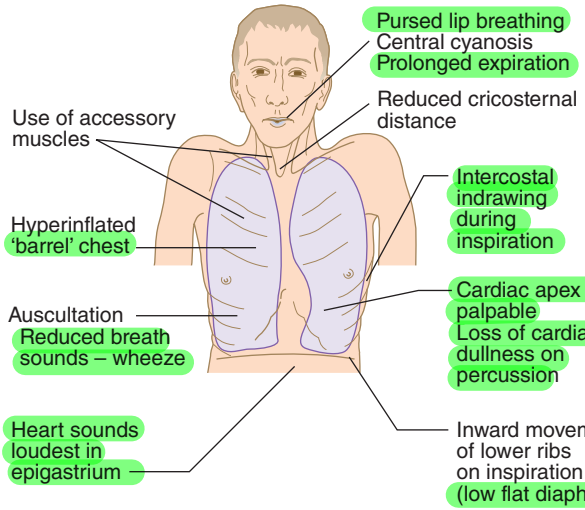
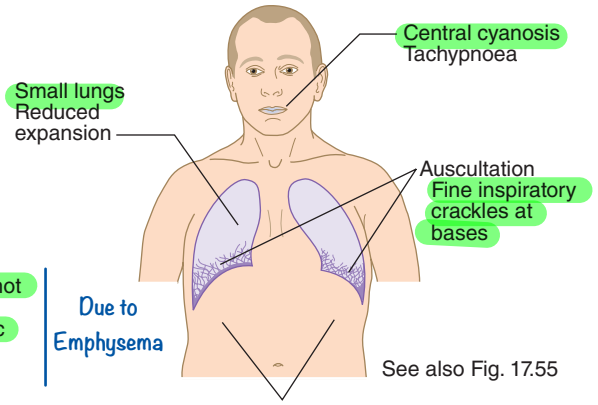
Chronic obstructive pulmonary disease



Also: raised jugular venous pressure (JVP), peripheral oedema from salt and water retention and/or cor pulmonale

Pulmonary fibrosis

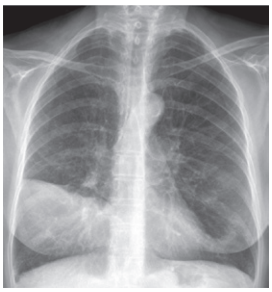


Due to Emphysema

See also Fig. 17.55

Also: finger clubbing common in idiopathic pulmonary fibrosis; raised JVP and peripheral oedema if cor pulmonale

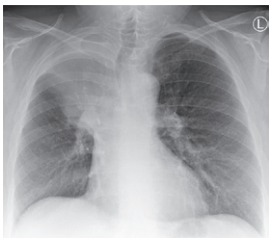
Right middle lobe pneumonia



Inspection
Tachypnoea
Central cyanosis (if severe)
Palpation
↓Expansion on R
Percussion
Dull R mid-zone and axilla
Auscultation
Bronchial breath sounds and ↑vocal resonance over consolidation and whispering pectoriloquy
Pleural rub if pleurisy

Obscures R heart border on X-ray

Right upper lobe collapse



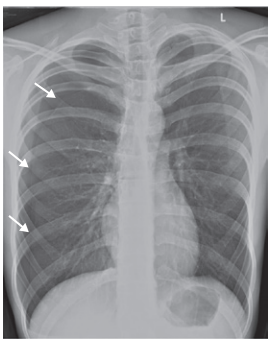
Inspection
↓Volume R upper zone
Palpation
Trachea deviated to R
↓Expansion R upper zone
Percussion
Dull R upper zone
Auscultation
↓Breath sounds with central obstruction

X-ray
Deviated trachea (to R)
Elevated horizontal fissure
↓Volume R hemithorax
Central (hilar) mass may be seen

Golden S sign

Previous FCPS Question

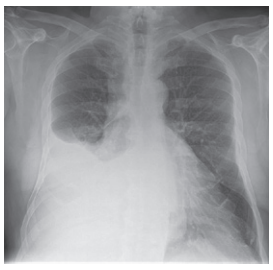
Right pneumothorax



Inspection
Tachypnoea (pain, deflation reflex)
Palpation
↓Expansion R side
Percussion
Resonant or hyper-resonant on R
Auscultation
Absent breath sounds on R

Tension pneumothorax also causes
Deviation of trachea to opposite side
Tachycardia and hypotension

Large right pleural effusion



Inspection
Tachypnoea
Palpation
↓Expansion on R
Trachea and apex may be moved to L
Percussion
Stony dull
R mid- and lower zones
Auscultation
Absent breath sounds and vocal resonance R base
Bronchial breathing or crackles above effusion

Insets (upper lobe collapse) From http://3.bp.blogspot.com; (pneumothorax) http://chestatlas.com; (pleural effusion) www.ispub.com.

Respiratory infections such as tuberculosis, pneumonia and virus infections such as influenza and COVID-19 represent a major burden of morbidity and mortality globally. The increasing prevalence of allergy, asthma and chronic obstructive pulmonary disease (COPD) contributes to the burden of chronic disease in the community. By 2030, the World Health Organization (WHO) predicts that the number of cigarette smokers worldwide will reduce to 1.2 billion; however, the ongoing tobacco exposure ensures a continuing burden of tobacco-related respiratory conditions.

Respiratory disease covers many pathologies, including infectious, inflammatory, neoplastic and degenerative processes. The practice of respiratory medicine thus requires collaboration with a range of disciplines. Recent advances have improved the lives of many patients with obstructive lung disease, cystic fibrosis, obstructive sleep apnoea and pulmonary hypertension, but the outlook remains poor for respiratory cancers and for some of the interstitial lung diseases.

Functional anatomy and physiology

The lungs occupy the upper two-thirds of the bony thorax, bounded medially by the spine, the heart and the mediastinum and inferiorly by the diaphragm. During breathing, free movement of the lung surface relative to the chest wall is facilitated by sliding contact between the parietal and visceral pleura, which cover the inner surface of the chest wall and the lung, respectively, and are normally closely apposed. Inspiration involves downward contraction of the diaphragm (innervated by the phrenic nerves originating from C3, 4 and 5) and upward, outward movement of the ribs, caused by contraction of the external intercostal muscles (innervated by intercostal nerves originating from the thoracic spinal cord). Expiration is largely passive, driven by elastic recoil of the lungs.

The conducting airways from the nose to the alveoli connect the external environment with the alveolar surface. As air is inhaled through the upper airways it is filtered in the nose, heated to body temperature and fully saturated with water vapour; partial recovery of this heat and moisture occurs on expiration. Total airway cross-section is smallest in the glottis and trachea, making the central airway particularly vulnerable to obstruction. Normal breath sounds originate mainly from the rapid turbulent airflow in the larynx, trachea and main bronchi.

The multitude of small airways within the lung parenchyma has a very large combined cross-sectional area (over 300 cm^2 in the third-generation respiratory bronchioles), resulting in very slow flow rates. Airflow is virtually silent here and gas transport occurs largely by diffusion in the final generations. Major bronchial and pulmonary divisions are shown in Figure 17.1.

The acinus (Fig. 17.2) is the gas exchange unit of the lung and comprises branching respiratory bronchioles and clusters of alveoli. Here the air makes close contact with the blood in the pulmonary capillaries (gas-to-blood distance < 0.4 µm), and oxygen uptake and CO_2 excretion occur. The alveoli are lined with flattened epithelial cells (type I pneumocytes) and a few, more cuboidal, type II pneumocytes. The latter produce surfactant, which is a phospholipid mixture that reduces surface tension and thereby counteracts the tendency of alveoli to collapse. Type II pneumocytes can divide to reconstitute type I pneumocytes after lung injury.

Lung mechanics

Healthy alveolar walls contain a fine network of elastin and collagen fibres (see Fig. 17.2). The volume of the lungs at the end of a tidal ('normal')

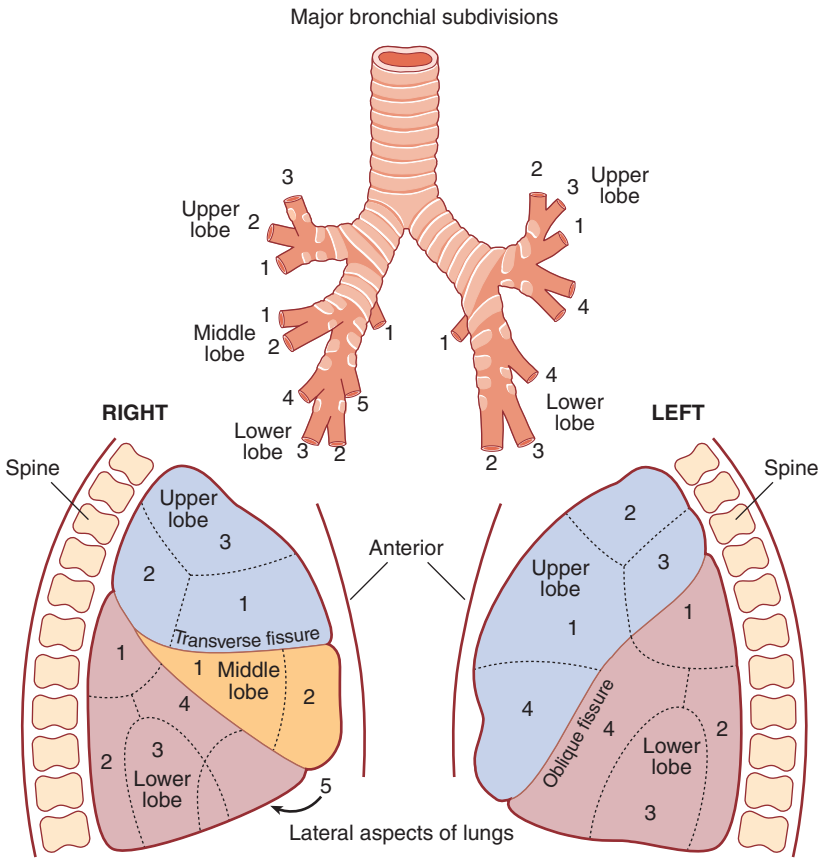


Fig. 17.1 The major bronchial divisions and the fissures, lobes and segments of the lungs. The angle of the oblique fissure means that the left upper lobe is largely anterior to the lower lobe. On the right, the transverse fissure separates the upper from the anteriorly placed middle lobe, which is matched by the lingular segment on the left side. The site of a lobe determines whether physical signs are mainly anterior or posterior. Each lobe is composed of two or more bronchopulmonary segments that are supplied by the main branches of each lobar bronchus. *Bronchopulmonary segments*: **Right** *Upper lobe*: (1) Anterior, (2) Posterior, (3) Apical. *Middle lobe*: (1) Lateral, (2) Medial. *Lower lobe*: (1) Apical, (2) Posterior basal, (3) Lateral basal, (4) Anterior basal, (5) Medial basal. **Left** *Upper lobe*: (1) Anterior, (2) Apical, (3) Posterior, (4) Lingular. *Lower lobe*: (1) Apical, (2) Posterior basal, (3) Lateral basal, (4) Anterior basal.

