, soles and sides of the digits. It usually occurs in young people and is associated with excessive sweating and warm weather.
- *Varicose eczema* is characterized by pruritic red eczematous patches over the shins. It commonly occurs secondary to venous hypertension. Varicose veins are often visible. Other changes may include oedema of the lower limbs, induration and hyperpigmentation caused by haemosiderin deposition in the skin. Ulceration may be precipitated by minor injury or infection.
- *Contact dermatitis* is an irritant or allergic eczematous reaction caused by an external substance coming into contact with the skin. Irritant contact dermatitis can affect anyone if they are exposed to a sufficient concentration of the irritant agent and for enough time. Allergic contact dermatitis is a delayed-type hypersensitivity allergic reaction that occurs only in predisposed people on every encounter with the allergen.

Answers

Clinical cases

CASE 13.7 – **An 18-year-old girl presents with painful weeping lesions over her face.**

A1: What is the likely differential diagnosis?

This is eczema herpeticum. Impetigo caused by staphylococci or streptococci (or a combination of these) is also a possibility, although it is more common in children.

A2: What issues in the given history support the diagnosis?

Eczema herpeticum is the most likely diagnosis in the light of the recent cold sore. Contrary to popular belief, this does not occur only when the eczema is in an active phase.

A3: What additional features in the history would you seek to support a particular diagnosis?

Start by finding out when, where and how the lesions began, whether the GP gave any treatment, whether the patient used any over-the-counter medication, and whether there was any improvement or deterioration from the medication. Are any other members of the family or friends affected in a similar way? Painful and weeping lesions indicate infection, so it is important to establish whether the patient has been feeling unwell in any way (e.g. fever, rigors). Finally, find out more about her past medical history and how her eczema was managed in the past.

A4: What clinical examination would you perform, and why?

Examine the patient's skin and document the extent and morphology of the lesions. Vesicles, yellow crusts or a combination of these is usually present. Look for associated lymphadenopathy. Examine the patient's eyes for any conjunctival involvement, as left untreated this may lead to corneal scarring and blindness.

A5: What investigations would be most helpful, and why?

Bacterial and viral swabs of the vesicle fluid or crusts will confirm the organism responsible. If the patient is pyrexial, blood cultures must be taken. An FBC may show a raised white cell count (WCC). C-reactive protein (CRP) will also be elevated in infection.

A6: What treatment options are appropriate?

Oral aciclovir 200 mg five times a day for 5 days is the treatment of choice for eczema herpeticum. If the infection is severe, intravenous (IV) aciclovir may be used. If the diagnosis is in doubt or secondary bacterial infection is also suspected, it is best to add in flucloxacillin and penicillin. Topical emollients will provide symptomatic relief and, once the infection has been treated, topical corticosteroids are usually necessary to treat the eczema. If there is eye involvement, an urgent assessment by an ophthalmologist is needed to exclude corneal ulceration, which may lead to blindness if left untreated.

The patient should be nursed in a side room and warned to avoid close physical contact with friends and family, because the herpes virus is contagious. Once the infection has been treated, it is important to educate the patient on management of her eczema with daily use of emollients and topical

corticosteroids over areas of active eczema. Bath oils and soap substitute emollients are useful to prevent dryness of the skin. Antihistamines can also be used to control pruritus.

CASE 13.8 – **A 24-year-old woman with sore red hands.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are allergic contact dermatitis, irritant contact dermatitis, pompholyx eczema, tinea and psoriasis.

A2: What issues in the given history support the diagnosis?

Allergic contact dermatitis is a delayed hypersensitivity reaction. Once the individual has been sensitized to a given allergen, dermatitis recurs on every subsequent exposure. Frequently the allergen responsible is encountered in the workplace and the dermatitis remits at weekends or holidays. Lesions are often pruritic or sore, and blisters are common with severe reactions. The distribution reflects the areas of contact with the allergen. Industrial dermatitis is commonly seen over the palms of the hands; the dorsum of the hands and wrists are typically affected with allergy to rubber gloves; and the earlobes and navel are affected with allergy to nickel in earrings and metal jeans studs.

A3: What additional features in the history would you seek to support a particular diagnosis?

The history is very important when allergic contact dermatitis is suspected. The distribution of dermatitis may give a clue to the responsible allergen, as indicated above. Common allergens responsible for contact dermatitis include metal (nickel and cobalt in costume jewellery), rubber, perfumes, nail varnish, plants, hair dyes, cosmetics, and colophony in adhesive dressings such as plasters. Ask the patient about any hobbies she has that may bring her into contact with potential allergens. Find out whether she has tried any topical preparations and whether they have improved or exacerbated the problem. Topical anaesthetics, antihistamines and rarely corticosteroids may occasionally be the culprit allergen.

A4: What clinical examination would you perform, and why?

Determine whether the dermatitis is confined to the palms of the hands or whether other areas are also involved. In palmoplantar psoriasis, the soles of the feet may be similarly involved. There may also be other clues for psoriasis, such as scaly plaques over the extensor surfaces of the limbs, scaling of the scalp, or pitting and onycholysis of the nails. On the other hand, tinea is almost always unilateral, and there may be a history or clinical evidence of athlete's foot as the source of infection.

