DISORDERS OF OXYGENATION AND CARBON DIOXIDE ELIMINATION

14

UNDERSTAND: CHAPTER VIDEOS

Watch the following videos to ease you into this chapter. If you are using the eBook just click on the play buttons. Alternatively go to **https://study.sagepub.com/essentialpatho/videos**

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (5:02)

ASTHMA (10:29)

PNEUMOTHORAX (10:52)

CYSTIC FIBROSIS (2:49)

CYSTIC FIBROSIS A-Z (6:36)

LEARNING OUTCOMES

When you have finished studying this chapter you will be able to:

1. Identify terms associated with disorders of the respiratory system.
2. Describe the pathophysiology of upper and lower respiratory tract infections.
3. Explain what happens when there is damage to the pleura.
4. Explain the pathophysiological changes that occur in pulmonary disorders.
5. Explain the pathophysiology of asthma and chronic obstructive pulmonary disease.
6. Describe the changes that occur with cystic fibrosis.
7. Identify the changes that occur when there are interruptions to the pulmonary circulation.
8. Explain the changes that occur in the respiratory system during acute lung disorders.

INTRODUCTION

In this chapter, you will consider disorders of pulmonary function; various types of **disease** can disrupt the normal processes associated with gaseous exchange. Pulmonary disease may be classified as infectious or non-infectious, acute or chronic, obstructive or restrictive. We look at these various diseases and the impact that they have on the person. Additionally, you will also consider the emotional/psychological and social implications of such pathophysiological changes, a central element of person-centred nursing.

Every cell in the body requires a constant supply of oxygen to undertake their metabolic function. In doing so, they produce carbon dioxide (a waste product) that must be removed. The respiratory system is therefore vital to how we function physically and is essential in maintaining **homeostasis**.

BODIE FAMILY CASE NOTES

PERSON-CENTRED CONTEXT: THE BODIE FAMILY

As a person-centred nurse, it is imperative that you understand that disorders of the respiratory system can have a significant impact on health-related quality of life; many conditions are long-term, progressive and can be life-limiting. The mature members of the family may start to notice changes in their respiratory systems. For example, Maud (age 77) and George (age 84) will have structural changes and may have reduced lung capacity that could impact on their activity levels as they may become short of breath more readily. They may also be more susceptible to respiratory tract infections such as **pneumonia** or bronchitis due to the decrease in the number of alveolar **macrophage**s; thus they receive the flu vaccine each year.

Derek Jones has asthma and needs to monitor his condition closely as exacerbations of his condition may occur; also due to his condition he needs to be careful that he does not develop chest infections. Danielle, as the youngest member of the family, may be susceptible to many respiratory tract infections as she does not yet have a fully developed immune system.

REVISE: A&P RECAP

Before reading this chapter, you may want to revise Chapter 10 in *Essentials of Anatomy and Physiology for Nursing Practice* (Boore et al., 2016). These videos may also help with revision. If you are using the eBook just click on the play button. Alternatively go to
https://study.sagepub.com/essentialpatho/videos

CONTROL OF RESPIRATION (7:48)

RESPIRATORY SYSTEM (15:47)

The principal function of the respiratory system is to ensure that the body extracts enough oxygen (O_2) from the atmosphere and that excess carbon dioxide (CO_2) is expelled (Boore et al., 2016). The process by which this happens consists of three distinct phases: pulmonary **ventilation**, external respiration and internal respiration (Boore et al., 2016). If for whatever reason these processes are interrupted, pulmonary function may become dysfunctional. There are a number of terms associated with pulmonary dysfunction presented in Table 14.1; it is essential that you understand these terms as they will be referred to frequently as we move through the rest of the chapter.