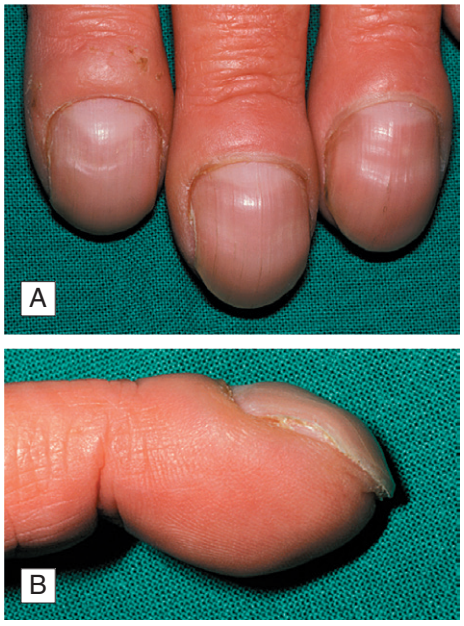


Fig. 17.10 Finger clubbing. A Anterior view. B Lateral view. *From Douglas G, Nicol F, Robertson C. Macleod's clinical examination. 13th ed. Edinburgh: Churchill Livingstone, Elsevier Ltd; 2013.*

toes but can be unilateral if caused by a proximal vascular condition such as an arteriovenous shunt for dialysis. Although clubbing is usually idiopathic, it can be associated with suppurative or malignant lung conditions (Box 17.8). Clubbing may recede if the underlying condition resolves, for example after successful lung transplantation for cystic fibrosis.

Haemoptysis

Coughing up blood is an alarming symptom, and patients nearly always seek medical advice. Care should be taken to establish that it is true haemoptysis and not haematemesis, or gum or nose bleeding. Haemoptysis must always be assumed to have a serious cause until this is excluded (Box 17.9).

Many episodes of haemoptysis remain unexplained, even after full investigation, and are likely to be due to simple bronchial infection. A history of repeated small haemoptysis, or blood-streaking of sputum, is highly suggestive of lung cancer. Fever, night sweats and weight loss suggest tuberculosis. Pneumococcal pneumonia often causes 'rusty'-coloured sputum but can cause frank haemoptysis, as can all suppurative respiratory infections. Lung abscess, bronchiectasis and intracavitary mycetoma can cause catastrophic bronchial haemorrhage. Finally, pulmonary thromboembolism is a common cause of haemoptysis and should always be considered.

Physical examination may reveal additional clues. Finger clubbing suggests lung cancer or bronchiectasis; other signs of malignancy, such as cachexia, hepatomegaly and lymphadenopathy, may also be observed. Fever, pleural rub and signs of consolidation occur in pneumonia or pulmonary infarction; a minority of patients with pulmonary infarction also have unilateral leg swelling or pain suggestive of deep venous thrombosis. Rashes, haematuria and digital infarcts point to an underlying systemic disease such as a vasculitis, which may cause haemoptysis.

Management

In severe acute haemoptysis the patient should be nursed upright (or on the side of the bleeding, if this is known), given high-flow oxygen and resuscitated as required. Bronchoscopy in the acute phase is difficult and often merely shows blood throughout the bronchial tree. Infusions of the antifibrinolytic agent tranexamic acid or the vasopressin receptor agonist terlipressin may help to limit bleeding, but evidence of efficacy is limited. If radiology shows an obvious central cause, then rigid bronchoscopy under general anaesthesia may allow intervention to stop bleeding; however, the source often cannot be visualised. Intubation with a divided endotracheal tube may allow protected ventilation of the unaffected lung to stabilise the patient. Bronchial arteriography and embolisation (Fig. 17.11), or even emergency surgery, can be life-saving in the acute situation. SBA

In the vast majority of cases, however, the haemoptysis itself is not life-threatening, and the following series of investigations should be performed:

- CXR – this may provide evidence of a localised lesion such as tumour, pneumonia, mycetoma or tuberculosis.
- Full blood count (FBC) and clotting screen – this may show anaemia or evidence of a bleeding disorder.
- CTPA – this may show underlying pulmonary thromboembolic disease or alternative causes not seen on the CXR, such as pulmonary arteriovenous malformation and small or hidden tumours.
- Bronchoscopic biopsy (after acute bleeding has settled) if the CT scan suggests an abnormality that needs biopsy.

Previous FCPS, MD Question

MCQ 17.8 Differential diagnosis of finger clubbing ★★★

Congenital or familial (5%–10%)	
Acquired	
Thoracic (~80%)	

• Chronic suppurative conditions:
  • Pulmonary tuberculosis
  • Bronchiectasis
  • Lung abscess
  • Empyema
  • Cystic fibrosis
	• Tumours:
	  • Lung cancer
	  • Mesothelioma
	  • Fibroma
	• Pulmonary fibrosis

Cardiovascular	
• Cyanotic congenital heart disease • Infective endocarditis	• Arteriovenous shunts and aneurysms
Gastrointestinal	
• Cirrhosis • Inflammatory bowel disease	• Coeliac disease
Others	
• Thyrotoxicosis (thyroid acropachy)	• Primary hypertrophic osteoarthropathy

Previous FCPS, MD Question

i 17.9 Causes of haemoptysis ★★★ MCQ

Bronchial disease	
• Cancer* • Bronchiectasis* • Acute bronchitis*	• Bronchial adenoma • Foreign body
Parenchymal disease	
• Tuberculosis* • Suppurative pneumonia • Parasites (e.g. hydatid disease, flukes)	• Lung abscess • Trauma • Actinomycosis • Mycetoma
Pulmonary vascular disease	
• Pulmonary infarction* • Goodpasture syndrome	• ANCA-associated vasculitis • Idiopathic pulmonary haemosiderosis
Cardiovascular disease	
• Acute left ventricular failure* • Mitral stenosis	• Aortic aneurysm
Blood disorders	
• Leukaemia • Haemophilia	• Anticoagulants

*Denotes a common cause.

Previous FCPS, MD Question

17.13 Pleural effusion: main causes and clinical features ★★★ SBA MCQ

Cause	Appearance of fluid	Type of fluid	Predominant cells in fluid	Other diagnostic features
Tuberculosis	Serous, usually amber-coloured	Exudate	Lymphocytes (occasionally polymorphs)	Positive tuberculin test Isolation of *Mycobacterium tuberculosis* from pleural fluid (20%) Positive pleural biopsy (80%) Raised adenosine deaminase
Malignant disease	Serous, often blood-stained	Exudate	Serosal cells and lymphocytes Often clumps of malignant cells	Positive pleural biopsy (40%) Evidence of malignancy elsewhere
Cardiac failure	Serous, straw-coloured	Transudate	Few serosal cells	Other signs of cardiac failure Response to diuretics
Pulmonary infarction	Serous or blood-stained	Exudate (rarely transudate)	Red blood cells Eosinophils	Evidence of pulmonary infarction Obvious source of embolism Factors predisposing to venous thrombosis
Rheumatoid arthritis	Serous Turbid if chronic	Exudate	Lymphocytes (occasionally polymorphs)	Positive: rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) antibodies Cholesterol in chronic effusion; very low glucose in pleural fluid
Systemic lupus erythematosus (SLE)	Serous	Exudate	Lymphocytes and serosal cells	Other signs of SLE Antinuclear factor and anti-double stranded DNA positive
Acute pancreatitis	Serous or blood-stained	Exudate	No cells predominate	Higher amylase in pleural fluid than in serum
Obstruction of thoracic duct	Milky	Chyle	None	Chylomicrons

★★ 17.14 Light's criteria for distinguishing pleural transudate from exudate

Exudate is likely if one or more of the following criteria are met:
- Pleural fluid protein:serum protein ratio > 0.5
- Pleural fluid LDH:serum LDH ratio > 0.6
- Pleural fluid LDH > two-thirds of the upper limit of normal serum LDH

(LDH = lactate dehydrogenase)

the presence of inflammatory or malignant cells. Microbiological staining can detect bacteria and mycobacteria. If a diagnosis of tuberculosis is being considered, adenosine deaminase (ADA) should be measured (see p. 559). A low pH suggests infection but may also occur in rheumatoid arthritis, ruptured oesophagus or advanced malignancy. Ultrasound- or CT-guided pleural biopsy provides tissue for pathological and microbiological analysis. Where necessary, video-assisted thoracoscopy allows visualisation of the pleura and direct guidance of a biopsy.

Management

Therapeutic aspiration may be required to palliate breathlessness, but removing more than 1.5 L at a time is associated with a small risk of re-expansion pulmonary oedema. An effusion should never be completely drained before establishing a diagnosis, as biopsy may be precluded until further fluid accumulates. Treatment of an underlying cause such as heart failure, pneumonia, pulmonary embolism or subphrenic abscess will often be followed by resolution of the effusion. The management of pleural effusion in pneumonia, tuberculosis and malignancy is dealt with below.

Empyema

An empyema is a collection of pus within the pleural space. Microscopically, neutrophil leucocytes are present in large numbers, and bacteria may be identified on Gram stain. An empyema may involve the whole pleural space or only part of it ('loculated' or 'encysted' empyema) and is usually unilateral. It is usually secondary to infection in a neighbouring structure, usually the lung, most commonly due to the bacterial pneumonia or tuberculosis. Over 40% of patients with community-acquired pneumonia develop an associated pleural effusion ('parapneumonic' effusion) and about 15% of these become secondarily infected. Other causes are infection of a haemothorax following trauma or surgery, oesophageal rupture and rupture of a subphrenic abscess through the diaphragm.

