D: Syndrome caused by systemic release of hormones from carcinoid (neuroendocrine) tumours.

A: Carcinoid tumours are slow-growing neuroendocrine tumours and secrete hormones, often 5-HT (serotonin) but also substances such as histamine, prostaglandins, bradykinin and peptide hormones. Common sites include appendix and rectum, where they are often benign and non-secretory, but are also found in other parts of small or large gut, stomach, thymus, bronchus and other organs. Hormones released into the portal circulation are metabolized in the liver, and symptoms typically do not appear until there are hepatic metastases or release into the systemic circulation from bronchial or extensive retroperitoneal tumours.

A/R: 10 % of patients with MEN type 1 have carcinoid tumours.

E: Rare, annual UK incidence is 1 in 1 000 000. Asymptomatic carcinoid tumours are more common and may be an incidental finding after rectal biopsy or appendectomy.

H: Paroxysmal flushing, diarrhoea, crampy abdominal pain (↑ gut motility), wheeze, sweating, palpitations.

E: Facial flushing, telangiectasia, wheeze.
Right-sided heart murmurs: Tricuspid stenosis, regurgitation or pulmonary stenosis may be prominent if carcinoid tumour is secreting hormones into systemic circulation.
Nodular hepatomegaly in cases of metastatic disease.
Carcinoid crisis: tachycardia and hypotension in severe cases.

P: **Macro:** Solid and yellow-tan in appearance, may be classified into fore-, mid- or hindgut tumours, depending on their site of origin. There is often an area of fibrosis surrounding the primary. Classic sites include the appendix and the small bowel.
Micro: Carcinoid tumours are derived from enterochromaffin cells also known as APUD cells. Electron microscopy shows dense cytoplasmic granules containing hormonal peptides.

I: **24-h urine collection:** 5-HIAA levels (a metabolite of serotonin, false-positive with high intake of bananas and avocados).
Blood: Plasma concentrations of chromogranin B, fasting gut hormones.
CT or MRI scan: Localizes the tumour.
Radioisotope scan: Radiolabelled somatostatin analogue helps localize tumour.
Investigations for MEN-1: (see footnote to Hyperparathyroidism).

M: **Carcinoid crisis:** Octreotide infusion, also IV antihistamine and hydrocortisone.
Chronic: Multidisciplinary approach (gastroenterologists, oncologists, radiologists and surgeons). Octreotide (or other somatostatin analogues) inhibit hormone release and tumour growth. Radiolabelled octreotide may be beneficial (receptor-targeted therapy).
Supportive: Ondansetron and cyproheptadine (5-HT antagonists) can alleviate symptoms, rehydration (for diarrhoea), antiemetics and antidiarrhoeal treatment (codeine, loperamide).
Advice: Avoid precipitating factors (e.g. alcohol, spicy food, strenuous exercise).
Surgery: Surgical resection or debulking of the tumour.
Hepatic metastases: Hepatic artery embolization, chemotherapy (e.g. interferon-α).

C: Electrolyte imbalance (secondary to diarrhoea), metastases, fibrosis near a gut primary can result in bowel obstruction, hormones can cause tricuspid and pulmonary valve stenosis with consequent right heart failure.

P: As these tumours are generally slow-growing, mean survival is usually 5–10 years but can range up to 20 years. Earlier detection and treatment should improve quality of life and survival.

D: Acute cessation of cardiac function.

A: The classical reversible causes of cardiac arrest are the four H's and four T's:

Hypoxia	Tamponade, cardiac
Hypothermia	Tension pneumothorax
Hypovolaemia	Thromboembolism
Hypo- or Hyperkalaemia	Toxins

(+ other metabolic disorders)(sepsis, drugs, therapeutic agents)

A/R: –

E: –

H: Management precedes or occurs at same time as history (e.g. from witnesses).

E: Unconscious, patient is not breathing, absent pulses.

P: –

I: **Cardiac monitor:** Classification of the rhythm directs management (see below).
Blood ABG, U&E, FBC, cross-match, clotting, toxic screen.

M: **Safety:** Approach any arrest scene with caution as the cause of the arrest may still pose a threat. Defibrillators and oxygen are hazards. Help should be summoned as soon as possible.
Basic life support:*
1 If the arrest has just occurred, give a precordial thump.
2 Clear and maintain **A**irway with head-tilt (if no spinal injury), jaw-thrust and chin-lift.
3 Assess **B**reathing by look, listen and feel.
If not breathing, give two effective breaths immediately.
4 Assess **C**irculation at carotid pulse for 10 s.
If absent, give 15 chest compressions at rate of about 100/min.
5 Continue cycle of 15 chest compressions for every two breaths.
Check circulation every minute.
6 Proceed to advanced life support as soon as possible.
Advanced life support:* Attach cardiac monitor and defibrillator.
1 Assess the rhythm and check pulse.
2 If **VF** or pulseless **VT**,† defibrillate × 3 (First cycle at 200J, 200J, 360J. Further cycles at 360J) CPR for 1 min, return to **1**.
(Make sure no one is touching patient or bed when defibrillating.)
3 If EMD‡ or asystole, CPR for 3 min, return to **1**.
4 During CPR: check electrode, paddle positions and contacts. Attempt endotracheal intubation, high-flow oxygen, IV access, adrenaline (1 mg IV every 3 min). Consider amiodarone, atropine, pacing, buffers (e.g. bicarbonate).

*See latest UK Resuscitation Council guidelines.
†VT: > 3 successive ventricular extrasystoles (broad QRS complexes: > 120 ms) at a rate of > 120/min. Acute treatment of VT in patients with no haemodynamic compromise is with IV amiodarone. Patients at high risk of recurrent VT should be considered for implantable defibrillator which has been shown to be more effective than amiodarone. VF: irregular, rapid ventricular activation with no cardiac output.
‡EMD: Absence of cardiac output despite ECG showing electrical activity.

Treatment of reversible causes:
Hypothermia: Warm slowly.
Hypo- or Hyperkalaemia: Correction of electrolytes.
Hypovolaemia: IV colloids, crystalloids or blood products.
Tamponade: Pericardiocentesis under xiphisternum upwards and leftwards.
Tension pneumothorax: Needle into second intercostal space, mid-clavicular line.
Thromboembolism: (see Pulmonary embolism and Myocardial infarction).
Toxins: (see drug formulary for antidotes).

C: Irreversible brain damage, death.

P: Resuscitation is less successful in the arrests that occur outside hospital. Poor prognosis even after successful resuscitation owing to underlying heart disease (e.g. ischaemic heart disease, hypertensive heart disease and cardiomyopathy).

D: Inability of the cardiac output to meet the body's demands despite normal venous pressures.

A: **Low output** (↓ cardiac output):
Left heart failure: Ischaemic heart disease, hypertension, cardiomyopathy, aortic valve disease, mitral regurgitation.
Right heart failure: Secondary to left heart failure, infarction, cardiomyopathy, pulmonary hypertension/embolus/chronic lung disease, pulmonary valve disease, tricuspid regurgitation, constrictive pericarditis/pericardial tamponade.
Biventricular failure: Arrhythmia, cardiomyopathy (dilated or restrictive), myocarditis, drug toxicity.
High output (↑ demand): Anaemia, beriberi, pregnancy, Paget's disease, hyperthyroidism, arteriovenous malformation.

A/R: (see Aetiology).

E: 10 % of > 65-year-olds.

H: **Left** (symptoms caused by pulmonary congestion): Dyspnoea (New York Heart Association classification):
1 no dyspnoea;
2 dyspnoea on ordinary activities;
3 dyspnoea on less than ordinary activities; and
4 dyspnoea at rest.
Orthopnoea, paroxysmal nocturnal dyspnoea, fatigue.
Acute LVF: Dyspnoea, wheeze, cough and pink frothy sputum.
Right: Swollen ankles, fatigue, ↑ weight (resulting from oedema), ↓ exercise tolerance, anorexia, nausea.