A5: What investigations would be most helpful, and why?

The diagnosis of allergic contact dermatitis can be confirmed by patch testing (see OSCE counselling case 13.5). If tinea is suspected, skin scrapings from the lesion can be taken and sent for mycology to look for the presence of fungus. In weeping lesions, superimposed infection can be identified by sending skin swabs for microbiology.

A6: What treatment options are appropriate?

If possible, the antigen should be completely removed from the patient's environment. This usually leads to complete recovery. This is not always possible, however, so the patient should be advised to avoid contact with the allergen as much as she can, e.g. by wearing rubber gloves when handling the allergen. Topical corticosteroids will provide symptomatic relief, but the dermatitis will recur on exposure to the allergen. In very severe cases, a short course of systemic steroids may be used.

OSCE counselling cases

OSCE COUNSELLING CASE 13.4 – 'Which creams should I use for my baby's eczema?'

Simple measures can help with the management of eczema. Skin contact with irritants such as woollen clothing (the clothing layer next to the skin should always be 100 per cent cotton), fragranced soaps and bubble baths should be avoided. Preventing the child from overheating will help reduce pruritus. This includes ensuring that bath water is not too warm and that the room temperature is controlled.

The daily use of emollients to prevent dryness of the skin is vital. These should be used at least first thing in the morning and after a bath at night, and more frequently in the winter months and if the skin is still dry. A soap substitute such as emulsifying ointment is good to help with skin hydration; a bath oil can also be added to the bath water. Some emollients, soap substitutes and bath oils also contain an antibacterial agent that is useful in treating and preventing infection, especially in children who often scratch at their eczema. The child should have a bath each night and then have an emollient applied. Olive oil is an effective emollient for the scalp in babies with cradle cap. A topical corticosteroid should be applied to areas of active eczema. Parents should be advised to use topical steroids sparingly, as liberal and continual use leads to thinning of the skin (skin atrophy). Ointment preparations are generally better than creams at hydration, but creams are used in preference over weeping areas, where ointments tend to slide off. A 20 min gap between emollient and steroid application will prevent dilution of the steroid. Topical steroids should not be used over areas of infected eczema. Occasionally a topical antibiotic and corticosteroid combination is prescribed for areas of mildly infected eczema. In children with severe eczema, a technique known as 'wet wrapping' can be very effective at controlling the disease. This is done by applying emollients or weak topical steroid cream to the skin and wrapping the child in moist gauze bandages.

If there is no evidence of infection and topical steroids have been ineffective, topical tacrolimus cream or topical pimecrolimus cream may be used in children over the age of 2 years. These immunomodulatory creams control the eczema by suppressing the immune system locally in the skin. They have been used widely in the UK only for the past 10 years and their long-term effects are unknown, but they are considered to be safe and, unlike steroid creams, they do not lead to thinning of the skin.

OSCE COUNSELLING CASE 13.5 – 'I have been referred for patch testing. What does this involve?'

When allergic contact dermatitis is suspected, patch testing is performed, whereby the suspected allergen is placed in direct contact with the skin. About 30 commonly encountered allergens are used in a standard battery, and other potential allergens are added, such as a range of plants in suspected plant-induced contact dermatitis, or the patient's own cosmetics in facial dermatitis. The allergens are placed in individual aluminium wells and applied to the patient's back with adhesive tape. They are left in place for 48 h and then removed. The skin is inspected at 96 h for areas of dermatitis corresponding to the application site of each allergen. Positive readings are interpreted with the clinical context in mind because they may not be relevant to the patient's symptoms.

PSORIASIS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 13.9 – **A 33-year-old woman presents with dry red patches over her elbows and knees.**

A 33-year-old woman presents with dry red scaly patches of skin over the elbows and knees. These have come on gradually over the years and are asymptomatic. She also has dandruff. This has recently become much worse and is causing her great embarrassment.

CASE 13.10 – **A 54-year-old man presents with reddened skin.**

A 54-year-old man has developed redness and discomfort of the skin over his trunk and limbs. He was diagnosed with chronic plaque psoriasis in his twenties. On examination, he is pyrexial and has confluent erythema over his chest, back, abdomen, arms and legs.

OSCE counselling cases

OSCE COUNSELLING CASE 13.6 – ‘Can I have some tablets instead of creams for my psoriasis?’

A 40-year-old woman has had chronic plaque psoriasis affecting her trunk, limbs and scalp for 20 years. This has been reasonably well controlled with topical preparations. She has recently read an article in a magazine describing a ‘miracle tablet that cures psoriasis’. She tells you that she is fed up with her messy creams and wants to have this tablet. What systemic therapies are commonly used to treat psoriasis? When are they used, and what does a specialist need to take into consideration when initiating treatment? What monitoring is required?

OSCE COUNSELLING CASE 13.7 – ‘Can I use a sunbed to treat my psoriasis?’