Macroscopically, the pleural surfaces are covered with an inflammatory exudate. The pus can be under considerable pressure. Inadequate treatment can result in rupture into a bronchus, causing a bronchopleural fistula and pyopneumothorax, or tracking through the chest wall forming a subcutaneous abscess or sinus ('empyema necessitans').

Clinical assessment

An empyema should be suspected in patients with pulmonary infection if there is severe pleuritic chest pain or persisting or recurrent pyrexia despite appropriate antimicrobial treatment. In other cases, the primary infection may be so mild that it passes unrecognised and the first definite clinical features are due to the empyema itself. Once an empyema has developed, systemic features are prominent (Box 17.15).

Investigations

The appearances on CXR may be indistinguishable from those of pleural effusion, although pleural adhesions may confine the empyema to form a 'D'-shaped shadow against the inside of the chest wall (Fig. 17.14). When air is present as well as pus (pyopneumothorax), a horizontal 'fluid level' marks the air/liquid interface. Ultrasound can show the position of the fluid, the extent of pleural thickening and whether fluid is in a single collection or multiloculated, containing fibrin and debris (Fig. 17.15). Imaging with CT provides information on the pleura, underlying lung parenchyma and patency of the major bronchi. Ultrasound or CT can be used to identify the optimal site for aspiration, which is best performed using a wide-bore needle. If the fluid is thick and turbid pus, empyema is confirmed. Other features suggesting empyema are a fluid glucose of less than 3.3 mmol/L (60 mg/dL), lactate dehydrogenase (LDH) of more than 1000 IU/L or a fluid pH of less than 7.2. However, pH measurement should be avoided if pus is thick, as it damages blood gas analysers. Bacterial culture may be negative if antibiotics have already been given. MCQ

New Box

17.22 Biological therapies for severe asthma* ★★★

Drug	Mechanism of action	Indication	Criteria for initiation	NICE guidance
Omalizumab	Antibody to IgE	Severe persistent allergic (IgE-mediated) asthma	Four or more courses, or continuous oral corticosteroids in the previous year, and IgE and weight in dosing range	TA278
Mepolizumab	Antibody to IL-5	Severe eosinophilic asthma	Blood eosinophils > 300 cells/μL and 4 courses of oral corticosteroids in the last 12 months or	TA671
Benralizumab	Antibody to IL-5 receptor		Blood eosinophils > 300 cells/μL and continuous oral corticosteroids greater than prednisolone 5 mg/day or	TA565
Reslizumab	Antibody to IL-5		Blood eosinophils > 400 cells/μL and 3 courses of oral corticosteroids in the last 12 months	TA479
Dupilumab	Antibody to IL-4 receptor alpha	Severe asthma with type 2 inflammation	Blood eosinophils > 150 cells/μL, FeNO > 25 ppb, and 4 courses of oral corticosteroids in the last 12 months	TA751
Tezepelumab	Antibody to thymic stromal lymphopoietin	Severe asthma	Three or more courses or maintenance oral corticosteroids in the previous year	TA880

*All biological therapies for severe asthma require assessment and an optimised standard treatment plan. Please see 'Further information' for links to the individual NICE Technology Appraisal documents.
(IgE = immunoglobulin E; IL = interleukin)

Previous FCPS, MD Question MCQ

17.23 Immediate assessment of acute severe asthma ★★★

Acute severe asthma

- PEF 33%–50% predicted (< 200 L/min)
- Heart rate ≥ 110 beats/min
- Respiratory rate ≥ 25 breaths/min
- Inability to complete sentences in 1 breath

Life-threatening features

- PEF < 33% predicted (< 100 L/min)
- SpO_2 < 92% or PaO_2 < 8 kPa (60 mmHg) (especially if being treated with oxygen)
- Normal or raised $PaCO_2$
- Silent chest
- Cyanosis
- Feeble respiratory effort
- Bradycardia or arrhythmias
- Hypotension
- Exhaustion
- Delirium
- Coma

Near-fatal asthma

- Raised $PaCO_2$ and/or requiring mechanical ventilation with raised inflation pressures

(PEF = peak expiratory flow)

Treatment includes the following measures:

- *Oxygen*. Controlled supplemental oxygen should be administered to maintain SaO_2 94%–98%. The presence of a high $PaCO_2$ should not be taken as an indication to reduce oxygen concentration but as a warning sign of a severe or life-threatening attack. Failure to achieve appropriate oxygenation is an indication for assisted ventilation.
- *High doses of inhaled bronchodilators*. Short-acting β_2-agonists such as salbutamol 5 mg nebulised are the agent of choice. If a nebuliser is not available then salbutamol can be administered via multiple doses of a metered dose inhaler (MDI) using a spacer device. Nebulised ipratropium bromide 500 μg can provide additional bronchodilation and should be added if there is a failure to respond to salbutamol or in life-threatening attacks.
- *Systemic corticosteroids*. These reduce the inflammatory response, reduce mortality, subsequent hospital admission and requirement for bronchodilators. They should be administered to all patients with an acute severe attack. They can usually be administered orally as prednisolone but intravenous hydrocortisone may be used in patients who are vomiting or unable to swallow.

There is no evidence base for the use of intravenous fluids but many patients are dehydrated due to high insensible water loss and may benefit. Potassium supplements may be necessary to counteract hypokalaemia caused by repeated doses of β-agonists.

If patients fail to improve or for patients with life-threatening or near-fatal attacks, a number of further options may be considered including intravenous magnesium and intravenous aminophylline, although cardiac monitoring and therapeutic drug level monitoring are recommended with these therapies.

The PEF should be recorded 15–30 minutes after starting therapy and thereafter according to response every 4–6 hours, and pulse oximetry should be monitored to ensure that SaO_2 94%–98% is maintained. Repeat arterial blood gases are necessary if the initial $PaCO_2$ measurements were normal or raised, the PaO_2 was below 8 kPa (60 mmHg) or the patient deteriorates. If the patient fails to respond adequately to these measures, endotracheal intubation and intermittent positive pressure ventilation (IPPV) may be required. Indications for this are shown in Box 17.24.

Prognosis

The outcome from acute severe asthma is generally good, but a considerable number of deaths occur in young people and many are preventable. Failure to recognise the severity of an attack, on the part of either the assessing physician or the patient, contributes to delay in delivering appropriate therapy and under-treatment.

Prior to discharge, patients should be stable on discharge medication (nebulised therapy should be discontinued for at least 24 hours), and the PEF should have reached 75% of predicted or personal best. The acute attack should prompt a review of any trigger factors, the delivery of asthma education, assessment of treatment concordance including inhaler technique, and the provision of a written self-management plan. The patient should be offered an appointment with a general practitioner or asthma nurse within 2 working days of discharge, and follow-up at a specialist hospital clinic within a month.

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease characterised by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities, usually caused by significant exposure to noxious particles or gases. The spectrum of COPD includes chronic bronchitis and emphysema. Chronic bronchitis is defined as cough and sputum for at least 3 consecutive months in each of 2 consecutive years. Emphysema is abnormal permanent enlargement of the airspaces distal to the terminal bronchioles, accompanied by destruction of their walls. Exacerbations MCQ

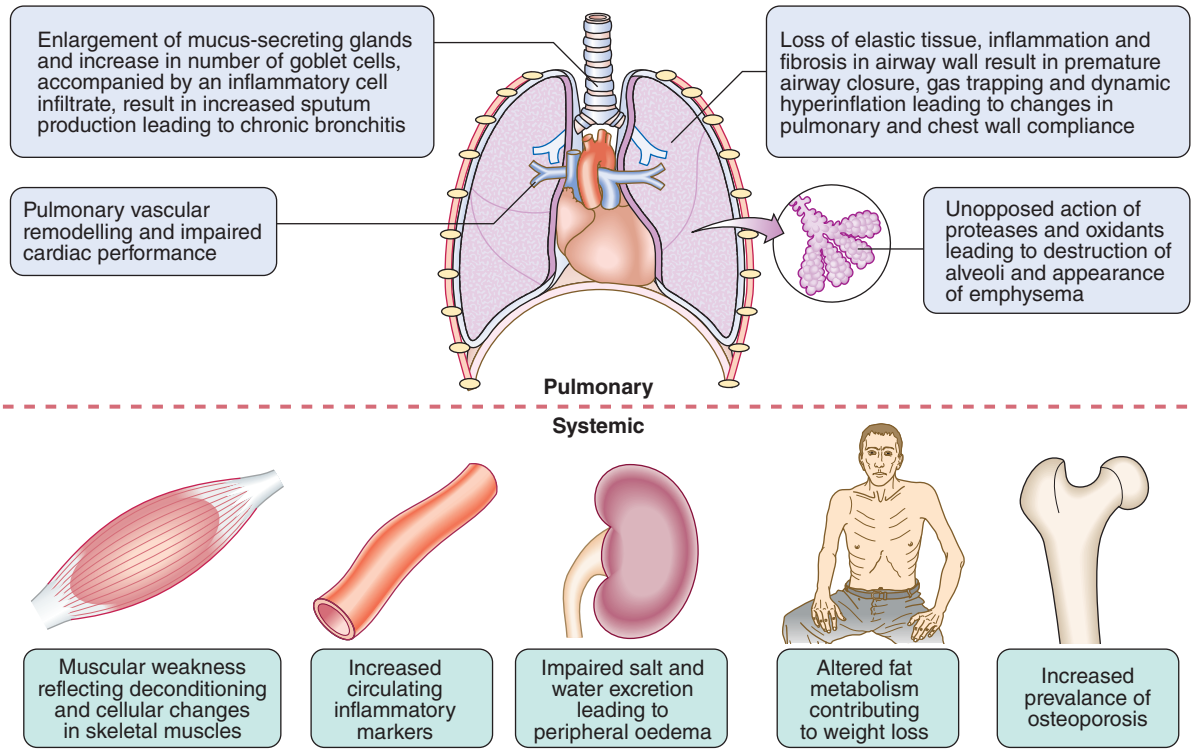


Fig. 17.25 The pulmonary and systemic features of chronic obstructive pulmonary disease.