E: **Left:** Tachycardia, tachypnoea, displaced apex beat, bilateral basal crackles, third heart sound ('gallop' rhythm: rapid ventricular filling), pansystolic murmur (functional mitral regurgitation).
Acute LVF: Tachypnoea, cyanosis, tachycardia, peripheral shutdown, pulsus alternans, gallop rhythm, wheeze 'cardiac asthma', fine crackles throughout the lung.
Right: ↑ JVP, hepatomegaly, ascites, ankle/sacral pitting, oedema, signs of functional tricuspid regurgitation (see Tricuspid regurgitation).

P: **Macro:** Depends on cause. Dilated or hypertrophic ventricles, areas of fibrosis from old infarctions or fibrosed pericardium may be seen.

I: **Blood:** FBC, U&E, lipids, TFT. In acute LVF, ABG and cardiac enzymes.
CXR (in acute LVF): Cardiomegaly (heart > 50 % of thoracic width), prominent upper lobe vessels, pleural effusion, interstitial oedema ('Kerley B lines'), perihilar shadowing ('bat's wings'), fluid in the fissures.
ECG: Normal, ischaemic changes, arrhythmia, left ventricular hypertrophy (seen in hypertension).
Echocardiogram, technetium-99 scan: To assess ventricular contraction. If ejection fraction < 50 %: systolic dysfunction. Diastolic dysfunction: ↓ compliance leading to a restrictive filling defect.
Swan–Ganz catheter: Allows measurements of right atrial, right ventricular, pulmonary artery, pulmonary wedge and left ventricular end-diastolic pressures.

M: **Acute LVF:** *Cardiogenic shock:* Severe cardiac failure with low BP requires the use of inotropes (e.g. noradrenaline (norepinephrine), dobutamine) and should be managed in ITU.

Pulmonary oedema: Sit up patient, 60–100 % O_2 and consider CPAP or BiPAP. Other first-line therapies are diamorphine (venodilator and anxiolytic effect), GTN infusion (↓ preload), IV furosemide (frusemide) if fluid overloaded (venodilator and later diuretic effect). Monitor temperature, BP, respiratory rate, sat O_2, urine output, ECG.

Chronic LVF: Treat the cause (e.g. hypertension). Treat exacerbating factors (e.g. anaemia).

Medical: The following drug therapies are evidence-based.*

ACE-inhibitors: Inhibit Na^+ and water retention, vasoconstriction and improve symptoms and prognosis.

β-Blockers: Block the effects of chronically activated sympathetic system.

Spironolactone (aldosterone antagonist): Consider combination with furosemide (frusemide) to prevent hyperkalaemia.

Digoxin: Positive inotrope. Reduces hospital admissions, but does not improve survival.

Surgical: Heart transplantation (if < 65 years).

C: Respiratory failure, cardiogenic shock, death.

P: 50 % of patients with severe heart failure die within 2 years.

*Important trials include CIBIS-II and US-Carvedilol (role of β-blockers), SOLVD and CONSENSUS (role of ACE-inhibitors) and DIG study (role of digoxin).

D: A primary disease of the myocardium. Cardiomyopathy (CM) may be dilated (**DCM**), hypertrophic (**HCM**) or restrictive (**RCM**).

A: The majority are idiopathic.
DCM: Postviral myocarditis, alcohol, drugs (e.g. doxorubicin, cocaine), familial (~25 % of idiopathic cases, usually autosomal dominant), thyrotoxicosis, haemochromatosis, peripartum.
HCM: Up to 50 % of cases are genetic (autosomal dominant) with mutations in β-myosin, troponin T or α-tropomyosin (components of the contractile apparatus).
RCM: Amyloidosis, sarcoidosis, haemochromatosis, endomyocardial fibrosis.

A/R: (see Aetiology).

E: Prevalence of **DCM** and **HCM** is ~0.05–0.20 %. **RCM** is rare.

H: **DCM:** Symptoms of heart failure, arrhythmias, thromboembolism, sudden death.
HCM: Usually none. Syncope, angina, arrhythmias, sudden death (more common in young patients).
RCM: Dyspnoea, fatigue, arrhythmias, ankle or abdominal swelling.
Enquire about family history of sudden death.

E: **DCM:** ↑ JVP, displaced apex beat, functional mitral and tricuspid regurgitations, third heart sound.
HCM: Jerky carotid pulse, double apex beat, ejection systolic murmur.
RCM: ↑ JVP (Kussmaul's sign: further ↑ on inspiration), palpable apex beat, third heart sound, ascites, ankle oedema, hepatomegaly.

P: **DCM:** Dilation and impaired contraction of ventricles. Mural thrombi are common.
HCM: Asymmetrical left ventricle hypertrophy, septal bulge may partially obstruct outflow to aorta. Microscopy shows myocyte hypertrophy and disarray, interstitial fibrosis.
RCM: Myocardial thickening, fibrosis or amyloid deposition. Diastolic ventricular filling is restricted by the rigid ventricular walls.

I: **CXR:** May show cardiomegaly and signs of heart failure.
ECG: *All types:* Non-specific ST or T wave changes, conduction defects, arrhythmias, plus:
HCM: Left axis deviation, signs of left ventricular hypertrophy (see Aortic stenosis), Q waves in inferior and lateral leads.
RCM: Low voltage complexes.
Echocardiography: *DCM:* Dilated ventricles with 'global' hypokinesia.
HCM: Ventricular hypertrophy with disproportionate involvement of the septum.
RCM: Non-dilated non-hypertrophied ventricles. Atrial enlargement, preserved systolic function, diastolic dysfunction; granular or 'sparkling' appearance of myocardium in amyloidosis.
Cardiac catheterization, endomyocardial biopsy, histological examination: (? RCM).
Pedigree or genetic analysis.

M: **DCM:** Treat heart failure and arrhythmias. Consider implantable cardioverter defibrillator for recurrent ventricular tachycardias.

HCM: Treat arrhythmias with drugs, implantable cardioverter defibrillator for survivors of sudden death, reduce outflow tract gradients, dual-chamber pacing, surgery (e.g. septal myectomy, septal ablation with ethanol). Screen family members with ECG or echocardiography.
RCM: No specific treatment. Manage the underlying cause. Cardiac transplantation may be considered in end-stage heart failure (all cardiomyopathy types).

C: **All types:** Heart failure, arrhythmias (atrial and ventricular).
DCM and HCM: Sudden death and embolism.
HCM: Infective endocarditis.

P: **DCM:** Depends on the aetiology, New York Heart Association functional class and ejection fraction.
HCM: Ventricular tachyarrhythmias are the major cause of sudden death.
RCM: Poor prognosis, many die within the first year after diagnosis.

D: Hand weakness and paraesthesia from compression of the median nerve in the carpal tunnel.

A: Narrowing of the carpal tunnel or enlargement of the contents compresses the median nerve which runs through it. Usually idiopathic but some common secondary causes include:

- fluid retention (e.g. in pregnancy, heart failure, liver failure, nephrotic syndrome);
- arthritis of the wrist (rheumatoid, osteoarthritis), previous wrist fractures, occupational misuse; and
- acromegaly, hypothyroidism, diabetes mellitus, obesity, amyloidosis.

A/R: Obesity and oral contraceptives are suggested risk factors.

E: Overall prevalence 2.7 %. Incidence in adults 0.1 % per year. Lifetime risk 10 %.

H: Tingling and pain in the hand and fingers (patients may be woken up at night). Weakness and clumsiness of hand.

E: Sensory impairment of median nerve (first 3 ½ fingers).
Tinel's sign: Tapping carpal tunnel triggers symptoms.
Phalen's test: Maximal flexion of the wrist for 1 min may cause symptoms.
Weakness and wasting of the thenar eminence (abductor pollicis brevis and opponens).
Signs of the underlying cause, e.g. hypothyroidism or acromegaly.

P: **Macro:** The carpal tunnel is made up of the flexor retinaculum anteriorly, the carpal bones posteriorly and laterally. It contains the median nerve, flexor pollicis longus, flexor digitorum profundus and superficialis tendons. There may be visible clues to the cause of compression: growths, oedema, inflammation or fibrosis.