Table 14.1 Terms associated with pulmonary dysfunction

Term	Definition
Dyspnoea	Difficulty in breathing
Hyperventilation	Ventilation in excess of what is needed for normal elimination of CO_2
Hypoventilation	Decreased ventilation, unable to eliminate adequate amounts of CO_2
Hyperpnoea	Increase in rate and depth of breathing (normal during exercise)
Tachypnoea	Increased respiratory rate
Bradypnoea	Decreased respiratory rate
Orthopnoea	Difficulty in breathing when lying flat
Hypoxia	Reduction in tissue oxygenation
Hypoxaemia	Decreased levels of oxygen in the blood
Hypercapnia	Increased levels of carbon dioxide content of the blood
Acidosis (can be either respiratory or metabolic)	Clinical condition as a result of a low blood pH (<7.35)
Alkalosis (can be either respiratory or metabolic)	Clinical condition as a result of a high blood pH (>7.45)
Atelectasis	Lack of gas exchange within alveoli, due to alveolar collapse or fluid **consolidation**
Cyanosis	Bluish discolouration of skin and/or mucous membrane due to increased levels of deoxygenated blood in the small vessels
Ventilation	The amount of air that enters the alveoli
Perfusion	The amount of blood perfusing the capillaries around the alveoli. Also refers to the delivery of blood to capillary bed in systemic circulation
Ventilation/Perfusion (V/Q) mismatch	Abnormal ventilation/perfusion ratio, e.g. when areas of the lungs are better perfused by blood than they are ventilated (e.g. lack of alveoli), or better ventilated than perfused with blood (e.g. lack of blood supply to a well-ventilated lung with sufficient alveoli)
Cough	Protective reflex that helps clear the airways
Acute cough	Resolves within 2–3 weeks of onset of illness or with treatment
Chronic cough	Persistent, does not resolve with treatment
Haemoptysis	Coughing up of blood or bloody secretions
Minute volume	Volume of air/gas inhaled (inhaled minute volume) or exhaled (exhaled minute volume) from a person's lungs in one minute.

Let's have a look at a few of these terms in more detail and how/why they occur.

HYPOVENTILATION AND HYPERVENTILATION

Hypoventilation refers to inadequate **alveolar ventilation** compared to the metabolic demands of the body. It occurs when the minute volume is reduced and is caused by changes in the mechanics of breathing or due to changes in the neurological control of breathing. Hypoventilation results in the accumulation of CO_2 (rate of production exceeds rate of excretion), leading to hypercapnia that may result in respiratory acidosis and affect the normal functioning of many tissues throughout the body.

Hyperventilation refers to increased alveolar ventilation that exceeds the metabolic demands of the body. It occurs when the excretion rate of CO_2 exceeds that which is produced by cellular **metabolism**, leading to hypocapnia that may result in respiratory alkalosis that can also affect the normal functioning of body tissues.

HYPOXIA AND HYPOXAEMIA

Hypoxia refers to a reduction in tissue oxygenation and can result from pulmonary alterations, or other abnormalities that are not related to pulmonary function, e.g. decreased **cardiac output**. **Hypoxaemia** refers to a reduction of oxygen in arterial blood and is caused by pulmonary dysfunction and may lead to hypoxia. There are four types of hypoxia:

1. **Ischaemic hypoxia** – when blood supply to the tissue is inadequate
2. **Anaemic hypoxia** – when blood is unable to carry enough oxygen to the tissues
3. **Hypoxic hypoxia** – when inadequate amounts of oxygen enter the lungs
4. **Histotoxic hypoxia** – when cells are unable to effectively use the oxygen reaching them.

Hypoxaemia may result from a number of factors. Hypoventilation, caused by neurological or muscular disorders restricting chest expansion, can lead to retention of CO_2 and a decrease in O_2. Ventilation/perfusion mismatch; either low V/Q, i.e. inadequate ventilation of well perfused areas of the lungs causing shunting (e.g. atelectasis, asthma, **pulmonary oedema** or pneumonia) or high V/Q, i.e. poor perfusion of lung areas that are well ventilated (e.g. pulmonary **embolus**). Signs and symptoms of hypoxaemia include cyanosis, altered mental state and confusion, **tachycardia** and decreased urinary output (Table 14.2).