Previous FCPS, MD Question

17.25 Risk factors for development of chronic obstructive pulmonary disease ★★★

Environmental factors

- Tobacco smoke: accounts for 95% of cases in the UK
- Indoor air pollution: cooking with biomass fuels in confined areas in low-income countries
- Occupational exposures, such as coal dust, silica and cadmium
- Low birth weight: may reduce maximally attained lung function in young adult life
- Lung growth: childhood infections or maternal smoking may affect growth of lung during childhood, resulting in a lower maximally attained lung function in adult life
- Infections: recurrent infection may accelerate decline in FEV_1; persistence of adenovirus in lung tissue may alter local inflammatory response, predisposing to lung damage; HIV infection is associated with emphysema
- Low socioeconomic status
- Cannabis smoking

Host factors

- Genetic factors: α_1-antitrypsin deficiency; other COPD susceptibility genes are likely to be identified
- Airway hyper-reactivity

(FEV_1 = forced expiratory volume in 1 sec)

tolerate) hypercapnia earlier and may develop oedema and secondary polycythaemia. In practice, these phenotypes often overlap.

Investigations

Although there are no reliable radiographic signs that correlate with the severity of airflow limitation, a CXR is essential to identify alternative diagnoses such as cardiac failure, lung cancer and the presence of bullae. A blood count is useful to exclude anaemia or document polycythaemia, and all patients should be tested for α_1-antitrypsin deficiency.

The diagnosis requires objective demonstration of airflow obstruction by spirometry and is established when the post-bronchodilator FEV_1/FVC is <70% or below the lower limit of normal. The severity of COPD may be defined in relation to the post-bronchodilator FEV_1 (Box 17.27).

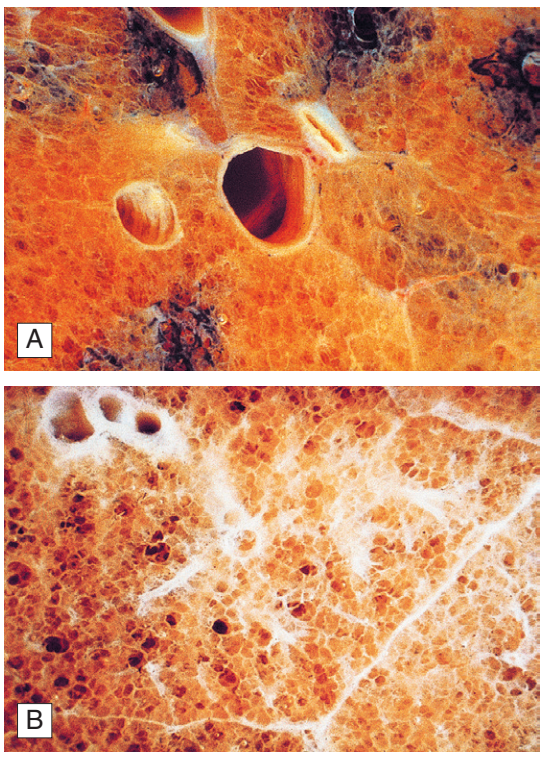


Fig. 17.26 The pathology of emphysema. A Normal lung. B Emphysematous lung, showing gross loss of the normal surface area available for gas exchange. *(B) Courtesy of the British Lung Foundation.*

Measurement of lung volumes provides an assessment of hyperinflation. This is generally performed by helium dilution technique (p. 526); however, in patients with severe COPD, and in particular large bullae, body plethysmography is preferred because the use of helium may under-estimate lung volumes. The presence of emphysema is suggested

SBA

17.31 Causes of bronchiectasis ★★★ MCQ

Congenital

- Cystic fibrosis
- Ciliary dysfunction syndromes:
  - Primary ciliary dyskinesia (immotile cilia syndrome)
  - Kartagener syndrome (sinusitis and transposition of the viscera)
- Primary hypogammaglobulinaemia

Acquired: children

- Severe infections in infancy (whooping cough, measles or pneumonia)
- Primary tuberculosis
- Inhaled foreign body

Acquired: adults

- Suppurative pneumonia
- Pulmonary tuberculosis
- Allergic bronchopulmonary aspergillosis complicating asthma
- Bronchial tumours

17.32 Symptoms of bronchiectasis ★★ MCQ SBA

- **Cough**: chronic, daily, persistent
- **Sputum**: copious, continuously purulent
- **Pleuritic pain**: when infection spreads to involve pleura, or with segmental collapse due to retained secretions
- **Haemoptysis**:
  - Streaks of blood common, larger volumes with exacerbations of infection
  - Massive haemoptysis requiring bronchial artery embolisation sometimes occurs
- **Infective exacerbation**: increased sputum volume with fever, malaise, anorexia
- **Halitosis**: frequently accompanies purulent sputum
- **General debility**: difficulty maintaining weight, anorexia, exertional breathlessness

Investigations

In addition to common respiratory pathogens, sputum culture may identify *Pseudomonas aeruginosa*, *Staphylococcus aureus*, fungi such as *Aspergillus fumigatus* and non-tuberculous mycobacteria.

Mild bronchiectasis may not be apparent on a plain CXR. In advanced disease, thickened airway walls, cystic bronchiectatic spaces and associated areas of pneumonic consolidation or collapse may be visible. CT is much more sensitive and shows thickened, dilated airways (Fig. 17.29).

SBA If the patient is suspected of having a ciliary dysfunction syndrome, a nasal FeNO sample should be taken as a screening test, then consideration of nasal brush biopsy and genetic testing. The nasal biopsies should be assessed for ciliary beat frequency and structural ciliary abnormalities assessed by electron microscopy.

Management

Physiotherapy

Patients should be shown how to perform regular daily physiotherapy to assist the drainage of excess bronchial secretions. This reduces the amount of cough and sputum and prevents recurrent episodes of bronchopulmonary infection. Patients should lie in a position in which the lobe to be drained is uppermost. Deep breathing, followed by forced expiratory manoeuvres (the 'active cycle of breathing' technique), helps to move secretions in the dilated bronchi towards the trachea, from which they can be cleared by vigorous coughing. Devices that increase airway pressure either by a constant amount (positive expiratory pressure mask) or in an oscillatory manner (flutter valve) aid sputum clearance in some patients, and a variety of techniques should be tried to find the one that suits the individual. The optimum duration and frequency of physiotherapy depend on the amount of sputum, but 5–10 minutes twice daily is a minimum for most patients.

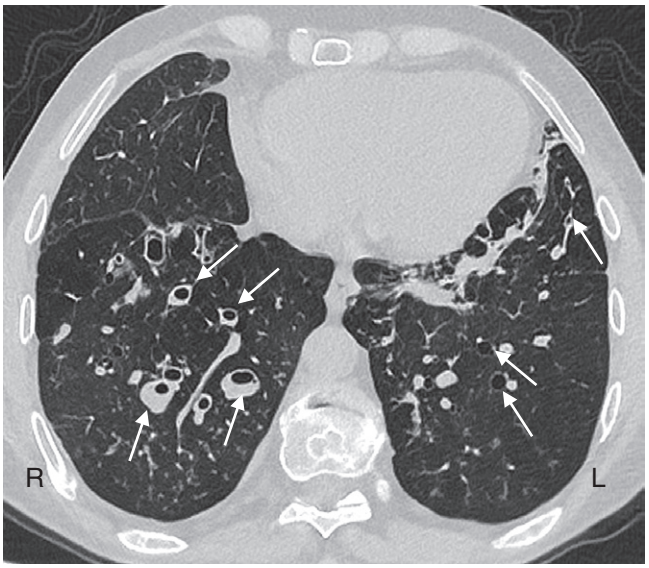


Fig. 17.29 Bronchiectasis. Chest CT demonstrating bilateral lower lobe bronchiectasis, more severe in the right lung base. The arrows indicate dilated bronchi which, on the right, are associated with bronchial wall thickening.

Antibiotic therapy

For most patients with bronchiectasis, the appropriate antibiotics are the same as those used in COPD but larger doses and longer courses are required. When secondary infection occurs with staphylococci and gram-negative bacilli, in particular *Pseudomonas* species, antibiotic therapy becomes more challenging and should be guided by microbiological sensitivities. For *Pseudomonas aeruginosa*, oral ciprofloxacin (500–750 mg twice daily) or an intravenous anti-pseudomonal β-lactam (such as piperacillin–tazobactam 4.5 g 4 times daily or ceftazidime 2 g 3 times daily) will be required. Haemoptysis in bronchiectasis often responds to treatment of the underlying infection, although percutaneous embolisation of the bronchial circulation by an interventional radiologist can be indicated in the event of massive or repeated haemoptysis.

Surgical treatment

Surgical resection of bronchiectatic areas is indicated in a minority of patients where the bronchiectasis is confined to a single lobe or segment on CT. Unfortunately, many of those in whom medical treatment proves unsuccessful are unsuitable for surgery because of either extensive bilateral bronchiectasis or reduced lung function. In progressive forms of bronchiectasis, resection of destroyed areas of lung that are acting as a reservoir of infection should be considered only as a last resort.

Prognosis

The disease is progressive when associated with ciliary dysfunction or cystic fibrosis and eventually causes respiratory failure. In other patients, the prognosis can be relatively good if physiotherapy is performed regularly and antibiotics are used aggressively.

Prevention

As bronchiectasis can start at a young age following measles, whooping cough or a primary tuberculous infection, adequate prevention and treatment of these conditions are essential. Early recognition and treatment of bronchiectasis is important to prevent progressive lung damage.

Cystic fibrosis

Genetics, pathogenesis and epidemiology

Cystic fibrosis (CF) is the most common life-limiting genetic disease in people of predominantly European descent. It is inherited in an autosomal

infection (North, Central or South America). Certain occupations may be associated with exposure to specific bacteria (p. 586).

Clinical examination should first focus on the respiratory and pulse rates, blood pressure and an assessment of the mental state, as these are important in assessing the severity of the illness. In the UK, severity is assessed using the CURB-65 score, which takes findings on physical examination and investigations into account (Fig. 17.32). Chest signs vary, depending on the inflammatory response, which proceeds through stages of acute exudation, red and then grey hepatisation, and finally resolution. When consolidated, the lung is typically dull to percussion and, as conduction of sound is enhanced, auscultation reveals bronchial breathing and whispering pectoriloquy; crackles are heard throughout. An assessment of the state of nutrition is important, particularly in old age and frailty. The differential diagnosis of pneumonia is shown in Box 17.39. in resolution stage

Investigations

The object of investigations, which are summarised in Box 17.40, is to confirm the diagnosis, assess severity and identify the development of complications.

Management

The most important aspects of management are oxygenation, fluid balance and antibiotic therapy. In severe or prolonged illness, nutritional support may be required.