I: **Blood:** TFT, ESR.
Nerve conduction study: Not always necessary. Shows conduction delay across wrist.

M: **Conservative:** Light wrist splint in a neutral position for a few weeks allows spontaneous resolution.
Medical: Local injection into carpal tunnel of long-acting steroid is effective. Worsens symptoms initially as a result of volume increase in carpal tunnel, diuretics are of uncertain benefit.
Surgical: Surgical decompression by division of the flexor retinaculum. Usually reserved for patients with intractable symptoms and motor involvement.

C: Permanent motor and sensory impairment of the hand.

P: Good. Majority of cases wax and wane over years. Secondary cases are more likely to progress further.

Cellulitis

D: Acute non-purulent spreading infection of the subcutaneous tissue, causing overlying skin inflammation.

A: Often results from penetrating injury (e.g. intravenous cannulation), local lesions (e.g. insect bites, sebaceous cysts, surgery) or fissuring (e.g. in anal fissures, toe web spaces), which allows pathogenic bacteria to enter the skin. In rare cases of septicaemia, it can arise spontaneously from blood-borne sources.

Most common organisms: *Streptococcus pyogenes* and *Staphylococcus aureus*. If occurring in the orbit, *Haemophilus influenzae* is the most common cause. The infection often arises from adjacent sinuses.

A/R: Main risk factors are poor hygiene and poor vascularization of tissue (e.g. diabetes mellitus).

E: Very common.

H: There may be history of a cut, scratch or injury.
Periorbital: Painful swollen red skin around eye.
Orbital cellulitis: Painful or limited eye movements, visual impairment.

E: **Lesion:** erythema, oedema, warm tender indistinct margins. Pyrexia may signify systemic spread.
Exclude abscess: Test for fluid thrill or fluctuation. Aspirate if pus suspected.
Periorbital: Swollen eyelids. Conjunctival injection.
Orbital cellulitis: Proptosis, impaired acuity and eye movement. Test for relative afferent pupillary defect, visual acuity and colour vision (to monitor optic nerve function).

P: **Micro:** Subdermal or subfascial bacterial growth. There is an acute inflammatory infiltrate composed mainly of polymorphs and macrophages. Localized vasodilation.

I: **Blood:** WCC, blood culture.
Discharge: Culture and sensitivity.
Aspiration: No pus. Not usually necessary unless abscess likely.
CT/MRI scan: When orbital cellulitis is suspected (to assess the posterior spread of infection).

M: **Medical:** Oral penicillins (e.g. flucloxacillin, benzylpenicillin, coamoxiclav) are effective in most community-acquired cases. In the hospital, treat empirically but change depending on sensitivity of any cultured organisms. IV use may be necessary.
Surgical: Orbital decompression may be necessary in orbital cellulitis. This is an emergency.
Abscess: Abscesses can be aspirated; incised and drained; or excised completely.

C: Sloughing of overlying skin. Localized tissue damage. In orbital cellulitis, there may be permanent vision loss and spread to brain, abscess formation, meningitis, cavernous sinus thrombosis.

P: Good with treatment.

D: Osteoarthritic degeneration of the lower cervical vertebral bodies causing compression of the spinal cord and/or nerve roots.

A: Degenerative change of vertebral bodies produces osteophytes, which protrude on to the exit foramina and spinal canal, and compress nerve roots (radiculopathy) or the anterior spinal cord (myelopathy).

A/R: Previous trauma, age and postmenopause.

E: Common in the elderly.

H: Neck pain or stiffness. Arm pain (stabbing or dull ache).
Paraesthesia, weakness, clumsiness in hands.
Weak and stiff legs.

E: **Arms:**

- Atrophy of forearm or hand muscles may be seen.
- Segmental muscle weakness in a nerve root distribution:
  C5: Shoulder abduction and elbow flexion weaknesses
  C6: Elbow flexion and wrist extension weaknesses
  C7: Elbow extension, wrist extension and finger extension weaknesses
  C8: Wrist flexion and finger flexion weaknesses.
- Hyporeflexia. In C5 and C6 lesions, 'inverted' reflexes (finger flexion seen on testing biceps or supinator tendon reflexes) may be seen as a result of LMN impairment at the level of compression and UMN impairment below the level.
- Sensory loss (mainly pain and temperature).
- Pseudoathetosis (writhing finger motions when hands are outstretched, fingers spread and eyes closed).

Legs (seen in those with cervical cord compressions):

- ↑ tone, weakness, hyper-reflexia and extensor plantars;
- ↓ Vibration and joint position sense (spinothalamic loss is less common) with a sensory level (few segments below the level of cord compression).

Lhermitte's sign: Neck flexion produces crepitus and/or paraesthesia down the spine.

P: **Macro:** Bony osteophytes and fibrocartilage protrude out into spinal canal and the exit foramina. The spinal vertebral bodies exhibit cystic changes subchondrally.

I: **Spinal X-ray (lateral):** Detects osteoarthritic change in the cervical spine, and excludes more serious causes. Poor sensitivity and specificity.
MRI: Assessment of root and cord compression and to exclude spinal cord tumour, many elderly people have some degree of cervical spondylosis and this may not be the cause of the symptoms.

M: **Conservative:** Physiotherapy. Soft neck collar to limit flexion–extension.
Medical: Supportive treatment with analgesia (e.g. NSAIDs, quinine sulphate).
Surgery: Spinal decompression, facetectomy, laminectomy (only about 50 % improve after surgery).

C: Acute spinal cord compression. Bladder and sphincter dysfunction.

P: If untreated, there can be a high quality of life impairment. Surgical treatment may only partially alleviate the impairment.

D: A chronic, slowly progressive lung disorder characterized by airflow obstruction, encompassing:
Chronic bronchitis: chronic cough and sputum production on most days for at least 3 months per year over 2 consecutive years; and
Emphysema: pathological diagnosis of permanent destructive enlargement of air spaces distal to the terminal bronchioles.

A: Bronchial and alveolar damage as a result of environmental toxins (e.g. cigarette smoke). A rare cause is α_1-antitrypsin deficiency ($< 1\,\%$) but should be considered in young patients or in those who have never smoked.

A/R: Risk factors are smoking (particularly if > 20 pack-years; 10–20 % of smokers will develop COPD), recurrent bronchopulmonary infections, occupational exposure in the mining and cotton industries. Overlaps and may often copresent with asthma.

E: Very common (prevalence up to 8 %). Presents in middle age or later. More common in males, but likely to change with ↑ female smokers. Responsible for large percentage of admissions. ~30 000 deaths/year.

H: Chronic cough and sputum production (see Definition). Breathlessness, wheeze, ↓ exercise tolerance.

E: **Inspection:** May have respiratory distress, use of accessory muscles, barrel-shaped overinflated chest, ↓ cricosternal distance, cyanosis. Note: clubbing is not normally a feature.
Percussion: Hyper-resonant chest, loss of liver and cardiac dullness.
Auscultation: Quiet breath sounds, prolonged expiration, wheeze, rhonchi and crepitations sometimes present.
Signs of CO_2 retention: Bounding pulse, warm peripheries, flapping tremor of the hands (asterixis). In late stages, signs of right heart failure (e.g. right ventricular heave, raised JVP, ankle oedema).

P: **Chronic bronchitis:** Narrowing of the airways resulting from inflammation of bronchioles (bronchiolitis) and bronchi with mucosal oedema, mucous gland hypertrophy, mucous hypersecretion and squamous metaplasia.
Emphysema: Destruction and enlargement of the alveoli distal to the terminal bronchioles, typically centriacinar in smokers and panacinar in α_1-antitrypsin deficiency. This results in loss of the elastic traction that keeps small airways open in expiration. Progressively larger emphyesematous spaces may develop, termed bullae when the diameter is > 1 cm.