HYPERCAPNIA

Hypercapnia refers to an increase in the CO_2 content of arterial blood and is usually caused by disorders that lead to hypoventilation or V/Q mismatching. Increased CO_2 production may result from increased metabolic activity, e.g. exercise, a rise in body temperature, disorders of respiratory muscle function or disorders of neural control of respiration. Hypercapnia can have profound effects on the body and its ability to function normally (Table 14.2).

Table 14.2 Effects of hypoxia and hypercapnia on the body

Hypoxia	Hypercapnia
Energy production reduced – anaerobic metabolism produces less **ATP**	Respiratory system – chemoreceptors stimulated – increased respiratory rate
pH – Increased lactic acid production (↓ pH)	Cardiovascular system – vasodilation of blood vessels, tachycardia, **diaphoresis**
Cell – oedema due to ↑ Na^+ and ↓ H_2O inside cell, ↑ membrane permeability, ↓ mitochondrial activity	Nervous system – vasodilation of cerebral vessels – headache, disorientation, coma
Central nervous system – restlessness, agitation, uncoordinated movements, impaired judgement, delirium, coma	
Cardiovascular system – tachycardia, peripheral vasoconstriction (cool moist skin), increased BP. Later leads to **bradycardia** and hypotension	
GI system – reduced gut function – **constipation**, **anorexia**. Reduced liver function – reduced plasma protein production	
Muscles – reduced function – fatigue	
Pulmonary circulation – **pulmonary hypertension** (vessels constrict in response to hypoxia), **pulmonary oedema**	
Cyanosis – excessive concentration of deoxygenated **haemoglobin** (5g/100 ml blood)	

PHASES IN RESPIRATORY DISEASE

Respiratory disease can be categorised into three phases: respiratory impairment, respiratory insufficiency and **respiratory failure**.

- Phase I: Respiratory impairment
  - Normal healthy adult has a very large functional reserve
  - Although having respiratory impairment, they will have no symptoms
  - Reduced respiratory function only identified through respiratory function tests
- Phase II: Respiratory insufficiency
  - Person becomes aware of respiratory discomfort during exertion
  - Exercise tolerance becomes progressively impaired
  - Blood gases remain within normal limits
- Phase III: Respiratory failure
  - Person loses the ability to maintain normal arterial blood gases at rest
  - PO_2 is low at rest
  - PCO_2 is raised at rest

In your practice as a nurse, you will be caring for people across this range of phases and so it is important to consider the physiological impact and what phase of respiratory disease this person is in. This will influence how much care they may require as a result of the impact on their independence and it may also require you to consider if they and their family need end of life care.

INFECTIONS OF THE RESPIRATORY TRACT

Respiratory tract infections (RTIs) refer to an infectious disease that can affect any part of the respiratory tract; they tend to be discussed in terms of upper respiratory tract infections (URTIs), i.e. infection of nose, oropharynx or larynx, or lower respiratory tract infections (LRTIs), i.e. lower airways and lungs. Diao et al. (2018) state that RTIs comprise as many as 34 kinds of infections. Whilst any **pathogen** can cause infection of the respiratory tract, **viruses** are the most frequent cause. RTIs are the most common diseases in humans; Hull et al. (2013) found that adults usually experience one to three episodes of URTIs per year. Signs and symptoms of RTIs depend on the structure infected, the severity of the infection and the person's age and health status. They are usually relatively limited, consisting mainly of sore throat, fever, cough, productive cough, rhinorrhoea with or without pus, shortness of breath, headache and/or general discomfort, earache and/or tinnitus (Diao et al., 2018).

Upper respiratory tract infections

The upper respiratory tract consists of the nasal cavity, sinuses, pharynx and larynx. The upper respiratory tract is continuously exposed to potential pathogens which are usually dealt with by the mucociliary escalator and coughing. Despite these defence mechanisms, infections are fairly common and include the common cold, **influenza**, **rhinitis**, **sinusitis** and **otitis media**.