A 22-year-old woman has recently been diagnosed with psoriasis. She tells you that her aunt also has the condition, which has almost completely cleared with UV treatment given by her specialist. She wants to know if buying a sunbed to use at home will help her psoriasis. Explain to her why it is not recommended for her to use a sunbed at home. What types of UV treatment are available for the treatment of psoriasis?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Psoriasis is a common chronic hyperproliferative and immunological condition, characterized by well-demarcated erythematous silvery scaled plaques, typically in a symmetrical distribution over extensor surfaces and in the scalp.

There are several types of psoriasis.

- *Chronic plaque psoriasis/psoriasis vulgaris* is characterized by well-defined, usually symmetrical raised red plaques with thick silvery scale, most commonly over the extensor surfaces of the elbows and knees, although it may occur at any skin site. The scalp is usually affected, and there may be nail involvement.
- *Flexural psoriasis* may occur alongside chronic plaque psoriasis. There are well-defined areas of erythema affecting the flexures (groin, perianally, axillae, umbilicus, inframammary folds).
- *Guttate psoriasis* usually affects adolescents and young adults, occurring days or a few weeks after a severe streptococcal throat infection. A history of this is not always obtained, however. It presents with widespread drop-like ('guttate') red papules with silvery scale over the trunk and limbs. It resolves within a few months but may recur in some patients.
- *Palmoplantar pustular psoriasis* is characterized by pustules occurring over the palms and soles, on the background of well-defined red scaly plaques. It is usually bilateral, and there may be psoriasis elsewhere.
- *Erythrodermic psoriasis:* worsening psoriasis can develop into erythroderma, a term used to describe abnormal reddening of the skin affecting over 90 per cent of the total body surface area. Patients are usually unwell and may be pyrexial. The redness is the result of capillary proliferation. Erythroderma may also be caused by eczema, drugs or cutaneous T-cell lymphoma (also known as mycosis fungoides).
- *Generalized pustular psoriasis* is an extreme form of psoriasis with extensive small sterile pustules and underlying erythema covering the skin. It can be provoked by abrupt cessation of potent steroids or a reduction in immunosuppressive treatment for psoriasis, or may be the result of concurrent infection, pregnancy or alcohol excess. There is a significant associated mortality.
- *Psoriasis of the nails:* about a third of patients with psoriasis and a quarter of patients with psoriatic arthropathy and psoriasis have nail changes. These may occur in isolation, however. Changes include pitting, onycholysis and subungual hyperkeratosis.
- *Psoriatic arthropathy:* arthropathy occurs in 8–10 per cent of patients with psoriasis, but it may also occur in the absence of skin changes. It may present in different forms, most commonly asymmetrical arthritis, symmetrical polyarthritis, ankylosing spondylitis and arthritis mutilans.

Answers

Clinical cases

CASE 13.9 – **A 33-year-old woman presents with dry red patches over her elbows and knees.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are psoriasis, eczema and tinea.

A2: What issues in the given history support the diagnosis?

The distribution of the lesions is characteristic of psoriasis. Apart from its cosmetic appearance, which causes significant distress to some patients, the condition is usually asymptomatic. Both eczema and tinea are typically pruritic.

A3: What additional features in the history would you seek to support a particular diagnosis?

It is important to find out how the condition has progressed up to now. Has it got gradually worse over the years, or does it come and go? Is it worse at any particular time of year? Most patients find that their psoriasis is worse in the winter and improves with sun exposure in the summer months. Find out whether there are any other exacerbating or relieving factors. Alcohol, nicotine, beta-blockers, lithium and antimalarial drugs can all make psoriasis worse. Enquire about nail and scalp involvement and whether the patient has any joint pains. Ask the patient about her family history – a third of patients with psoriasis recall a family member with the condition.

A4: What clinical examination would you perform, and why?

Examine the skin, scalp and nails for changes consistent with psoriasis. Plaques vary in size and shape and may coalesce into large areas. Pay particular attention to the elbows, knees and natal cleft as these are typical sites for psoriasis plaques. The Auspitz sign may be elicited by scraping away the surface of a scaly plaque to reveal tiny bleeding points from the dilated superficial capillaries.

A5: What investigations would be most helpful, and why?

Psoriasis is a diagnosis made clinically, and usually no investigations are necessary. If tinea is suspected, skin scrapings sent for mycology may differentiate between the diagnoses.

A6: What treatment options are appropriate?

There are many treatments for psoriasis. Daily emollients are used alongside other topical preparations such as coal tar, dithranol, corticosteroids and vitamin D analogues, some being available in combined preparations. For scalp psoriasis, tar shampoos and topical corticosteroid scalp applications usually achieve good results. Psoralen and ultraviolet A treatment (PUVA), or short-wave UV (UVB) radiation without psoralen, also known as TL-01, can be used for widespread psoriasis. The number of treatments that can be given to a patient in their lifetime is limited because UV radiation increases the risk of skin malignancies. Cytotoxic drugs such as methotrexate, ciclosporin and oral retinoids can be very effective for severe psoriasis but require careful blood monitoring to avoid complications. Patients with severe psoriasis who have not shown a response to these conventional systemic agents may be offered treatment with a new class of agents known as biologics (etanercept, adalimumab, infliximab,

ustekinumab). These are administered by injection or infusion every week or every few weeks and may be highly effective, but they are very expensive and patients need to be selected carefully before treatment.