I: **Blood:** FBC (↑ Hb and PCV as a result of secondary polycythemia, ↑ WCC in acute infective exacerbations).
ABG: May show hypoxia (↓ PaO_2), normal or ↑ $PaCO_2$.
Pulmonary function tests: Obstructive picture as reflected by ↓ PEFR, ↓ FEV_1: FVC ratio (mild, 60–80 %; moderate, 40–60 %; severe $< 40\,\%$), ↑ lung volumes and carbon monoxide gas transfer coefficient ↓ when significant alveolar destruction.
CXR: May appear normal or show hyperinflation (> 6 ribs visible anteriorly, flat hemi-diaphragms), ↓ peripheral lung markings, elongated cardiac silhouette.
ECG and echocardiogram: For cor pulmonale.
Sputum and blood cultures: In acute exacerbations for treatment.

M: Most important: stop smoking.

Medical:* *Bronchodilators:* β_2*-Agonists* (e.g. salbutamol) and anticholinergics (e.g. ipratropium), delivered by inhalers or nebulizers, provide symptomatic relief.

Steroids: Trial of inhaled beclometasone (6–8 weeks) and continue treatment if FEV_1 improves by $>15\,\%$. In non-responders, long-term corticosteroid therapy is controversial. Oral corticosteroids are mainly reserved for acute exarcebations.

Oxygen therapy (only for those who stop smoking): Long-term home oxygen therapy has been shown to improve mortality. Indications are:

- $PaO_2 < 7.3$ kPa on air during a period of clinical stability.
- PaO_2 7.3–8.0 kPa and signs of secondary polycythaemia, nocturnal hypoxaemia, peripheral oedema or pulmonary hypertension.

Oxygen concentrators are more economical and useful in those requiring it for >8 h/day.

Treatment of complications:

Acute infective exacerbations: 24 % O_2 via non-variable flow Venturi mask. Raise slowly if no improvement (measured by ABG) as there is a danger that a loss of hypoxic drive might cause respiratory arrest. Start empirical antibiotic therapy (first-line are amoxicillin or erythromycin). Corticosteroids (oral or inhaled) are of proven benefit. Vigorous chest physiotherapy is essential. Consider early ventilation in severe cases.

Prevention of infective exacerbations: Vaccination against pneumococcus and influenza.

C: Acute respiratory failure, infections (*Streptococcus pneumoniae*, *Haemophilus influenzae*), pulmonary hypertension and right heart failure, pneumothorax (resulting from bursting of emphysematous bullae), secondary polycythaemia.

P: High level of morbidity. 3-year survival rate of 90 % if age <60 years and $FEV_1 > 50\,\%$ predicted; 75 % if >60 years and FEV_1 40–49 % predicted.

*Refer to British Thoracic Society guidelines (*Thorax* 1997; **52**: S1–S28) and the UK Department of Health guidelines (available at http://www.prodigy.nhs.uk/) for complete information.

Cirrhosis

D: End-stage of chronic liver damage with replacement of normal liver architecture with diffuse fibrosis and nodules of regenerating hepatocytes. **Decompensated** when there are complications such as ascites, jaundice, encephalopathy or GI bleeding (see Liver failure).

A: **Chronic alcohol misuse:** Most common UK cause (see Alcoholic hepatitis and Alcohol dependence).
Chronic viral hepatitis: Hepatitis B or C are the most common causes worldwide.
Autoimmune hepatitis.
Inherited: α_1-Antitrypsin deficiency, haemochromatosis, Wilson's disease, galactosaemia, cystic fibrosis.
Drugs: e.g. methotrexate, hepatotoxic drugs.
Vascular: Budd–Chiari syndrome or hepatic venous congestion.
Chronic biliary diseases: Primary biliary cirrhosis, primary sclerosing cholangitis, biliary atresia.
Cryptogenic: In 5–10 %.

A/R: NASH are at ↑ risk of developing cirrhosis (NASH is associated with obesity, diabetes, TPN, short bowel syndromes, hyperlipidaemia and drugs, e.g. amiodarone, tamoxifen).
Decompensation can be precipitated by infection, GI bleeding, constipation, high protein meal, electrolyte imbalances, alcohol and drugs, tumour development or portal vein thrombosis.

E: Among the top 10 leading cause of deaths worldwide.

H: Early non-specific symptoms: anorexia, nausea, fatigue, weakness, weight loss.
Symptoms caused by ↓ liver synthetic function: Easy bruising, abdominal swelling, ankle oedema.
Reduced detoxification function: Jaundice, personality change, altered sleep pattern, amenorrhoea.
Portal hypertension: Abdominal swelling, haematemesis, PR bleeding or melaena.

E: Stigmata of chronic liver disease:
Asterixis ('liver flap')
Bruises
Clubbing
Dupuytren's contracture
Erythema (palmar).
Jaundice, gynaecomastia, leuconychia, parotid enlargement, spider naevi, scratch marks, ascites ('shifting dullness' and fluid thrill), enlarged liver (shrunken and small in later stage), testicular atrophy, caput medusae (dilated superficial abdominal veins), splenomegaly (indicating portal hypertension).

P: **Micro:** Periportal fibrosis, loss of normal liver architecture and nodular appearance, either micronodular (<3 mm, often caused by alcohol) or macronodular (>3 mm). Grade refers to the assessment of degree of inflammation, whereas stage refers to the degree of architectural distortion, ranging from mild portal fibrosis to cirrhosis.

Macro: Enlarged liver or shrunken cirrhotic liver in later stages.

I: **Blood:** *FBC:* ↓ Hb, ↓ platelets as a result of hypersplenism.

LFT: May be normal or often ↑ transaminases, AlkPhos, γ-GT, bilirubin, ↓ albumin.
Clotting: Prolonged PT (↓ synthesis of clotting factors).
Serum AFP: ↑ In chronic liver disease, but high levels may suggest HCC.
Other investigations: To determine the cause, e.g. viral serology, α_1-antitrypsin, caeruloplasmin (Wilson's disease), iron studies (serum ferritin, iron, total iron binding capacity) for haemochromatosis, antimitochondrial antibody (primary biliary cirrhosis), ANA, SMA (autoimmune hepatitis).
Ascitic tap: Microscopy, culture and sensitivity, biochemistry (protein, albumin, glucose, amylase) and cytology. If neutrophils $>250/mm^3$, this indicates SBP.
Liver biopsy: Percutaneous or transjugular if clotting deranged or ascites present.
Imaging: Ultrasound, CT or MRI, MRCP.
Endoscopy: Examine for varices, portal hypertensive gastropathy.
Child–Pugh grading: Class A is score 5–6, Class B is score 7–9, Class C is score 10–15.

Score	1	2	3
Albumin (g/L)	>35	28–35	<28
Bilirubin (mg/dL)	<2	2–3	>3
Prothrombin time (s prolonged)	<4	4–6	>6
Ascites	None	Mild	Moderate or severe
Encephalopathy	None	Grade 1–2	Grade 3–4

M: **Medical:** Treat the cause if possible, avoid sedatives, opiates, NSAIDs and drugs that affect the liver. Nutrition is very important and if intake is poor, dietitian review and enteral supplements should be given; nasogastric feeding may be indicated.
Treat the complications:
Encephalopathy: Treat infections. Exclude a GI bleed. Lactulose, phosphate enemas and avoid sedation.
Ascites: Diuretics (spironolactone ± furosemide (frusemide)), salt restriction, therapeutic paracentesis (with human albumin replacement IV).
SBP: Antibiotic treatment (e.g. cefuroxime and metronidazole), prophylaxis against recurrent SBP with ciprofloxacin.
Surgical: Consider insertion of TIPS to relieve portal hypertension (if recurrent variceal bleeds or diuretic-resistant ascites) although it may precipitate encephalopathy. Liver transplantation is the only curative measure.

C: Portal hypertension with ascites, encephalopathy or variceal haemorrhage, SBP, hepatocellular carcinoma, renal failure (hepatorenal syndrome), pulmonary hypertension (hepatopulmonary syndrome).

P: Depends on the aetiology and complications. Generally poor; overall 5-year survival is ~50 %. In the presence of ascites, 2-year survival of ~50 %.

CNS tumours

D: Primary tumours arising from any of the brain tissue types.