Common cold

The common cold is the most frequent cause of upper respiratory tract infection and is usually caused by one of a number of viruses, including rhinovirus, coronavirus, **adenovirus**, parainfluenza, influenza and respiratory syncytial types, which together have around 200 **serotypes** (Hemilä and Chalker, 2017). Due to the large number of causative agents, it would be impossible for a person to develop immunity to all, hence they can occur frequently throughout the year. The common cold is spread by respiratory droplets that can be directly inhaled or **acquired** through contamination of objects by infected secretions. It is highly contagious, especially during the first three days following onset of signs and symptoms; incubation may last up to five days. Signs and symptoms include nasal congestion, **rhinorrhoea**, sneezing, increased secretions and watery eyes. As the nose is congested, mouth breathing may be common and there may be a change in the person's voice. The person may also complain of a sore throat, headache, mild fever and general **malaise**.

Influenza

Influenza is a viral infection that can affect both the upper and lower respiratory tract. Influenza is caused by viruses that belong to the Orthomyxoviridae family; there are three different groups of influenza virus that cause disease in humans: type A (most prevalent), type B and type C. Regardless of the type, they mutate constantly, meaning that initiating an effective immune response for a long time is prevented. Influenza type A and type B can cause seasonal epidemics (World Health Organisation [WHO], 2018a) (see Go Deeper box). Influenza C is responsible for causing mild URTIs in adults and children. Influenza may cause three types of infection: uncomplicated URTI, viral pneumonia (discussed later) and respiratory viral infection that is then followed by a **bacterial** infection. Once a virus establishes an URTI, it then targets and destroys mucus secreting cells, ciliated **epithelium** and other epithelial cells, thereby leaving large spaces between the underlying basal cells, allowing extracellular fluid to escape, i.e. rhinorrhoea. If the infection spreads to the lower respiratory tract, it can cause diffuse shedding of bronchial and alveolar cells.

Signs and symptoms of flu are usually similar to those of other viral infections. Onset is abrupt with fever, chills, malaise, **myalgia**, headache, rhinorrhoea, non-productive cough and a sore throat.

GO DEEPER

Influenza subtypes/lineages

- *Influenza A* viruses can be categorised into subtypes based on two **glycoproteins**: haemagglutinin (H) that allows the virus to anchor to the epithelium of the respiratory tract and neuraminidase (N) that facilitates digestion of host secretions and release of viral particles from host cells (Labella and Merel, 2013). There are 16 variants of haemagglutinin (H1– H16) and nine variants of neuraminidase (N1–N9). For example, in the winter of 2017/2018 the main **strains** circulating were Influenza A(H3N2) and A(H1N1).
- *Influenza B* viruses are not classified into subtypes but can be broken down into lineages, e.g. B-Victoria lineage, B-Yamagata lineage.
- *Influenza C* virus does not present public health importance as it is detected less frequently and usually only causes mild infections (WHO, 2018a).

Epidemics (type A and type B) and pandemics (only caused by type A) result from the ability of viruses to mutate and develop new subtypes against which the population has no protection. Worldwide, these annual

epidemics are estimated to result in about 3–5 million cases of severe illness, and about 290,000 to 650,000 deaths (WHO, 2018a).

In winter 2017/2018, influenza A H3N2 caused widespread disease as it is a particularly virulent strain of influenza type A, mutating at a faster rate and being more dominant. This particular strain spreads with much more severity, is harder to vaccinate against and increases health complications.

Rhinitis

Rhinitis refers to **inflammation** of the nasal passages. B cells produce immunoglobulin (Ig) IgE against **allergens**. IgE binds to **mast cells** and causes degranulation with the release of **histamine**, **proteases**, **prostaglandins**, cysteinyl leukotrienes and **cytokines**. These inflammatory mediators cause the acute symptoms including sneezing, itch, rhinorrhoea and nasal congestion. Allergens presented to T cells cause the release of **interleukins** (IL), IL-4 and IL-13, that further stimulate B cells to release IL-5, IL-9 and granulocyte macrophage colony-stimulating factor. This results in a switch from a T-**helper cell** 1 (T_h1) response to a T_h2 response to activate **eosinophils**, **basophils**, **neutrophils** and T **lymphocytes**, leading to nasal obstruction, hyper-reactivity and **anosmia**.