Oxygen

Oxygen should be administered to all patients with tachypnoea, hypoxaemia, hypotension or acidosis to maintain the target oxygen saturations specified on p. 232. Continuous positive airway pressure (CPAP) should be considered in those who remain hypoxic despite high-concentration oxygen therapy, and these patients should be managed in a high-dependency or critical care environment where invasive ventilation is available. Indications for referral to a critical care unit are summarised in Box 17.41.

Fluid balance

Intravenous fluids should be considered in those with severe illness, in older patients and those with vomiting. It may be appropriate to discontinue hypertensive agents temporarily, particularly if there is evidence of acute kidney injury secondary to sepsis. Otherwise, an adequate oral intake of fluid should be encouraged. Vasopressor support may be required in patients with shock.

Antibiotic treatment

Prompt administration of appropriate antibiotics improves the outcome. The initial choice of antibiotic is guided by clinical context, severity assessment, local knowledge of antibiotic resistance patterns and antibiotic guidelines. Current treatment regimens are detailed in Box 17.42. In most patients with uncomplicated pneumonia a 5-day course is adequate, although treatment is usually required for longer in patients with pneumonia due to *Legionella pneumophila*, *Staph. aureus* or *Klebsiella pneumoniae*.

Treatment of pleural pain

It is important to relieve pleural pain in order to allow the patient to breathe normally and cough efficiently. For the majority, simple analgesia with paracetamol, co-codamol or NSAIDs is sufficient. In some patients, opiates may be required but must be used with caution in individuals with poor respiratory function.

Physiotherapy

Physiotherapy is not usually indicated in patients with CAP, although it may be helpful to assist expectoration in patients who suppress cough because of pleural pain.

Prognosis

Most patients respond promptly to antibiotic therapy. Fever may persist for several days, however, and the CXR often takes several weeks or even months to resolve, especially in old age. Delayed recovery suggests either that a complication has occurred (Box 17.43) or that the diagnosis is incorrect (see Box 17.39). Alternatively, the pneumonia may be secondary to a proximal bronchial obstruction or recurrent aspiration. The mortality rate of adults with mild pneumonia is low (< 5%); hospital death

★★ 17.39 Differential diagnosis of pneumonia MCQ

- Pulmonary infarction
- Pulmonary/pleural tuberculosis
- Pulmonary oedema (can be unilateral)
- Pulmonary eosinophilia
- Malignancy: bronchoalveolar cell carcinoma
- Cryptogenic organising pneumonia/bronchiolitis obliterans organising pneumonia (COP/BOOP)

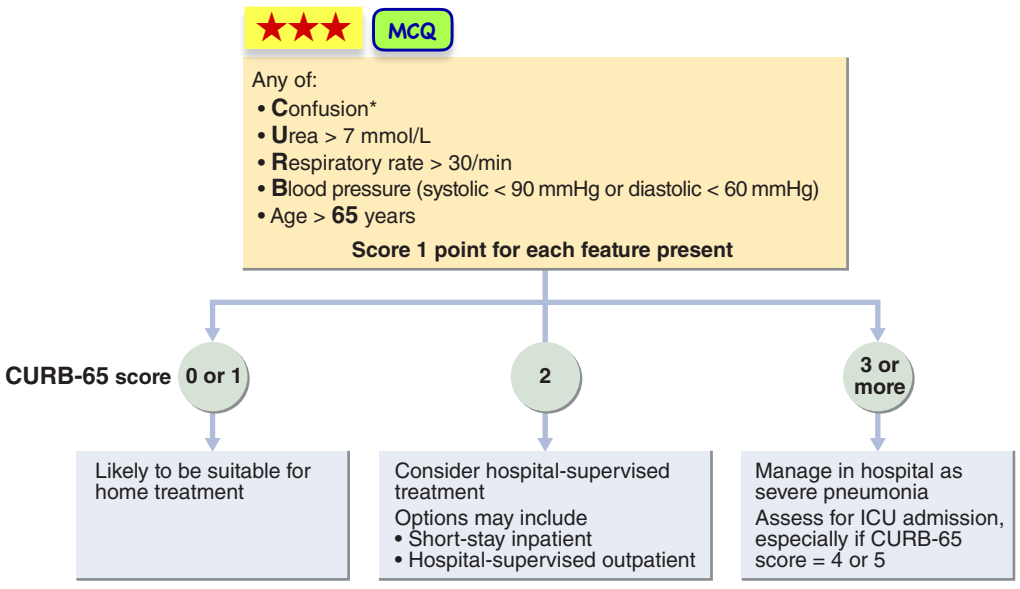


Fig. 17.32 Hospital CURB-65 score. Confusion is defined as an Abbreviated Mental Test Score of 8 or less or new disorientation in person, place or time. (ICU = intensive care unit; urea of 7 mmol/L ≅ 42 mg/dL)

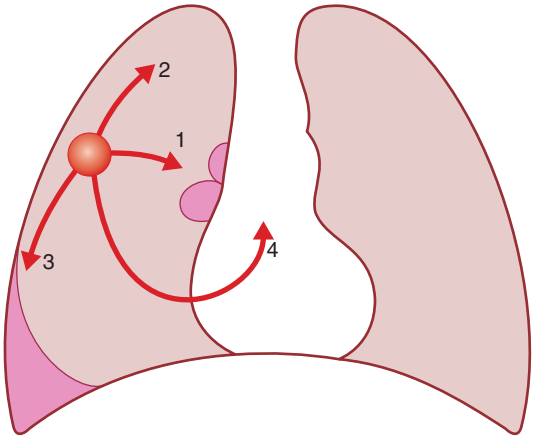


Fig. 17.36 Primary pulmonary tuberculosis. (1) Spread from the primary focus to hilar and mediastinal lymph glands to form the 'primary complex', which heals spontaneously in most cases. (2) Direct extension of the primary focus – progressive pulmonary tuberculosis. (3) Spread to the pleura – tuberculous pleurisy and pleural effusion. (4) Blood-borne spread: *few bacilli* – pulmonary, skeletal, renal, genitourinary infection, often months or years later; *massive spread* – miliary pulmonary tuberculosis and meningitis.

Previous FCPS Question SBA MCQ

★★★ **17.48 Natural history of untreated primary tuberculosis**

Time from infection	Manifestations
3–8 weeks	Primary complex, positive tuberculin skin test
3–6 months	Meningeal, miliary and pleural disease
Up to 3 years	Gastrointestinal, bone and joint, and lymph node disease
Around 8 years	Renal tract disease
From 3 years onwards	Post-primary disease due to reactivation or re-infection

Adapted from Davies PDO, ed. Clinical tuberculosis. London: Hodder Arnold; 1998.

★ **17.49 Features of primary tuberculosis**

Infection (4–8 weeks)

- Influenza-like illness
- Skin test conversion
- Primary complex

Disease

- Lymphadenopathy: hilar (often unilateral), paratracheal or mediastinal
- Collapse (especially right middle lobe)
- Consolidation (especially right middle lobe)
- Obstructive emphysema
- Cavitation (rare)
- Pleural effusion
- Miliary disease
- Meningitis
- Pericarditis

Hypersensitivity ★★★ MCQ Previous FCPS, MD Question

- Erythema nodosum
- Phlyctenular conjunctivitis
- Dactylitis

★★★ **17.47 Risk factors for tuberculosis** MCQ

Patient-related

- Age (children > young adults < old age)
- First-generation immigrants from high-prevalence countries
- Close contacts of patients with smear-positive pulmonary TB
- Overcrowding (prisons, collective dormitories); homelessness (shelters and hostels)
- CXR evidence of primary TB infection
- Primary infection < 1 year previously
- Smoking: cigarettes, bidis (Indian cigarettes made of tobacco wrapped in tembhurni leaves) and cannabis

Associated diseases

- Immunosuppression: HIV (reduced by ART), anti-tumour necrosis factor (TNF) and other biologic therapies, high-dose glucocorticoids, cytotoxic agents
- Malignancy (especially lymphoma and leukaemia)
- Diabetes mellitus
- Chronic kidney disease
- Silicosis
- Gastrointestinal disease associated with malnutrition (gastrectomy, jejuno-ileal bypass, cancer of the pancreas, malabsorption)
- Deficiency of vitamin D or A
- Recent measles in children

(ART = antiretroviral therapy; HIV = human immunodeficiency virus; TB = tuberculosis)

★★ **17.50 Clinical presentations of pulmonary tuberculosis** MCQ

- Chronic cough, often with haemoptysis
- Pyrexia of unknown origin
- Unresolved pneumonia
- Exudative pleural effusion
- Asymptomatic (diagnosis on CXR)
- Weight loss, general debility
- Spontaneous pneumothorax

Post-primary pulmonary TB

Post-primary disease refers to new exogenous infection or endogenous infection (reactivation of a dormant primary lesion) in a person who has been sensitised by earlier exposure. It is most frequently pulmonary and characteristically occurs in the apex of an upper lobe, where the oxygen tension favours survival of the strictly aerobic organism. The onset is usually insidious, developing slowly over several weeks. Systemic symptoms include fever, night sweats, malaise and loss of appetite and weight, and are accompanied by progressive pulmonary symptoms (Box 17.50). Radiological changes include ill-defined opacification in one or both of the upper lobes, and as progression occurs, consolidation, collapse and cavitation develop to varying degrees (Fig. 17.37). It is often difficult to distinguish active from quiescent disease on radiological criteria alone, but the presence of a miliary pattern or cavitation favours active disease. In extensive disease, collapse may be marked and results in significant displacement of the trachea and mediastinum. Occasionally, a caseous lymph node may drain into an adjoining bronchus, leading to tuberculous pneumonia.

Clinical features: extrapulmonary disease

Extrapulmonary TB accounts for 20% of cases in those who are HIV-negative but is more common in HIV-positive patients.