A: In children, it probably reflects embryonic errors in development. In adults, the aetiology is unknown.

A/R: Neurofibromatosis type I is associated with gliomas. Previous brain trauma is a postulated risk factor.

E: Annual incidence of primary tumours 5–9 in 100 000. Two peaks of incidence (children and the elderly).

H: Headache or vomiting (↑ intracranial pressure), epilepsy (focal or generalized), focal neurological deficits (dysphagia, hemiparesis, ataxia, visual field defects, cognitive impairment), personality change.

E: Papilloedema/false localizing signs (↑ intracranial pressure), focal neurological deficits (visual field defects, dysphasia, agnosia, anopia, hemiparesis, ataxia, dysdiadochokinesis, hemispheric disconnection).
Specific localizing syndromes:
Olfactory groove tumours: Anosmia, frontal lobe dysfunction.
Cavernous sinus tumours: Opthalmoplegia (III, IV, VI nerve palsies), V_1 and V_2 sensory loss.
Foster Kennedy syndrome: Sphenoid wing meningioma compresses II nerve causing ipsilateral optic atrophy and contralateral papilloedema.
Pituitary adenomas: Endocrine signs, bitemporal hemianopia (suprasellar expansion and optic chiasm compression), hypopituitarism or hypersecretion of specific hormones from functioning tumours (e.g. acromegaly, hyperprolactinaemia, Cushing's disease).
Parinaud's syndrome: In pineal region impairing upgaze (because of proximity of the lesion to the superior midbrain) or obstructive hydrocephalus (at the level of third ventricle).
Parasagittal region tumours: Spastic paraparesis (mimicking cord compression).
Cerebellopontine tumours: Unilateral deafness, facial weakness, nystagmus.

P: **Meningioma:** Benign and most common primary CNS tumour.
Fibrilliary astrocytoma: Most common form, usually in cerebrum.
Pilocytic astrocytoma: Cystic, in cerebellum and brainstem.
Glioblastoma multiforme: High-grade invasive tumour.
Haemangioblastoma: Vascular tumours, often in the cerebellum.
Pituitary adenoma: Benign. Space-occupying and endocrine effects.
Oligodendroglioma: 10 % of gliomas. Epileptogenic.
Medulloblastoma: Invasive midline cerebellar tumour in children.
Ependymoma: Benign, in spinal cord and fourth ventricle.
Lymphoma: In immunosuppressed patients, highly malignant. 80 % occur in the posterior fossa in children, while in adults divided roughly equally between anterior and posterior fossa.

I: **CT/MRI:** To localize and characterize the lesion.
Blood: CRP, ESR, HIV screen.
Brain biopsy: Type and grading (degree of differentiation of tumour).
Caution: Lumbar puncture is contraindicated, may cause cerebral coning.

M: **Medical:** Anticonvulsants for epilepsy. Dexamethasone to reduce brain oedema. Chemotherapy and radiotherapy to reduce tumour size.

Surgery: Debulk or total resection of the tumour (especially for benign tumours). Not preferred if on dominant hemisphere or near speech centres. In pituitary adenomas, trans-sphenoidal resection is possible. Intraventricular shunts for hydrocephalus. Surgery may be inappropriate for low-grade glioma causing epilepsy only or for multiple metastases.

C: Pressure effect on surrounding tissue; herniation (falcine, tentorial, tonsillar); cerebrovascular accident (haemorrhage; see Stroke); focal or generalized fits (see Epilepsy).

P: Generally good for benign tumours, that are extra-axial (originate from meninges or cranial nerves). Malignant tumours that are intra-axial are generally incurable. Median survival is good in low-grade tumours (>5 year) but very poor in glioblastomas (about 9 months).

Coeliac disease

D: Inflammatory disease caused by intolerance to gluten, causing chronic intestinal malabsorption.

A: Sensitivity to the gliadin component of the cereal protein, gluten, triggers an immunological reaction in the small intestine leading to mucosal damage and loss of villi.

A/R: 10 % risk of first-degree relatives being affected. Strongly associated with dermatitis herpetiformis. There is a clear genetic susceptibility associated with *HLA-B8*, *DR3* and *DQW2* haplotypes.

E: Prevalence in UK is 1 in 2000. Very variable: 1 in 300 in the west of Ireland; very rare in East Asia.

H: May be asymptomatic.
Abdominal discomfort, pain and distention.
Steatorrhoea (pale bulky stool, with offensive smell and difficult to flush away), diarrhoea.
Tiredness, malaise, weight loss (despite normal diet).
Failure to 'thrive' in children, amenorrhoea in young adults.

E: **Signs of anaemia:** pallor.
Signs of malnutrition: Short stature, abdominal distension and wasted buttocks in children. Mid-arm muscle circumference or triceps skinfold thickness gives an indication of fat stores.
Signs of vitamin or mineral deficiencies (e.g. osteomalacia, easy brusing).
Intense, itchy blisters on elbows, knees or buttocks (dermatitis herpetiformis).

P: **Macro:** Villous atrophy in the small intestine (particularly the jejunum and ileum) giving the mucosa a flat smooth appearance.
Micro: Villous atrophy with crypt hyperplasia of the duodenum. The epithelium adopts a cuboidal appearance, and there is an inflammatory infiltrate of lymphocytes and plasma cells in the lamina propria.

I: **Blood:** FBC (↓ Hb), iron and folate, U&E, albumin, Ca^{2+} and phosphate.
Stool: Culture to exclude infection, faecal fat tests for steatorrhoea.
D-xylose test: Reduced urinary excretion after an oral xylose load indicates small bowel malabsorption.
Serology: Presence of IgA antigliadin, antiendomysial (against tissue trans-glutaminase) or antireticulin antibodies can be diagnostic. As IgA deficiency is common (1 in 50 with coeliac disease), immunoglobulin levels should also be measured.
Endoscopy: Visualization and biopsy of duodenum.

M: **Advice:** Withdrawal of gluten from the diet, with avoidance of all wheat, rye and barley products. Education and expert dietary advice is essential. The Coeliac Society offers patient support and advice.
Medical: Vitamin and mineral supplements. Oral corticosteroids may be used if the disease does not subside with gluten withdrawal.

C: Iron, folate and vitamin B_{12} deficiency, osteomalacia, ulcerative jejunoileitis, gastrointestinal lymphoma (particularly T cell), bacterial overgrowth.

P: With strict adherence to gluten-free diet, most patients make a full recovery. Symptoms usually resolve within weeks. Histological changes may take longer to resolve. A gluten-free diet needs to be followed for life.

D: A growth from the bowel wall that projects into the colonic lumen.

A: Classified into non-neoplastic and neoplastic polyps. Most are benign proliferations of mucosal epithelium (adenomas). Clinically significant because of malignant potential (see Colorectal carcinoma).

A/R: Multiple colonic polyps occur in some rare syndromes:
Peutz–Jeghers syndrome: Diffuse GI polyposis (most common in the small intestine) with mucocutaneous pigmentation of lips and gums. Autosomal dominant. Benign.
Inflammatory bowel disorder: Mucosal sloughing causes pseudopolyps. Colitis increases risk of malignancy.
Familial polyposis coli: Multiple colonic adenomas. Autosomal dominant. Caused by mutation in *APC* gene. Pre-malignant.
Gardner's syndrome: Osteomas, soft-tissue tumours, sebaceous cysts, congenital hypertrophy of retinal pigment epithelium and multiple colonic adenomas. Autosomal dominant. Pre-malignant.
Turcot's syndrome: Glioblastomas or medulloblastomas, with multiple colonic adenomas. Autosomal dominant. Pre-malignant.
Cronkhite–Canada syndrome: Alopecia, nail atrophy, pigmentation, watery diarrhoea and multiple stomach, small intestine and colonic adenomas. Pre-malignant.

E: Common. Prevalence is $>50\,\%$ of those over 60 years old.

H: Usually asymptomatic.
May cause a change in bowel habit.
Mucoid diarrhoea.
PR bleeding.
Symptoms of anaemia.

E: Usually no findings on examination.