CASE 13.10 – **A 54-year-old man presents with reddened skin.**

A1: What is the likely differential diagnosis?

Causes of erythroderma include psoriasis, eczema, drugs and cutaneous T-cell lymphoma (also known as mycosis fungoides).

A2: What issues in the given history support the diagnosis?

Erythroderma is a term used to describe abnormal reddening of the skin affecting over 90 per cent of the total body surface area. In this case, the patient's psoriasis is most probably the cause.

A3: What additional features in the history would you seek to support a particular diagnosis?

Find out when the patient's symptoms began. Was there a preceding illness (e.g. sore throat) or did the patient become unwell once the skin erythema developed? What is the extent of the patient's psoriasis normally, and how is it managed? Determine whether there have been any changes made to his psoriasis treatment recently. Abrupt cessation of topical corticosteroids or oral immunosuppressive medication can precipitate erythroderma. An increase in alcohol consumption can cause an exacerbation of psoriasis.

A4: What clinical examination would you perform, and why?

Erythrodermic psoriasis is deep red in colour. It may also be exfoliative, with scaling or peeling of the skin. Thick white or silvery scaly plaques may cover the body or be confined to the extensor surfaces of the elbows and knees. In most patients with psoriasis, there is also scalp involvement, which may vary from fine flakes to thick scaly plaques. The nails may also be affected, with pitting, ridging or onycholysis.

A5: What investigations would be most helpful, and why?

The diagnosis is usually made on history and examination. An FBC may show a leucocytosis, and inflammatory markers such as CRP or erythrocyte sedimentation rate (ESR) may be raised. An infection screen (e.g. blood cultures, chest radiograph) is necessary if there is any history or sign of infection. It is important to monitor renal function because vasodilation leads to increased percutaneous water loss, with consequent decreased urine output, which may lead to renal failure. Liver function must also be measured if the patient admits to excess alcohol consumption.

A6: What treatment options are appropriate?

Correction of hypovolaemia and hypothermia and treatment of concomitant sepsis are vital in the early stages of erythroderma. Emollients are applied daily. Systemic therapy (e.g. retinoids, methotrexate, ciclosporin) is usually needed to control the underlying psoriasis. Corticosteroids and UV light therapy are usually avoided.

OSCE counselling cases

OSCE COUNSELLING CASE 13.6 – 'Can I have some tablets instead of creams for my psoriasis?'

The decision to start systemic therapy can be difficult and is made by a specialist. It is generally a long-term commitment, using drugs with potential side effects, which require careful monitoring. The patient must be told that the drug is not a cure for psoriasis and that the disease usually returns to its previous state after stopping treatment. Drug interactions may occur, so it is important to take a drug history before initiating treatment. Systemic therapies are used to treat erythrodermic psoriasis, generalized pustular psoriasis, and extensive psoriasis where other therapy has failed, multiple admissions to hospital have been necessary or the disease interferes with function or restricts the patient's quality of life.

The most commonly used systemic therapies are methotrexate, ciclosporin and acitretin.

Methotrexate is given as a once-weekly dose of 0.2–0.4 mg/kg. A test dose of 2.5–5 mg is given before starting therapy to detect idiosyncratic myelosuppression, which may occur within 7–10 days (an FBC is necessary). Bone marrow toxicity may occur, so the FBC must be monitored. Regular LFTs are needed because hepatotoxicity may occur. Occasionally a liver biopsy is necessary if hepatic fibrosis is suspected. Methotrexate is excreted by the kidneys so renal function is also monitored. It is teratogenic in early pregnancy; all women need adequate contraception and must be told to avoid pregnancy for at least 3 months after cessation of treatment.

Ciclosporin is given as either a low-dose regimen (2.5 mg/kg/day, increased slowly) or a high-dose regimen (5 mg/kg/day). These are usually well tolerated. The risk of nephrotoxicity means that careful monitoring of renal function is vital. Treatment is usually limited to a few months at a time, as long-term ciclosporin increases the risk of renal damage. There is also a risk of hypertension, and blood pressure checks are mandatory.

Acitretin is taken as tablets, usually 20–30 mg a day; higher doses lead to side effects. Hyperlipidaemia and hepatotoxicity may occur, so monitoring of cholesterol, triglycerides and liver function is necessary. Acitretin is highly teratogenic and should be avoided in women of childbearing age. Unlike methotrexate and ciclosporin, acitretin is not immunosuppressive.

OSCE COUNSELLING CASE 13.7 – 'Can I use a sunbed to treat my psoriasis?'

Ultraviolet treatment can be very beneficial for the treatment of psoriasis, but it must be initiated by a specialist and given in a controlled manner. The dose given (in joules per square centimetre, or J/cm^2) depends on the patient's skin type. There is a risk of cutaneous malignancy, which is cumulative and becomes highly significant after a total dose of 1200 J/cm^2. People with psoriasis often require repeated courses of UV treatment to keep the disease under control. A record is kept of the cumulative exposure, which is kept to a minimum where possible. It is not recommended that patients use sunbeds because there is no monitoring of the dose given.