Lymphadenitis

SBA

Lymph nodes are the most common extrapulmonary site of disease. Cervical and mediastinal glands are affected most frequently, followed by axillary and inguinal, and more than one region may be involved. Disease may represent primary infection, spread from contiguous sites or reactivation. Supraclavicular lymphadenopathy is often the result of spread from mediastinal disease. The nodes are usually painless and initially mobile but become matted together with time. When caseation and liquefaction occur, the swelling becomes fluctuant and may discharge through the skin with

Previous FCPS, MD Question

★★★ MCQ

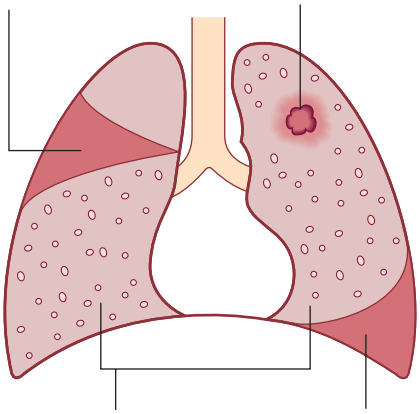


Fig. 17.37 **Major manifestations and differential diagnosis of pulmonary tuberculosis on chest X-ray**. Less common manifestations include pneumothorax, acute respiratory distress syndrome (ARDS), cor pulmonale and localised emphysema.

the formation of a 'collar-stud' abscess and sinus formation. Approximately half of cases fail to show any constitutional features, such as fevers or night sweats. During or after treatment, paradoxical enlargement, development of new nodes and suppuration may all occur but without evidence of continued infection; surgical excision is rarely necessary. In non-immigrant children in the UK, most mycobacterial lymphadenitis is caused by opportunistic mycobacteria, especially of the *M. avium* complex.

Pleural tuberculosis

Tuberculous pleural effusions are common. Patients present with pleuritic chest pain in addition to the classic clinical features of pulmonary TB. Effusions are caused by both primary and reactivated TB but can also result from a delayed hypersensitivity reaction to TB in the pleural cavity. Pseudochylothorax, due to compression from TB lymphadenitis, and empyema occur infrequently. Pleural fluid analysis demonstrates a lymphocytic exudate, with low glucose and pH. Pleural fluid smear and culture have sensitivities of only 10% and 25%, respectively; however, pleural tissue culture increases this to 80%. Raised adenosine deaminase has high sensitivity but low specificity as it occurs in malignancy and empyema also. Effusion volume fluctuates during treatment, even when successful. Therapeutic drainage is performed when necessary and steroids are sometimes used as an alternative.

MCQ

Gastrointestinal tuberculosis

Any part of the bowel can be affected by TB and patients may present with a wide range of symptoms and signs (Fig. 17.38). Upper gastrointestinal tract involvement is rare and is usually an unexpected histological finding in an endoscopic or laparotomy specimen. Ileocaecal disease accounts for approximately half of abdominal TB cases. Fever, night sweats, anorexia and weight loss are usually prominent and a right iliac fossa mass may be palpable. Up to 30% of patients present with an acute abdomen. Ultrasound or CT may reveal thickened bowel wall, abdominal

17

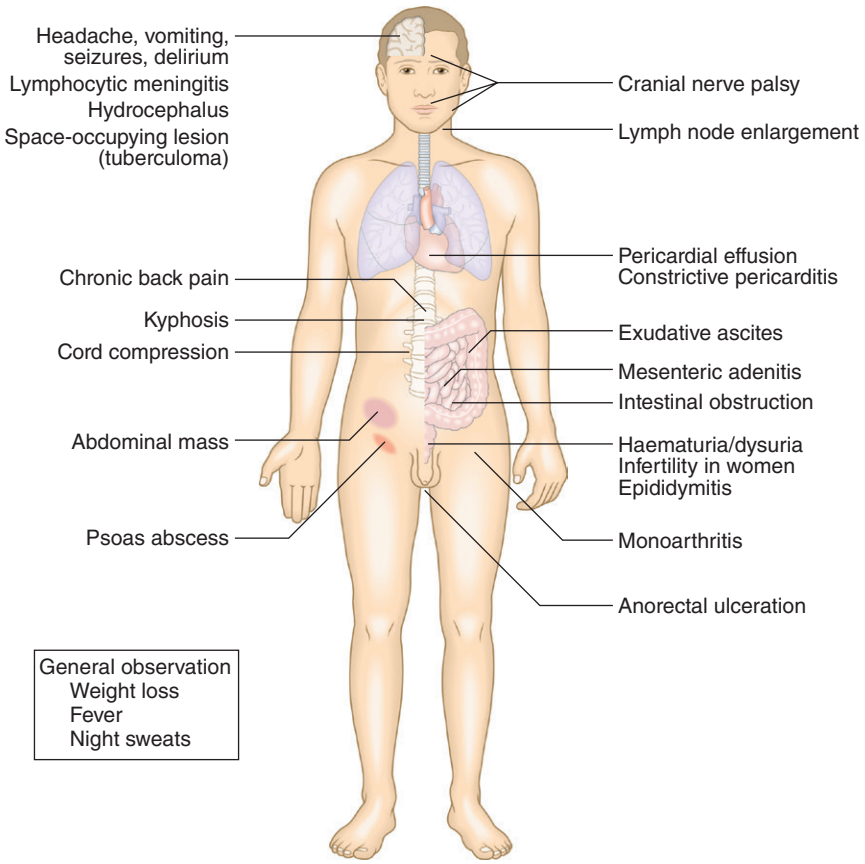


Fig. 17.38 **Systemic presentations of extrapulmonary tuberculosis.**

microscopy and Ziehl–Neelsen stain. A positive smear is sufficient for the presumptive diagnosis of TB, but definitive diagnosis requires either culture or the detection of *M. tuberculosis* DNA. The probability of visualising acid-fast bacilli (AFB) is proportional to the bacillary burden in the sputum. Smear-negative sputum should also be cultured, as only 10–100 viable organisms are required for sputum to be culture-positive. A diagnosis of smear-negative TB may be considered in advance of culture if the CXR appearances are typical of TB.

The slow growth of MTB on solid (typically between 4 and 6 weeks) and liquid (typically around 2 weeks) culture media has prompted the development of rapid NAATs. The WHO now recommends use of the GeneXpert MTB/RIF as an initial diagnostic test for MTB detection and rifampicin-resistance in sputum rather than smear microscopy, although for practical purposes a smear is still usually performed first, particularly in countries of low TB prevalence.

New info

The diagnosis of extrapulmonary TB can be more challenging. There are generally fewer organisms (particularly in meningeal or pleural fluid), so culture, histopathological examination of tissue and/or NAAT may be required. Stimulation of T cells by mycobacterial antigens leads to increased levels of adenosine deaminase (ADA) in pleural, pericardial, cerebrospinal and ascitic fluid, so measuring ADA in these fluids may support a diagnosis of TB but should not replace culture. The IGRA and tuberculin skin tests have low sensitivity and specificity, and are not routinely used in the diagnosis of active TB infection.

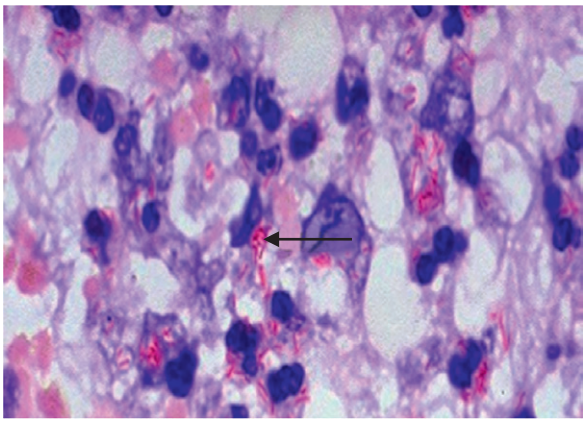


Fig. 17.40 Auramine-stained sputum sample. *Mycobacterium tuberculosis* and other mycobacteria retain the auramine stain after washing with acid and alcohol and are therefore seen as fluorescent organisms against a dark background. *Courtesy of Richard Hobson.*

Drug sensitivity testing

The rapid detection of drug resistance is central both to the management of the individual with TB and to control of the disease in the population. Molecular tests are increasingly used to provide rapid drug sensitivity testing (DST), particularly with regard to the detection of rifampicin resistance, which is important because rifampicin forms the cornerstone of 6-month chemotherapy. The GeneXpert MTB/RIF (see above) can detect molecular markers of rifampicin resistance in less than 2 hours. The gold standard is culture, followed where possible by whole genome sequencing (WGS), which is now being used routinely in resource-rich settings both for identification of mycobacterium and to predict antimicrobial susceptibility, at least to first-line agents.

SBA

Management

Chemotherapy

The treatment of TB is based on the principle of an initial intensive phase to reduce the bacterial population rapidly, followed by a continuation phase to destroy any remaining bacteria. Treatment options for newly diagnosed TB are summarised in Box 17.52. Standard WHO-recommended treatment involves 6 months' treatment with isoniazid and rifampicin (the continuation phase), supplemented in the first 2 months (the intensive phase) with pyrazinamide and ethambutol. Ethambutol is given throughout the continuation phase in countries with high levels of isoniazid resistance in new TB patients, and where DST is not performed (or results are unavailable) before the continuation phase begins. Fixed-dose tablets combining two, three or four drugs are preferred to reduce pill burden and increase adherence. A 4-month regimen of isoniazid, rifapentine, and moxifloxacin in the continuation phase, supplemented in the first 2 months with pyrazinamide in the intensive phase, was introduced by WHO in 2022. However, poor access to rifapentine, lack of fixed-dose combination tablets, and high cost have limited implementation. Unless there is reason to suspect drug resistance or non-tuberculous mycobacterium, treatment should be commenced immediately in any patient who is smear-positive, and in those who are smear-negative but with typical CXR changes and no response to standard antibiotics. Where drug resistance is not anticipated, patients can be assumed to be non-infectious after 2 weeks of appropriate therapy.

New info

17

Six months of therapy is appropriate for most patients with pulmonary or extrapulmonary TB. However, extended courses of therapy are recommended for CNS and bone and joint TB (12–18 months). Extended durations of treatment should also be considered in patients whose sputum remains culture positive following the intensive phase, having first reassessed for drug resistance, poor adherence and malabsorption. Note that treatment extension relates to prolonged therapy with drugs used in the continuation phase rather than continued therapy with drugs used in the intensive phase.

New info

17.52 Treatment of newly diagnosed tuberculosis

MCQ

Intensive phase	Continuation phase	Comments
Standard regimen		
2 months of HRZE daily	4 months of HR daily	
2 months of HRZE daily	4 months of HRE	Applies only in countries with high levels of isoniazid resistance in new TB patients, and where isoniazid drug susceptibility testing in new patients is not done (or results are unavailable) before the continuation phase begins
Dosing frequency		
Daily*	Daily	Optimal
Daily*	3 times/week	No longer recommended but sometimes used in practice for patients receiving directly observed therapy
3 times/week	3 times/week	No longer recommended but sometimes used in practice for patients receiving directly observed therapy, provided the patient is *not* living with HIV or living in an HIV-prevalent setting

*Daily (rather than 3 times weekly) intensive-phase dosing may help to prevent acquired drug resistance in TB patients starting treatment with isoniazid resistance.
(H = isoniazid; R = rifampicin; Z = pyrazinamide; E = ethambutol; HIV = human immunodeficiency virus)
Adapted from World Health Organization. Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update.