May be palpable on PR examination if low in rectum.
Associated features of multiple polyposis syndromes.

P: **Macro:** It may be sessile or pedunculated and size ranges from millimetres to centimetres in diameter.
Micro: Non-neoplastic polyps include metaplastic (hyperplastic), inflammatory and hamartomatous polyps. Neoplastic polyps are adenomas, either tubular, tubulovillous or villous, the latter with a greater tendency to malignancy.

I: **Blood:** FBC (anaemia).
Stool: Occult or frank blood in stool.
Endoscopy: Colonoscopy is gold standard investigation. For multiple polyposis syndromes, an upper GI endoscopy is necessary to look for upper GI polyps. Polyps removed need to be histologically examined to determine their malignant potential.

M: **Endoscopy:** Colonoscopic polypectomy for small isolated polyps.
Surgical: Large polyps may have to be surgically resected. In multiple polyposis syndromes (particularly familial polyposis coli), early subtotal colectomy is recommended to reduce risk of malignancy.
Follow-up: Patients should be followed by colonoscopy every 2–4 years. Genetic screening of relatives may be necessary in multiple polyposis syndromes.

C: Malignant change, with highest risk in villous adenomas and in multiple polyposis syndromes. Risk of bowel obstruction.

P: Good if detected and treated before any malignant change.

Colorectal carcinoma

D: Malignant adenocarcinoma of the large bowel.

A: Environmental and genetic factors have been implicated. A sequence from epithelial dysplasia leading to adenoma and then carcinoma is thought to occur, involving accumulation of genetic changes in oncogenes (e.g. *APC*, *K-ras*) and tumour suppressor genes (e.g. *p53*, *DCC*).

A/R: Low-fibre diet (controversial), presence of colorectal polyps, previous colorectal cancer, family history,* inflammatory bowel disease (particularly long-standing ulcerative colitis). Inherited (autosomal dominant) disorders: Hereditary non-polyposis colorectal cancer (HNPCC) caused by mutations in mismatch repair genes (1–5% of colorectal cancers), familial adenomatous polyposis (FAP) caused by mutation in the APC gene.
NSAIDS and postmenopausal HRT may be protective.

E: Second most common cause of cancer death in the West. 20 000 deaths per year in the UK. Average age at diagnosis 60–65 years. Rectal carcinomas ♂ > ♀, colon carcinomas ♀ > ♂.

H: Symptoms will depend on the location of the tumour.
Left-sided colon and rectum: Change in bowel habit, rectal bleeding or blood/mucous mixed in with stools. Rectal masses may also present as tenesmus (sensation of incomplete emptying after defecation).
Right-sided colon: Later presentation, with symptoms of anaemia, weight loss and non-specific malaise or, more rarely, lower abdominal pain.
Up to 20 % of tumours will present as an emergency with pain and distension caused by large bowel obstruction, haemorrhage or peritonitis as a result of perforation.

E: Anaemia may be only sign, particularly in right-sided lesions, abdominal mass, with metastatic disease, hepatomegaly, 'shifting dullness' of ascites. Low-lying rectal tumours may be palpable on rectal examination.

P: **Macro:** 60 % rectum and sigmoid colon; 15–20 % in the ascending colon; and the remainder in the transverse and descending colon. Distal colon tumours tend to form an annular encircling ring around the bowel wall, causing 'napkin ring' constrictions, while proximal colon tumours tend to form polypoid exophytic masses.
Micro: Neoplastic change with deranged adenomatous or anaplastic cells and varying degrees of bowel wall penetration. Staging systems include Dukes' (see below) and the TNM system.

I: **Blood:** FBC (for anaemia), LFT, tumour markers (CEA to monitor treatment response or disease recurrence).
Stool: Occult or frank blood in stool (can be used as a screening test).
Endoscopy: Sigmoidoscopy, colonoscopy. Allows visualization and biopsy. Polypectomy can also be performed if isolated small carcinoma *in situ*.
Barium contrast studies: 'Apple core' stricture on barium enema.
Ultrasound scan for hepatic metastases.
Other staging investigations include CXR, CT or MRI, endorectal ultrasound.

*Risk of colorectal Cancer = 1:17 if one first degree relative affected, 1:10 if two affected, 1:50 if no close relative affected.

M: **Surgery:** Surgery is the only curative treatment. Operation depends on circumstances.
Caecum, *ascending colon, proximal transverse colon:* right hemicolectomy.
Distal transverse colon, descending colon: left hemicolectomy.
Sigmoid colon: sigmoid colectomy.
High rectum: anterior resection.
Low rectum: abdoperineal resection and end colostomy formation.
Emergency: Hartmann's procedure (proximal colostomy, resection of tumour and oversew of distal stump).
Survival in rectal tumours is improved if total mesorectal excision (removal of surrounding fascia). Isolated hepatic metastases may be successfully resected.
Radiotherapy: May be given in a neoadjuvent setting to downstage rectal tumours prior to resection or as adjuvant therapy to reduce risk of local recurrence.
Chemotherapy: Used as adjuvant therapy in Dukes' C, or sometimes B. 5-Fluorouracil (+folinic acid); many others are being assessed in clinical trials. Used to treat metastatic or recurrent disease, either systemically or regionally, e.g. liver infusion of chemotherapeutic drugs, often combined with embolization in hepatic metastases.

C: Bowel obstruction or perforation, fistula formation. Recurrence. Metastatic disease.

P: Prognosis varies depending on Dukes' staging.

Dukes'	Extent of spread	5-year survival (%)
A	Confined to bowel wall	80–90
B	Breached serosa but no lymph nodes	60
C	Breached serosa with lymph nodes	30
D	Distant metastases (usually liver)	<5

Congenital adrenal hyperplasia

D: Inherited disorders of adrenal steroid synthesis.

A: Autosomal recessive genetic defects in the steroid synthesis pathway result in ↓ cortisol (and, in some cases, ↓ aldosterone) synthesis. This produces a secondary rise in pituitary ACTH secretion causing enlargement of the adrenal glands and build-up of precursor steroids (e.g. androgenic steroids). Common defective enzymes include 21-hydroxylase (most common), 11β-hydroxylase and 17α-hydroxylase.

A/R: Associated with consanguinity.

E: Annual incidence of 21-hydroxylase deficiency and 11β-hydroxylase deficiency are 1 in 10 000 and 1 in 100 000, respectively. The rest are less common. 21-Hydroxylase deficiency is common among the Yupik Eskimos.

H & E: **21-Hydroxylase deficiency** (↓ aldosterone, ↑ androgens): Salt-losing crisis in infants (hypotension, hyponatraemia, hyperkalaemia).

Females: Virilization of fetuses, ambiguous genitalia (cliteromegaly, fused labia) or virilization, acne, hirsutism later in life, ↑ skeletal maturation.

Males: Precocious puberty (early pubic hair, penile and muscle enlargement, ↑ skeletal maturation).

11β-Hydroxylase deficiency (↑ 11-deoxycorticosterone (a mineralocorticoid), ↓ androgens): Hypertension, hypokalaemia.

Females: As 21-hydroxylase deficiency.

Males: As 21-hydroxylase deficiency.

17α-Hydroxylase deficiency (↑ 11-deoxycorticosterone (a mineralocorticoid), ↓ androgens): Hypertension, hypokalaemia.

Females: Failure to develop secondary sexual characteristics at puberty.

Males: Ambiguous or female genitalia.

P: **Macro:** Enlarged adrenal glands.

I: **Blood:** ^{17}OH-progesterone (↑ in 21-hydroxylase deficiency and 11β-hydroxylase deficiency), testosterone, ↑ basal ACTH, LH, FSH, U&E.

ACTH stimulation test: Inappropriately elevated ^{17}OH-progesterone levels after IM ACTH (should be performed in follicular phase of menstrual cycle).

Pelvic ultrasound: Excludes PCOS.

Karyotyping: Confirms gender of infant with ambiguous genitalia.

Molecular genetic testing: To confirm location of mutation.

M: **Acute salt-losing crisis:** IV saline, dextrose and hydrocortisone.