PUVA, or UVB radiation without psoralen, can be used in the treatment of psoriasis. Psoralens may also be applied topically or added to the bath before UVA exposure (bath PUVA). Treatment is usually given two to three times a week for about 20 treatments to obtain clearance of the disease. Multiple courses of treatment are usually necessary in a patient's lifetime. Patients must be warned of the risks of developing cutaneous malignancies.

PRURITUS

Questions

Clinical cases

For each of the case scenarios given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 13.11 – **A 36-year-old Asian woman presents with a 2-month history of generalized pruritus.**

The patient has no associated rash. She has been feeling tired for a few months now but has no other symptoms. On examination, she has pale conjunctivae.

CASE 13.12 – **An 88-year-old man who lives in a residential home has developed a generalized itchy rash.**

The rash is particularly bad over the patient's hands, arms, groin and thighs. The itching is worse at night and prevents him from sleeping. Some of the other residents at the home have developed a similar itchy rash.

OSCE counselling case

OSCE COUNSELLING CASE 13.8 – **'I have been told I have urticaria. What is this?'**

A 33-year-old man has had intermittent episodes of a nettle-like rash over his body for the past 6 months. Each episode lasts for a few hours. He has not identified any triggers but has noticed that the rash becomes less itchy and fades slowly after taking antihistamine tablets. He has been told the diagnosis is urticaria. Explain to him what this diagnosis means. Are there any investigations he can have to determine the cause?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

The common causes of generalized pruritus include:

- *haematological:*
  - iron deficiency anaemia
  - polycythaemia rubra vera
  - paraproteinaemia
- *hepatic disease:*
  - extrahepatic obstructive jaundice
  - primary biliary cirrhosis
  - cholestasis of pregnancy
- *renal disease:*
  - chronic renal failure
- *endocrine disease:*
  - hyper- or hypothyroidism
  - diabetes mellitus
- *internal malignancy:*
  - lymphoma
  - leukaemia
  - abdominal cancer
  - bronchial carcinoma
- *drugs:*
  - oral contraceptive pill (causes cholestasis)
  - opiates (cause histamine release)
  - alcohol and drug withdrawal
- *psychological.*

The common pruritic skin disorders are eczema, scabies, urticaria, insect bites, lichen planus, drug eruptions, bullous pemphigoid, dermatitis herpetiformis and polymorphic light eruptions.

Answers

Clinical cases

CASE 13.11 – **A 36-year-old Asian woman presents with a 2-month history of generalized pruritus.**

A1: What is the likely differential diagnosis?

Causes of generalized pruritus must be considered (see 'Key concepts' above).

A2: What issues in the given history support the diagnosis?

The most likely diagnosis is pruritus secondary to iron deficiency anaemia. Patients with anaemia often have non-specific symptoms and complain of lethargy. The pale conjunctivae also suggest anaemia.

A3: What additional features in the history would you seek to support a particular diagnosis?

Find out whether the patient has any other associated symptoms. The tiredness and pale conjunctivae suggest anaemia, although iron deficiency in the absence of anaemia can also cause pruritus. Is there anything in the history to suggest iron deficiency? Is she vegetarian or vegan, and does she eat a balanced diet? Enquire about any history of blood loss (e.g. bleeding per rectum, heavy menstrual blood loss). Find out whether the pruritus occurs at any specific time (e.g. pruritus after a hot bath is classically associated with polycythaemia). Are there symptoms suggesting internal malignancy such as weight loss, haemoptysis, chronic cough, fevers or night sweats? Drugs such as opiates and their derivatives may also cause pruritus, so ask the patient about any medication she is taking.

A4: What clinical examination would you perform, and why?

A full general examination is necessary to look for coexisting skin disease or a cause for the pruritus. Often, the only positive findings are the excoriations caused by the patient scratching. Look for scabies burrows in the finger webs or pruritic papules over the genitals. Examine for evidence of chronic liver disease, hypo- or hyperthyroidism, and renal failure or malignancy, all of which may present with pruritus.

A5: What investigations would be most helpful, and why?

An FBC to look for anaemia or polycythaemia rubra vera is necessary. Iron studies (ferritin, total iron-binding capacity) can determine whether iron deficiency is present. It may be necessary to investigate further for a cause with faecal occult blood, e.g. by sigmoidoscopy. Liver function tests may indicate cholestasis. Renal function tests may reveal uraemia secondary to chronic renal failure as the cause of pruritus. Thyroid function tests may show thyrotoxicosis or hypothyroidism. Diabetes can also cause generalized pruritus, so check the patient's fasting glucose.

A6: What treatment options are appropriate?