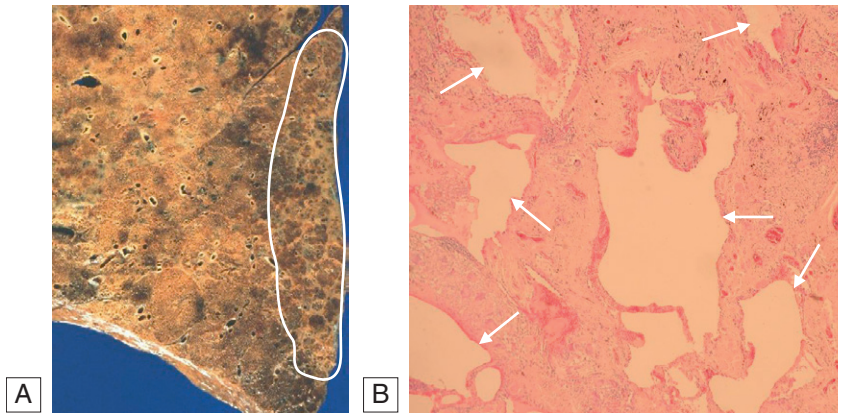


Fig. 17.56 Pathological features of usual interstitial pneumonia. A Lung tissue showing subpleural scarring, most prominently down the posterior edge of the lower lobe (highlighted). This distribution of fibrosis is typical of usual interstitial pneumonitis. The fibrosis may be associated with prominent cystic change known as 'honeycomb lung'. B Histology showing severe interstitial fibrosis with loss of the normal alveolar architecture and the development of 'honeycomb' cysts (arrows). *Courtesy of Dr William Wallace, Department of Pathology, Royal Infirmary of Edinburgh.*

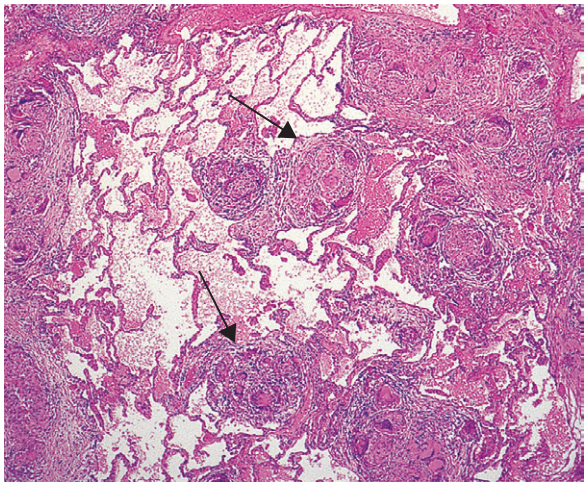


Fig. 17.57 Sarcoidosis of the lung. Hematoxylin and eosin–stained section showing non-caseating granulomas (arrows). *Courtesy of Dr William Wallace, Department of Pathology, Royal Infirmary of Edinburgh.*

Lofgren Syndrome =Young female + E. nodosum+ arthropathy+uveitis+BHL

Clinical features

Sarcoidosis is considered with other DPLDs, as over 90% of cases affect the lungs, but the condition can involve almost any organ (Fig. 17.58 and Box 17.74). Löfgren syndrome – an acute illness characterised by erythema nodosum, peripheral arthropathy, uveitis, bilateral hilar lymphadenopathy (BHL), lethargy and occasionally fever – is often seen in young women. Alternatively, BHL may be detected in an otherwise asymptomatic individual undergoing a CXR for other purposes. Pulmonary disease may also present in a more insidious manner with cough, exertional breathlessness and radiographic infiltrates; chest auscultation is often surprisingly unremarkable. Fibrosis occurs in around 20% of cases of pulmonary sarcoidosis and may cause a silent loss of lung function. Pleural disease is uncommon and finger clubbing is not a feature. Complications such as bronchiectasis, aspergilloma, pneumothorax, pulmonary hypertension and cor pulmonale have been reported but are rare.

SBA

MCQ

Investigations

Lymphopenia is characteristic and liver function tests may be mildly deranged. Hypercalcaemia may be present (reflecting increased formation of calcitriol – 1,25-dihydroxyvitamin D – by alveolar macrophages), particularly if the patient has been exposed to strong sunlight or is taking high-dose vitamin D supplements. Hypercalciuria may also be seen and can lead to nephrocalcinosis. Serum angiotensin-converting enzyme (ACE) provides a non-specific marker of disease activity and can assist in monitoring the clinical course. Chest radiography is commonly used to stage sarcoidosis (Box 17.75). In patients with pulmonary infiltrates, pulmonary function testing may show a restrictive defect accompanied by impaired gas exchange. Exercise tests may reveal oxygen desaturation. Bronchoscopy may demonstrate a 'cobblestone' appearance of the mucosa, and bronchial and transbronchial biopsies usually show non-caseating granulomas, as may samples from the mediastinal nodes obtained by EBUS. Bronchoalveolar lavage fluid typically contains an increased CD4:CD8 T-cell ratio. Characteristic HRCT appearances include reticulonodular opacities that follow a perilymphatic distribution centred on bronchovascular bundles and the subpleural areas. FDG PET scanning can detect extrapulmonary disease.

SBA

17

The occurrence of erythema nodosum with BHL on CXR is often sufficient for a confident diagnosis, without recourse to a tissue biopsy. Similarly, a typical presentation with classical HRCT features may also be accepted. In other instances, however, the diagnosis should be confirmed by histological examination of the involved organ. The presence of anergy to tuberculin skin tests (an injection of protein derived from *M. tuberculosis*) can support the diagnosis.

Management

Patients who present with acute illness and erythema nodosum should receive NSAIDs and, on occasion, a short course of corticosteroids. The majority of patients enjoy spontaneous remission and so, if there is no evidence of organ damage, systemic corticosteroid therapy can be withheld for 6 months. However, prednisolone (at a starting dose of 20–40 mg/day) should be commenced immediately in the presence of hypercalcaemia, pulmonary impairment, cardiac involvement, renal impairment or uveitis. Topical corticosteroids may be useful in cases of mild uveitis, and inhaled corticosteroids have been used to shorten the duration of systemic corticosteroid use in asymptomatic parenchymal sarcoidosis. Patients should be warned that strong sunlight and high-dose vitamin D supplements may precipitate hypercalcaemia and endanger renal function.

Features suggesting a less favourable outlook include age over 40, African Caribbean ancestry, persistent symptoms for more than 6 months, the involvement of more than three organs, lupus pernio (see Fig. 17.58) and a stage III/IV CXR. In patients with severe disease, methotrexate (10–25 mg/week), azathioprine (50–150 mg/day) and biological therapies inhibiting tumour necrosis factor alpha (TNF-α) may be effective in suppressing disease activity. Chloroquine, hydroxychloroquine and low-dose thalidomide may be useful in cutaneous sarcoidosis with limited pulmonary involvement. Selected patients may be referred for consideration of single lung transplantation. The overall mortality is low (1%–5%) and usually reflects cardiac involvement or pulmonary fibrosis.

MCQ

Previous FCPS, MD Question

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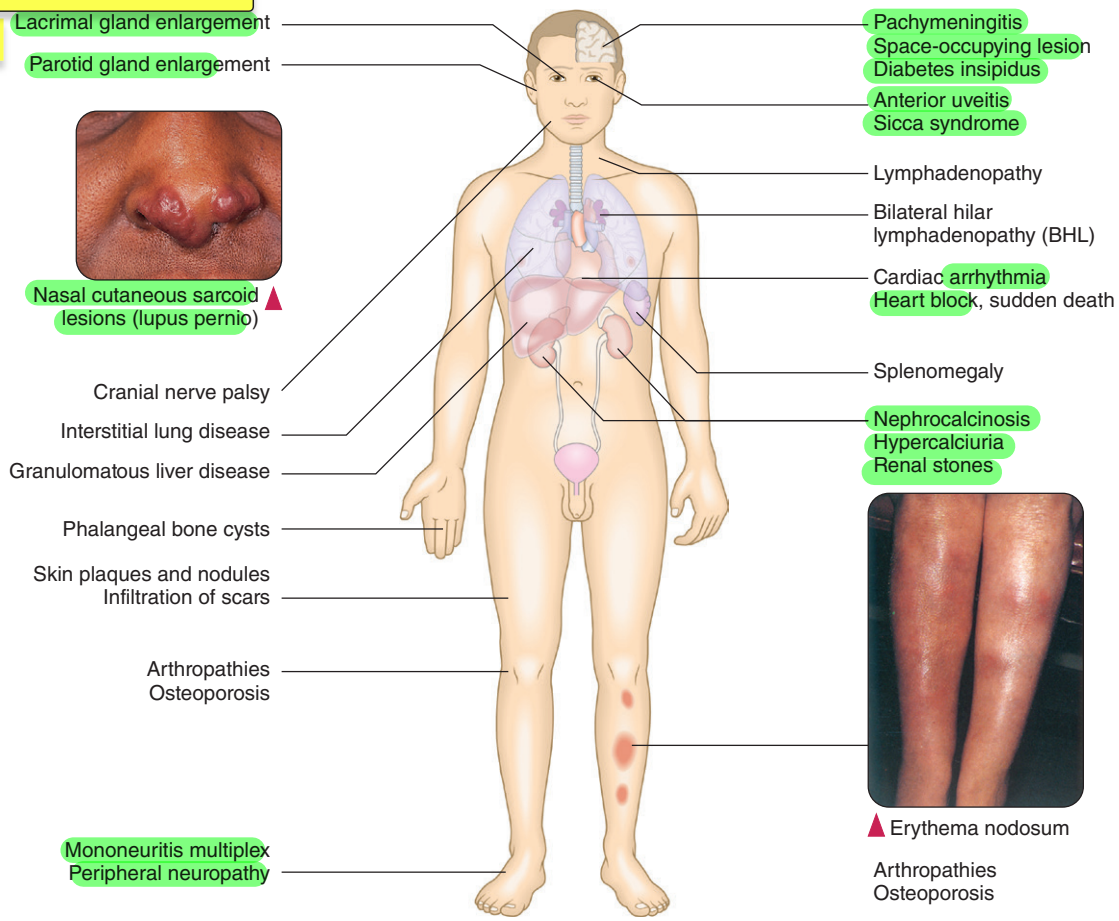