Medical: Glucocorticoid replacement with dexamethasone or hydrocortisone. Fludrocortisone in salt-losers. Treatment is monitored by measuring serum levels of ^{17}OH-progesterone and growth.

Advice: Genetic counselling. Antenatal screening occurs in UK.

C: Infertility. Short final adult height (because of premature epiphyseal closure without treatment).

P: Undiagnosed infants may die from salt-losing crisis. Otherwise, quality of life is usually good.

D: Chronic granulomatous inflammatory disease that can affect any part of the gastrointestinal tract. Grouped with ulcerative colitis and together they are known as inflammatory bowel disease.

A: Cause has not yet been elucidated, but thought to involve an interplay between genetic and environmental factors.

A/R: **Genetic:** *NOD2* gene (chromosome 16), *HLA-B27* in those with ankylosing spondylitis.
Environmental: Smoking (4–6 × risk), refined sugar intake. Infectious agents (e.g. *Mycobacterium*) proposed.
May be associated with autoimmune diseases (e.g. SLE, autoimmune thyroid disease).

E: Annual UK incidence is 5–8 in 100 000. Prevalence is 50–80 in 100 000. Affects any age but peak incidence is in the teens or twenties.

H: Crampy abdominal pain (caused by transmural and peritoneal inflammation, fibrosis or obstruction of bowel).
Diarrhoea (may be bloody or steatorrhoea).
Fever, malaise, weight loss.
Symptoms of complications.

E: Weight loss, clubbing, signs of anaemia.
Aphthous ulceration of the mouth.
Perianal skin tags, fistulae and abscesses.
Signs of complications.

P: **Macro:** Inflammation can occur anywhere along GI tract (40 % involving the terminal ileum), 'skip' lesions with inflamed segments of bowel interspersed with normal segments. Mucosal oedema and ulceration with 'rose-thorn' fissures (cobblestone mucosa), fistulae, abscesses.
Micro: Transmural chronic inflammation with infiltration of macrophages, lymphocytes and plasma cells. Granulomas with epithelioid giant cells may be seen in blood vessels or lymphatics.

I: **Blood:** FBC (↓ Hb, ↑ platelets, ↑ WCC), U&E, LFTs (↓ albumin), ↑ ESR, CRP (↑ or may be normal), haematinics to look for deficiency states: ferritin, vitamin B_{12} and red cell folate.
Stool microscopy and culture.
AXR for evidence toxic megacolon.
Erect CXR if risk of perforation.
Small bowel follow through: May reveal fibrosis/strictures (string sign of Kantor), deep ulceration (rose thorn), cobblestone mucosa.
Endoscopy (OGD, colonoscopy) and biopsy: May help to differentiate between ulcerative colitis and Crohn's disease, useful monitoring for malignancy and disease progression.
Radionuclide-labelled neutrophil scan: Localization of inflammation (when other tests are contraindicated).

M: **Acute exacerbation:** Fluid resuscitation, IV or oral corticosteroids, high dose 5-ASA analogues (e.g. mesalazine, sulfasalazine) may induce a remission in colonic Crohn's disease. Analgesia. Elemental diet may induce remission (more often used in children). Parenteral nutrition may be necessary.
Monitor: Temperature, pulse, respiratory rate, BP and markers of activity (ESR, CRP, platelets, stool frequency, Hb and albumin). Assess for complications.

Long-term: Steroids for acute exacerbations, regular 5-ASA analogues to ↓ number of relapses in Crohn's colitis. Alternatively, steroid-sparing agents (e.g. azathioprine, 6-mercaptopurine, methotrexate, infliximab).
Advice: Stop smoking, dietitian referral. Education and advice (e.g. from inflammatory bowel disease nurse specialists).
Surgery: Failure of medical treatment, failure to thrive in children, or the presence of complications.

C: **GI:** Haemorrhage, bowel strictures, perforation, fistulae (between bowel, bladder, vagina), perianal fistulae and abscess, GI carcinoma (5 % risk in 10 years), malabsorption.
Extraintestinal: Uveitis, episcleritis, gallstones, kidney stones, arthropathy, sacroiliitis, ankylosis spondylitis, erythema nodosum and pyoderma gangrenosum, amyloidosis.

P: Chronic relapsing condition. Two-thirds will require surgery at some stage and two-thirds of these >1 surgical procedure. Mortality rate twice that of general population.

D: Inflammatory condition of the lung resulting in fibrosis of alveoli and interstitium.

A: Unknown; proposed factors include environmental dusts, viral trigger or environmental injury potentiated by viral infection and immunological derangement. Certain drugs can produce a similar illness (e.g. bleomycin, methotrexate and amiodarone).

A/R: Occupational exposure to metal (steel, brass, lead) or wood (pine) in ~20 % cases; smoking (in 75 %); other associations reported are farming, hairdressing, stone cutting, animal and vegetable dusts.

E: Rare. Prevalence in UK is ~6 in 100 000. 2 × more ♂ affected. Mean age 67 years.

H: Gradual onset of progressive dyspnoea on exertion.
Dry irritating cough. No wheeze.
Symptoms may be preceded by a viral-type illness.
Fatigue and weight loss are common.
Full occupational and drug history important.

E: Finger clubbing (~50 %).
Bibasal fine late inspiratory ('velcro') crepitations.
Signs of right heart failure in advanced stages (e.g. right ventricular heave, raised JVP, peripheral oedema).

P: Varying areas of chronic inflammatory alveolitis with abundant lymphocytes, plasma cells and macrophages and fibrosis. Three histological patterns: usual interstitial pneumonia (UIP: patchy interstitial fibrosis, later: 'honeycomb' lung); desquamative interstitial pneumonia (DIP: Diffuse intra-alveolar accumulation of macrophages, mild thickening of alveolar septa, lymphoid aggregates); and non-specific interstitial pneumonia (NSIP).

I: **Blood:** ABG (normal in early disease, but ↓ PO_2 on exercise. Normal P_{CO_2} which rises in late disease).
Serology: One-third have rheumatoid factor or antinuclear antibodies.
CXR: Usually normal at presentation. Early disease may feature small lung fields and 'ground glass' shadowing. Later, there is reticulonodular shadowing (especially at bases), signs of cor pulmonale and eventually, in advanced disease, honeycombing.
High-resolution CT: More sensitive in early disease than CXR. Affecting mainly lower zones and subpleural areas, with reticular densities, honeycombing and traction bronchiectasis.
Pulmonary function tests: Restrictive ventilatory defect (↓ FEV_1, ↓ FVC with preserved or increased ratio), ↓ lung volumes, ↓ lung compliance and ↓ TLCO.
Bronchoalveolar lavage: To exclude infection and malignancy.
Lung biopsy: Gold standard for diagnosis but may not be appropriate.
Radionucleotide scans: Gallium scan is sensitive, but not specific. Raised clearance of inhaled radiolabelled-DPTA indicates ongoing inflammation.

M: **Medical:** No curative treatment available. Dual therapy trial with corticosteroids and azathioprine for 1 month is recommended. If responsive or disease stable (in up to 30 %), continue treatment. Corticosteroids should be stopped if there is deterioration. Cyclophosphamide can be used if azathioprine not tolerated.

Cryptogenic fibrosing alveolitis continued

Supportive care: Home oxygen may be necessary. Aggressive treatment of infections. Opiates in terminal stages for relieving distressing breathlessness. Psychosocial support is necessary because of poor long-term prognosis.
Surgical: Single lung transplantation is an option in selected patients.

C: Right heart failure, lung cancer (12 %), pulmonary embolus. Death from respiratory failure.

P: Poor; mean survival is only about 3 years. Good prognostic factors:
Clinical: young age, female, response to steroids.
Radiological: predominantly 'ground glass' shadowing.
Histology: DIP and NSIP better response to treatment than UIP.

D: Syndrome associated with chronic inappropriate elevation of free circulating cortisol.