Treatment is that of the underlying cause. Prevent dryness of the skin that can cause or exacerbate pruritus. Menthol in aqueous cream can be very soothing. Bath oils and emollients used as soap substitutes can also provide symptomatic relief. Antihistamines may provide symptomatic relief. A sedating antihistamine may help the patient sleep at night, but a non-sedating antihistamine is better for daytime use so it does not interfere with driving and work.

CASE 13.12 – **An 88-year-old man who lives in a residential home has developed a generalized itchy rash.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are scabies, eczema, tinea corporis and tinea cruris and drug eruption.

A2: What issues in the given history support the diagnosis?

Itching that is particularly bad over the hands and groin area and is worse at night suggests a diagnosis of scabies, especially if other members of the family or residential home are also complaining of pruritus. The itch intensifies with time and, apart from sparing the face, affects the whole body.

A3: What additional features in the history would you seek to support a particular diagnosis?

A very observant patient may have noticed the scabies burrows and describe them as very pruritic, but usually they go unnoticed. Ask whether the patient has any small itchy lumps between the fingers, around the nipples, or on the buttocks and genitalia. Pruritic papules on the penis or scrotum are characteristic of scabies. Find out whether the patient has tried any treatments – topical corticosteroids are often wrongly prescribed if the rash is mistaken for eczema, and they often provide temporary symptomatic relief from itching but actually make the condition worse.

A4: What clinical examination would you perform, and why?

Finding a scabies burrow is diagnostic. Look carefully over the webs of the fingers, dorsum of the hands, around the wrists and on the palms. Multiple serpiginous slightly raised linear tracks of a few millimetres in length are characteristic. The *Sarcoptes scabiei* mite may be just visible as a black dot at one end of the burrow. The pruritus and rash associated with scabies are a result of an allergic reaction to the mite's faeces and present as an extremely itchy erythematous papular eruption. Multiple excoriations are often present, and bruising from vigorous scratching may occur.

A5: What investigations would be most helpful, and why?

The diagnosis is made on history and examination, although occasionally a mite can be carefully extracted from a burrow using a fine needle and visualized under the microscope.

A6: What treatment options are appropriate?

Scabies is easily treatable, but the patient must apply the treatment correctly and be warned that the itching (which is caused by an allergic reaction to the mite's faeces) typically persists for a few weeks after the mite has been eradicated. The treatment should be applied to all the skin areas except the face. Most lotions for scabies need to be applied and left on for 12–24 h before being washed off. Usually two applications applied 7 days apart are recommended – the treatment kills the mite but not the eggs, and it is possible for new eggs to hatch a week later and lead to reinfestation. Permethrin 5% cream or malathion 0.5% lotion is usually used. Close contacts such as family members and carers may also need treatment. Other measures include washing the patient's bedding, towels and undergarments at a high temperature. As the itch and eczema persist for weeks, application of crotamiton, with or without a topical corticosteroid, and a sedating antihistamine tablet can provide symptomatic relief.

OSCE counselling case

OSCE COUNSELLING CASE 13.8 – **'I have been told I have urticaria. What is this?'**

Urticaria is a term used to describe intermittent transient itchy red swellings of the skin that occur secondary to histamine and other vasoactive substances being released from granules within mast cells in blood vessels. Angio-oedema occurs if the mucous membranes are also involved, with swelling around the eyes and of the lips, tongue and larynx. This may be life-threatening because of the possibility of asphyxia. Patients often describe the rash as itchy wheals and blisters, 'nettle rash' or 'hives'. They typically appear as raised annular areas with a red periphery and central pallor. The rash lasts for several hours and the skin appears completely normal afterwards. In most patients, a cause is never identified (idiopathic urticaria), but the following are some common causes of urticaria:

- *drugs* – aspirin and other non-steroidal anti-inflammatory drugs, antibiotics (especially penicillin and cephalosporins), angiotensin-converting enzyme (ACE) inhibitors
- *foods* – e.g. nuts, dairy products, shellfish, dyes, additives
- *infection* – focal sepsis
- *physical* – cold, heat, UV light, pressure
- *blood transfusion reactions*.

Treatment involves avoiding any identified precipitating cause and controlling the symptoms with antihistamines. If there is a history of angio-oedema leading to anaphylaxis, the patient must be provided with an adrenaline injection for self-administration.

The diagnosis is usually made on the history alone. Investigations are rarely helpful. Blood tests are usually normal and therefore not indicated. It can be helpful to ask the patient to make a list of things ingested in the 24 h before each attack to try to identify the trigger. An elimination diet may be worth trying. Skin-prick and radioallergosorbent (RAST) tests are often positive in a non-specific way, but the results must be interpreted in the clinical context.

ACNE

Questions

Clinical case

For the case scenario given, consider the following:

Q1: What is the likely differential diagnosis?
Q2: What issues in the given history support the diagnosis?
Q3: What additional features in the history would you seek to support a particular diagnosis?
Q4: What clinical examination would you perform, and why?
Q5: What investigations would be most helpful, and why?
Q6: What treatment options are appropriate?

CASE 13.13 – **A 17-year-old girl presents to her GP complaining of spots over her face for the past 4 years.**

The patient has tried multiple over-the-counter acne preparations, with no improvement. She is very concerned about the scarring left behind.