Fig. 17.58 Systemic involvement in sarcoidosis. *Inset (Erythema nodosum): From Savin JA, Hunter JAA, Hepburn NC. Skin signs in clinical medicine. London: Mosby–Wolfe; 1997.*

i 17.74 Presentation of sarcoidosis ★★ MCQ

- Asymptomatic: abnormal routine CXR (~30%) or abnormal liver function tests
- Respiratory and constitutional symptoms (20%–30%)
- Erythema nodosum and arthralgia (20%–30%)
- Ocular symptoms (5%–10%)
- Skin sarcoidosis (including lupus pernio) (5%)
- Superficial lymphadenopathy (5%)
- Other (1%), hypercalcaemia, diabetes insipidus, cranial nerve palsies, cardiac arrhythmias, nephrocalcinosis

i 17.75 CXR changes in sarcoidosis ★★ SBA

Stage I: BHL (usually symmetrical); paratracheal nodes often enlarged

- Often asymptomatic but may be associated with erythema nodosum and arthralgia. The majority of cases resolve spontaneously within 1 year

Stage II: BHL and parenchymal infiltrates

- Patients may present with breathlessness or cough. The majority of cases resolve spontaneously

Stage III: parenchymal infiltrates without BHL

- Disease less likely to resolve spontaneously

Stage IV: pulmonary fibrosis

- Can cause progression to ventilatory failure, pulmonary hypertension and cor pulmonale

(BHL = bilateral hilar lymphadenopathy)

Lung diseases due to systemic inflammatory disease

The acute respiratory distress syndrome

The pathogenesis and treatment of this disorder is discussed in Chapter 10.

Respiratory involvement in connective tissue disorders

Pulmonary complications of connective tissue disease are common, affecting the airways, alveoli, pulmonary vasculature, diaphragm and chest wall muscles, and the chest wall itself (Box 17.76). In some instances, pulmonary disease may precede the appearance of the connective tissue disorder. Indirect associations between connective tissue disorders and respiratory complications include those due to disease in other organs, such as thrombocytopenia causing haemoptysis; pulmonary toxic effects of drugs used to treat the connective tissue disorder; and secondary infections due to the disease itself, neutropenia or immunosuppressive drug regimens.

Rheumatoid disease

Pulmonary involvement in rheumatoid disease is important, accounting for around 10%–20% of the mortality associated with the condition. The majority of cases occur within 5 years of the rheumatological diagnosis, but pulmonary manifestations may precede joint involvement in 10%–20%. Pulmonary fibrosis is the most common pulmonary manifestation. All forms of interstitial disease have been described, but NSIP is probably the most common. A rare variant of localised upper lobe fibrosis and cavitation is occasionally seen.

Exam Related Extra Information

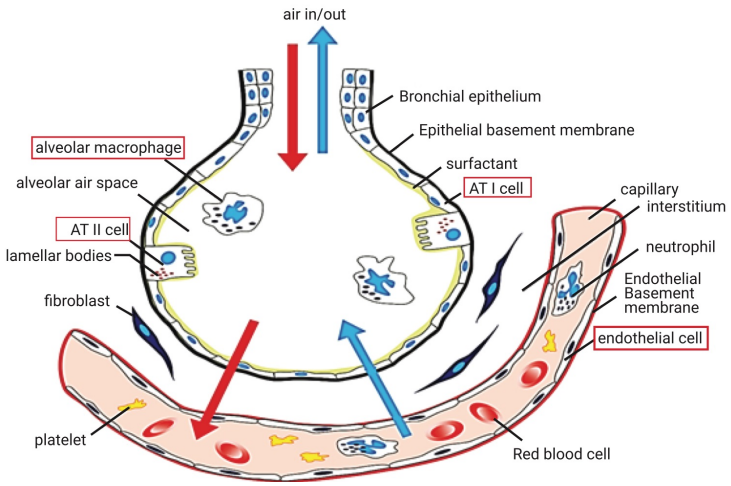
Functional Division of Respiratory Tract

1) Conducting Zone
(Trachea to Terminal Bronchiole)
* No gaseous exchange occurs.

2) Respiratory Zone
(From Respiratory Bronchiole to Alveolar Sac)
* Gaseous exchange occurs.

Layers of Respiratory Membrane

1. Surfactant layer: (A layer of fluid lining the alveolus and containing surfactant.)
2. Alveolar epithelium layer.
3. Epithelial basement membrane.
4. A very thin interstitial space between the alveolar epithelium and the capillary membrane.
5. Capillary basement membrane (in many places it fuses with the epithelial basement membrane).
6. Capillary endothelial membrane.



Factors Affecting Diffusion Capacity through Respiratory Membrane

1. Thickness of the membrane.
2. Surface area of the membrane.
3. Diffusion coefficient of the gas in the substance of the membrane.
4. Pressure difference between the two sides of the membrane.
5. Molecular weight of the gas.
6. Solubility of the gas in the fluid.
7. Distance over which diffusion must occur.

Muscles of Respiration

A. Inspiration
In quiet inspiration
* The diaphragm (75%)
* External intercostal muscle

In forceful inspiration
The above muscles + additional muscles:
* Sternocleidomastoid muscles
* Scaleni
* Anterior serrati
* Scalenus posterior
* Latissimus dorsi muscle

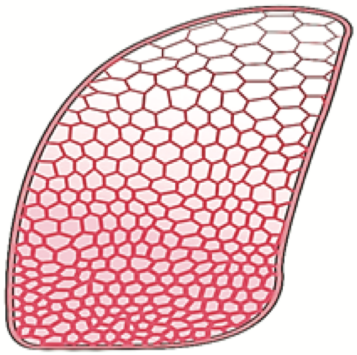
B. Expiration

1. In quiet expiration
* Does not involve any muscle.

2. In forceful expiration (Additional muscles)
* Rectus abdominis
* Internal intercostal
* Serratus posterior inferior muscle

Muscles common in both inspiration and expiration
1. Intercostal
2. Serratus posterior

At apex
Intrapleural pressure
At apex
Intrapleural pressure
more negative
Greater transmural
pressure
Large alveoli
Lower intravascular
Pressure
Less blood flow
So less ventilation
And perfusion



SBA Pearls

1. Progressive dyspnoea + Dry cough + Finger clubbing + Bibasal Velcro crackles + HRCT: UIP pattern (basal subpleural honeycombing) → Idiopathic Pulmonary Fibrosis (IPF)

2. Exertional dyspnoea + Occupational asbestos exposure + Finger clubbing + Bibasal end-inspiratory crackles + HRCT: Pleural plaques + Lower lobe fibrosis → Asbestosis

3. Acute episodic wheeze + Nocturnal cough + Chest tightness + Spirometry: FEV_1 increase ≥12% and ≥200 mL after bronchodilator → Bronchial Asthma

4. Smoker + Chronic productive cough + Progressive dyspnoea + Barrel chest + Post-bronchodilator $FEV_1/FVC < 0.70$ → COPD

5. Copious foul-smelling sputum + Clubbing + Recurrent chest infection + Haemoptysis + HRCT: Signet-ring sign / Tram-track appearance → Bronchiectasis

6. Fever + Productive cough + Pleuritic chest pain + Bronchial breathing + Chest X-ray: Lobar consolidation → Community-Acquired Pneumonia

7. Chronic cough + Weight loss + Evening fever + Night sweats + Haemoptysis + Xpert MTB/RIF positive → Pulmonary Tuberculosi
8.
9. Sudden dyspnoea + Pleuritic chest pain + Tachycardia + DVT risk factors + ECG: $S_1Q_3T_3$ pattern + CTPA: Pulmonary artery filling defect → Pulmonary Embolism

9. Sudden pleuritic chest pain + Hyper-resonance + Absent breath sounds + Chest X-ray: Visible pleural line with absent lung markings → Pneumothorax

10. Dyspnoea + Stony dullness + Reduced breath sounds + Pleural fluid meeting Light's criteria → Pleural Effusion

11. Bilateral hilar lymphadenopathy + Erythema nodosum + Uveitis + Biopsy: Non-caseating granuloma → Sarcoidosis
12. Young female + E. nodosum+arthropathy+uveitis+BHL → Lofgren Syndrome

12. Asthma + Eosinophilia + Recurrent fleeting pulmonary infiltrates + Central bronchiectasis + Total IgE >1000 IU/mL → ABPA

13. Previous TB cavity + Recurrent haemoptysis + CT: Mobile intracavitary fungal ball (air-crescent sign) → Aspergilloma
14. Profound neutropenia + Immunosuppression + Halo sign ± Air-crescent sign + CT chest: Dense nodular lesion → Invasive Pulmonary Aspergillosis
15. Persistent cough + Weight loss + Haemoptysis + Smoker + Clubbing + CECT chest + Bronchoscopy biopsy positive → Bronchogenic Carcinoma

Previous FCPS, MD Question

Q. A 30-year-old man complained of persistent purulent cough, with finger clubbing. He has a childhood history of TB. Which is the cause of finger clubbing?

a) COPD
b) TB
c) Bronchiectasis
d) Bronchial carcinoma
e) Empyema
Answer: C

Q. Gaseous exchange takes place in the (Residency March 2026)

a) Alveolar duct
b) Alveolus
c) Respiratory bronchiole
d) Segmental bronchus
e) Terminal bronchiole
Answer: T T T F F
Explanation:
* (a, b, c) Respiratory zone / Gas exchange zone.
* (d, e) Conducting zone.

Q. Causes of type II respiratory failure include (Diploma July 2023)

a) Acute interstitial pneumonia
b) Barbiturate overdose
c) Pneumothorax
d) Poliomyelitis
e) Pulmonary embolism
Answer: F T F T F

Q. A patient with poorly controlled asthma is started on mepolizumab. What is the mechanism of action of this drug?

a) Anti IL-5 monoclonal antibody
b) Monoclonal antibody directed against IgE
c) Leukotriene receptor antagonist
d) Phosphodiesterase type-4 inhibitor
e) Short-acting β2 agonist
Answer: A