A: **ACTH-dependent:** ACTH-releasing pituitary adenoma (Cushing's disease most common endogenous cause). Ectopic ACTH from oat cell bronchocarcinoma, carcinoid tumours, phaeochromocytoma.
Non-ACTH dependent: Adrenal adenoma/carcinoma/hyperplasia.
Iatrogenic: Steroids (most common overall cause).
(Rare) Meal dependent adrenal nodules.*

A/R: Associated with MEN-1. Rare associations in Carney's syndrome† and McCune–Albright syndrome.‡

E: ♂ : ♀ = 4:1. Peak incidence is 20–40 years; adrenal carcinomas more commonly present in childhood.

H: Increasing weight and fatigue.
Muscle weakness, myalgia, thin skin, easy bruising, poor wound healing, fractures (resulting from osteoporosis).
Polydipsia and polyuria.
Hirsutism, acne, frontal balding.
Oligo- or amenorrhoea, infertility, impotence.
Depression or psychosis.

E: Moon face (with plethoric complexion), buffalo hump.
Central obesity (because of altered fat distribution), pink/purple striae on abdomen, breast, thighs.
Proximal myopathy (difficulty rising from squat), thin skin, bruises.
Evidence of fractures (kyphosis in vertebral fracture).
Hirsutism, acne, frontal balding and poorly healing wounds.
Hypertension.
Ankle oedema (salt and water retention as a result of mineralocorticoid effect of excess cortisol).
Pigmentation in ACTH-dependent cases.

P: **ACTH dependent:** Excess ACTH causes bilateral diffuse or nodular hyperplasia of the adrenal glands and excess glucocorticoid synthesis and secretion.
ACTH independent: Hypersecretion of glucocorticoid by adrenal cortex, causing a negative feedback on ACTH production.

I: **Blood:** U&E (may show hypokalaemia), ↑ glucose, ↑ cortisol with loss of diurnal variation.
Screening test: ↑ 24-h Urinary free cortisol.
Confirmation tests: *Low-dose dexamethasone suppression test:* 0.5 mg orally every 6 h for 48 h. Normally, serum ACTH and cortisol are suppressed. In Cushing's syndrome, cortisol is not suppressed because the pituitary is less sensitive to negative feedback control.

*↑ Cortisol after meals, patients have ectopic overexpression of gastrointestinal peptide receptors in the adrenal cortex.
†Carney's syndrome: spotty skin pigmentation, atrial myxomas and peripheral nerve tumours.
‡McCune–Albright syndrome: fibrous dysplasia of bones with cysts, skin pigmentation and gonadal (precocious puberty), adrenal, pituitary and thyroid hyperfunction caused by a somatic mutation in α-subunit of the G protein and constitutive activation of hormone receptors in those tissues expressing the Gsα mutation.

To determine the underlying cause:

ACTH-independent (adrenal adenoma): ↓ ACTH.

- CT or MRI of adrenals shows structural lesions.

ACTH-dependent (pituitary adenoma): ↑ ACTH.

- *High-dose dexamethasone suppression test:* 2 mg orally every 6 h for 48 h. Serum cortisol is suppressed (> 50 %) in Cushing's disease.
- *Inferior petrosal sinus sampling:* Central:peripheral ratio of venous ACTH > 2:1.
- *CRH test:* Exaggerated ACTH and cortisol response to IV bolus CRH.

Pituitary MRI: Shows structural lesion.

ACTH-dependent (ectopic):

- If lung cancer is suspected: CXR, sputum cytology, bronchoscopy, CT scan.
- To find the ectopic cause: whole body venous sampling for ACTH.

M: **Medical:** Pre-operative or if unfit for surgery. Inhibition of cortisol synthesis with metyrapone or ketoconazole. Treat osteoporosis and provide physiotherapy for muscle weakness. In iatrogenic cases, discontinue administration, lower steroid dose, or use an alternative steroid-sparing agent.

Radiotherapy.

Surgical:

In pituitary adenomas: Trans-sphenoidal adenoma resection (hydrocortisone until pituitary function recovers).

In adrenal carcinoma: Surgical removal of tumour (> 5 cm) ± mitotane.

In ectopic ACTH production: Treatment is directed at the tumour.

C: Predisposition to infections (onychomycosis, dermatomycosis, pityriasis vesicolor), diabetes, osteoporosis.

Cardiovascular: Hypertension, IHD, thromboembolism.

Complications of surgery: CSF leakage, meningitis, sphenoid sinusitis, hypopituitarism.

Complications of radiotherapy: Hypopituitarism, radionecrosis, malignancy.

P: In the untreated, 5-year survival rate is 50 %.

D: Autosomal recessive inherited multisystem disease characterized by recurrent respiratory tract infections, pancreatic insufficiency, malabsorption and male infertility.

A: Caused by a defective *CFTR* gene on chromosome 7q, which encodes a cAMP-dependent Cl^- channel. This channel regulates Na^+ and Cl^- concentrations in exocrine secretions, especially in the lung and pancreas. Any loss of function mutations result in thick viscous secretions. >800 mutations reported, most common is ΔF508 phenylalanine deletion (75 % cases in UK).

A/R: Persons with obstructive azoospermia have an increased frequency of mutations in *CFTR* genes, but may be asymptomatic for cystic fibrosis.

E: Most common life-threatening autosomal inherited condition in white people. Incidence is 1 in 2500 live births. In UK, 1 in 25 are carriers.

H: **Lung:** Recurrent chest infections, chronic cough, wheeze, sputum, haemoptysis.
Gut: Meconium ileus (in neonates), steatorrhoea (caused by ↑ fat in the stool).
Other: Chronic sinusitis, nasal polyps, male infertility, arthritis.

E: **Chest:** Chest wall deformities, coarse crepitations and wheeze.
Signs of malnutrition: Anaemia, weight loss, signs of vitamin deficiencies, slow growth, failure to thrive in children, delayed puberty in adolescents.
Other: Clubbing, nasal polyps, signs of diabetes, hepatomegaly.

P: At birth, the lung is normal histologically but as the lung matures there is mucous gland hyperplasia, recurrent infection leads to fibrosis, consolidation and bronchiectasis. The pancreas shows fatty replacement, ductal obstruction from accumulation of thick secretions, reduced exocrine parenchyma and fibrosis.

I: **Sweat test:** Pilocarpine iontophoresis (low electrical current) stimulates sweat secretion which is collected and analysed for Na^+ and Cl^- (Cl^- levels >60 mmol is diagnostic of cystic fibrosis).
Neonatal screening: Standard day 6 Guthrie heal prick, blood is tested for immunoreactive trypsin (raised by 2–5 $\times$ in babies with cystic fibrosis).
CXR: May be normal in mild disease or show increased bronchial markings, ring shadows, fibrosis (often upper zone). Consolidation or bronchiectasis in more advanced cases.
Pancreatic assessment: Faecal elastase, faecal fat content, GTT, HbA1c.
Genetic analysis: For *CFTR* mutations.
Pulmonary function tests: To assess general lung function and to predict long-term prognosis.

M: Multidisciplinary specialist care is necessary.
Respiratory: Chest physiotherapy (postural drainage, regular exercise), positive expiratory pressure masks.
Bronchodilator therapy (if responsive).
Antibiotic prophylaxis and aggressive treatment of infections (especially *Pseudomonas*).
Influenza vaccination.

GI: Adequate nutritional intake is vital, using high-calorie oral supplements and oral pancreatic enzyme replacement, vitamin (especially fat-soluble) supplements.
Endocrine: Insulin replacement therapy if diabetes develops.
Surgical: Single lung or heart–lung transplants is an option in end-stage disease (5-year survival is 55 %).

C: Recurrent chest infections, bronchiectasis (particularly *Haemophilus*, *Staphylococcus* and *Pseudomonas*).
Malabsorption, meconium ileus, intussusception, rectal prolapse.
Diabetes mellitus Type I (30 % by late teens).
Male infertility (females are fertile but conception may be difficult).
Gallstones.

P: Life expectancy is in the third decade, but steadily improving. Those with pancreatic insufficiency and those colonized by *Pseudomonas* have poorer prognosis. Gene replacement therapy may be possible in the future.