OSCE counselling case

OSCE COUNSELLING CASE 13.9 – **'Can I have isotretinoin for my acne?'**

A 23-year-old woman has been treated for acne with various topical preparations and different courses of antibiotics for the past 2 years, with little success. Her friend was recently given isotretinoin tablets, which have cured her acne. The patient wishes to have the same treatment. What are the indications for prescribing isotretinoin? What are the side effects that she needs to know about before starting treatment?

Key concepts

To work through the core clinical cases in this section, you will need to understand the following key concepts.

Acne is a chronic disorder of the pilosebaceous apparatus of the skin. It results from overactivity of the sebaceous glands and blockage of its ducts, leading to the formation of open (blackheads) and closed (whiteheads) comedones. The sebaceous glands are under the control of androgens and produce sebum, which may be converted into comedogenic and irritant free fatty acids by the anaerobic bacterium *Propionibacterium acnes* within the pilosebaceous duct.

There are various treatments for acne. The choice of treatment depends on the disease severity and the individual patient.

- *Topical therapy* is used for mild acne and as an adjunct to other acne treatments. Examples include benzoyl peroxide, retinoic acid, antibiotics and salicylic acid.
- *Systemic antibiotics* such as tetracyclines and erythromycin are used to treat acne that does not respond to topical treatment alone.
- *Hormone therapy:* a combined preparation of cyproterone acetate and ethinylestradiol (co-cyprindiol) reduces sebum production and is helpful in some patients.
- *Systemic retinoid therapy:* 13-cis-retinoic acid (isotretinoin) is a synthetic derivative of vitamin A. It acts by reducing sebum secretion by 90 per cent, microorganisms (especially *P. acnes*), plugging of the pilosebaceous ducts and inflammation. It also influences epithelial proliferation and differentiation so that the sebaceous glands return to their prepubertal state.

Answers

Clinical case

CASE 13.13 – **A 17-year-old girl presents to her GP complaining of spots over her face for the past 4 years.**

A1: What is the likely differential diagnosis?

The likely differential diagnoses are acne vulgaris, rosacea (usually occurs from the fourth decade onwards) and perioral dermatitis (may be secondary to misuse of topical corticosteroids).

A2: What issues in the given history support the diagnosis?

Acne is a very common problem in adolescents. The hallmark of acne is the comedone, which may be open (blackhead) or closed (whitehead). The characteristic lesions and their distribution give the diagnosis away.

A3: What additional features in the history would you seek to support a particular diagnosis?

Find out when the lesions started and their distribution. Do they affect only the face, or are the patient's back, chest or upper arms also involved? Ask the patient to describe the lesions – are they small papules or large cysts? What type of scars do the lesions leave when they resolve? Post-inflammatory hyperpigmentation is common and appears as a brown mark when the lesion resolves. It is not a permanent scar but can take many months to fade away. The colour tends to be more intense in patients with darker skin. Pitted atrophic scars ('ice-pick scars') may occur after severe nodulocystic acne and are permanent. Rarely, patients may have hypertrophic or keloid scarring, which is disfiguring.

A4: What clinical examination would you perform, and why?

The skin may appear greasy with red papules, pustules, comedones, and sometimes nodules, cysts, post-inflammatory hyperpigmentation and pitted or hypertrophic scars. Determine the distribution of the acne.

A5: What investigations would be most helpful, and why?

The diagnosis is made on history and clinical examination. If the lesions look infected, a swab may be sent for microbiology. Bear in mind that pustules are typically sterile.

A6: What treatment options are appropriate?

Topical benzoyl peroxide is antibacterial and comedolytic. Combined preparations with an antibiotic are also available. It can be very drying and cause irritation, so the treatment is started at the weakest concentration. Topical antibiotics alone are also used. Topical retinoic acid is a keratolytic agent and useful for comedonal acne and post-inflammatory hyperpigmentation. Salicylic acid can also be used as a keratolytic agent. Systemic antibiotics are the mainstay of acne treatment. Tetracyclines (oxytetracycline, doxycycline, minocycline, lymecycline), erythromycin or trimethoprim can be very effective but need to be taken for at least 3–6 months before a benefit is seen. As a rule, acne over the trunk responds slower than facial acne, and antibiotics may need to be continued for longer. For antibiotic-resistant acne or severe acne leading to scarring, systemic retinoid therapy is the treatment of choice.

OSCE counselling case

OSCE COUNSELLING CASE 13.9 – **'Can I have isotretinoin for my acne?'**

Isotretinoin is used in the treatment of the following:

- nodulocystic acne – severe chronic acne that is usually resistant to standard therapy; it is most frequent in males and presents with deep painful papules and nodules that lead to scars, occasionally with keloid formation
- acne leading to scarring
- antibiotic-resistant acne
- acne causing significant psychological distress to the patient.

Isotretinoin is given as 1 mg/kg/day in tablet form for 16 weeks. The effect is usually evident within 6 weeks. One course is usually sufficient to clear most patients' acne.

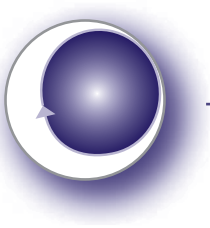
The main side effect noticed by patients is dryness of the skin and mucous membranes; patients must be advised to use an emollient and lip balm to alleviate this. Patients who usually wear contact lenses are advised to wear spectacles instead during the treatment period. Nosebleeds may occur in patients with a predisposition. Isotretinoin is metabolized through the liver and may cause hyperlipidaemia; liver function tests and cholesterol and triglyceride levels are taken before starting and during treatment. Patients should be warned of the risk of depression – there have been cases of suicide reported in patients receiving treatment with isotretinoin, and therefore depression is a relative contraindication to starting treatment.

It is vital that patients are informed that the drug is highly teratogenic, especially as most female patients on treatment are of childbearing age. A pregnancy test is mandatory before starting therapy. Patients are entered into a pregnancy prevention programme whereby they are prescribed treatment each month only if they have a negative pregnancy test. Patients are counselled to use two forms of contraception (oral contraception and a barrier method) during treatment and for at least 3 months after cessation of treatment.

REVISION PANEL

- A malignant melanoma may arise de novo or present as a pre-existing mole that is enlarging and changing in colour. It usually looks different from the patient's other moles.
- A suspected melanoma must be excised urgently so that it can be analysed for Breslow depth. The Breslow depth is a good prognostic indicator and determines whether further investigations are needed.
- Melanoma may present as an enlarging freckle in elderly people (lentigo maligna).
- Subungual melanoma presents with discoloration under a nail, which may mimic haemorrhage from trauma.
- Actinic keratoses result from chronic sun damage and usually occur as rough red asymptomatic lesions that are often multiple and on sun-exposed sites.
- Actinic keratosis and Bowen's disease (in situ SCC of the skin) can progress to SCC and must be treated.
- Treatment for actinic keratosis, Bowen's disease and superficial BCC can be with cryotherapy, 5FU, imiquimod cream, photodynamic therapy or surgery (curettage and cautery or excision).
- SCCs must be excised urgently, as they have the potential to metastasize. Patients need follow-up after excision for early detection of recurrence.
- A BCC is best excised, but it does not need follow-up if removed completely as they very rarely metastasize.

- Atopic eczema is the most common type of eczema and is typically associated with hayfever and asthma.
- Infected eczema can be a dermatological emergency. Eczema herpeticum can also affect the eye and lead to corneal scarring and blindness.
- Patients with suspected contact dermatitis must be patch-tested to identify the allergen(s) responsible.
- The treatment of eczema includes patient education, emollients, soap substitutes and topical steroids for exacerbations.
- Patients with eczema should be advised to limit the use of topical steroids and use them sparingly, as continual use leads to skin atrophy.
- Psoriasis can affect the skin, scalp, nails and joints
- Erythrodermic psoriasis can be a life-threatening emergency, and the patient may be systemically unwell.
- Topical treatments for psoriasis include emollients and preparations containing coal tar, dithranol, corticosteroids and vitamin D analogues.
- PUVA or UVB radiation without psoralen (TL-01) can be used for widespread psoriasis, but patients should be warned that phototherapy increases the risk of skin cancer.
- Severe psoriasis can be treated with systemic agents such as methotrexate, ciclosporin and acitretin, or with biologic injections or infusions, which can be prescribed only by a dermatologist.
- Patients presenting with pruritus can be subdivided into those with pruritus and a rash where the itch is secondary to the skin condition, and those presenting without a rash, in which case an internal or medical cause is usually responsible for the itching.
- Blood investigations are necessary for patients presenting with pruritus in the absence of a skin rash.
- If scabies is suspected, look for burrows in the finger webs and on the hands.
- Scabies is highly infectious, and all contacts need to be treated at the same time as the patient.
- If urticaria is accompanied by angio-oedema, the patient must be given an adrenaline injection for self-administration to use in case of anaphylaxis.
- The hallmark of acne is the comedone, which may be open (blackhead) or closed (whitehead).
- Acne can lead to scarring, which may be permanent and disfiguring.
- If topical acne treatments have been ineffective, systemic antibiotics should be prescribed for at least 3–6 months.
- In women with acne, the oral contraceptive pill containing cyproterone acetate can be effective in treating acne.
- If systemic antibiotics have been ineffective, or the acne is severe, oral isotretinoin can be given. This needs careful monitoring, especially in female patients.



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Series Editor: Janesh K. Gupta, Professor of Obstetrics and Gynaecology, University of Birmingham, Birmingham Women's Hospital, Birmingham, UK

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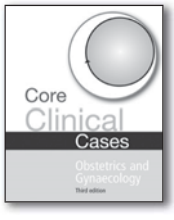

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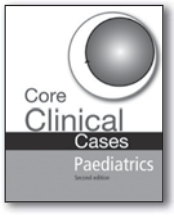

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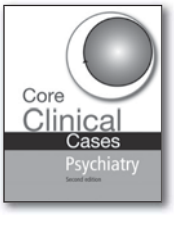

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