Sinusitis

Sinusitis refers to inflammation/infection of the paranasal sinuses, caused mainly by *Streptococcus pneumoniae* and *Haemophilius influenzae*; occasionally it may be caused by a fungal infection. The infection leads to obstruction and prevents drainage of the paranasal sinuses into the nasal cavity. Pressure builds up inside the sinus cavity due to the accumulation of exudate, causing severe facial pain that can be confused with toothache (due to blockage of the maxillary sinus) or headache (blockage of the ethmoid sinus).

Otitis media

Otitis media, whilst technically not an infection of the respiratory tract, refers to infection of the middle ear seeded from an upper respiratory tract infection through the eustachian tube. *Streptococcus pneumoniae* and *Haemophilius influenzae* are the most common bacteria that cause otitis media. Infection causes inflammation of the middle ear **mucosa** and inflammatory exudate in the middle ear space. It usually presents with **otalgia** (ear pain) and hearing disturbances. If it does not resolve it can lead to tympanic membrane **perforation** and discharge.

Croup

Croup is a condition that affects the airways of babies and young children aged between 3 months and 3 years (NICE, 2017c). It is usually caused by viruses, and the parainfluenza virus accounts for 75% of cases (Johnson, 2014) with the remaining 25% caused by **adenoviruses**, respiratory syntical virus and influenza types A and B (Zoorob et al., 2011). Whilst the disease is well defined in children, it remains an uncommon cause of respiratory distress in adults (Patel et al,. 2018). However, it is believed that adult croup syndrome takes a more severe course than in children and may require definitive airway management and intensive care monitoring (Patel et al., 2018). Croup is characterised by abrupt onset

although it is usually preceded by upper respiratory tract infections. Symptoms are most often worse at night and can fluctuate rapidly depending on whether the child is calm or agitated (Bjornson and Johnson, 2013). As the larynx and subglottic area become inflamed, oedema and exudate can cause obstruction, leading to the characteristic barking cough, hoarse voice, inspiratory stridor and respiratory distress. Symptoms are usually short-lived, with about 60% of children having resolution of the barking cough within 48 hours; less than 2% of children have symptoms persisting for more than 5 nights (Bjornson and Johnson, 2013).

LOWER RESPIRATORY TRACT INFECTIONS

Pneumonia

Pneumonia refers to infection of the pulmonary parenchyma, i.e. bronchioles and alveoli. It may develop as an acute primary infection or may occur as a secondary infection due to another respiratory or systemic condition. In the majority of cases, organisms enter the lungs by inhalation, aspiration or **translocation** of resident bacteria that spread along the mucosa. Pneumonia can be classified in a number of ways based on the pathogen (typical or atypical) or the area of infection (lobar pneumonia or bronchopneumonia). Pneumonia may also be classified according to the setting in which they occur and referred to as community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), health care-associated pneumonia (HCAP) or ventilator-associated pneumonia (VAP) (Table 14.3).

Table 14.3 Classification of pneumonia

Pathogen	Typical – bacterial Atypical – variety of organisms including: *Mycoplasma pneumoniae*, viruses and **fungi**
Area of infection	Lobar pneumonia – confluent consolidation involving one or more lung lobes. Most often due to *Streptococcus pneumoniae* (the pneumococcus) Bronchopneumonia – widespread small patches usually affecting both lungs, especially lower lobes. Causative organisms more varied including: *Streptococcus pneumoniae*, *Haemophilus influenza*, *Staphylococcus*, anaerobes, coliforms
Setting	Community-acquired – describes infection caused by organisms (bacterial or viral) found in the community, begins outside the hospital or develops within 48 hours after admission to hospital Health care-associated – occurs in someone who has had a recent hospitalisation or resides in a care home, receiving chronic dialysis or home infusion therapy Hospital-acquired – nosocomial infection, LRTI not present on admission or develops 48 hours or more following admission Ventilator-associated – nosocomial infection that occurs in a person requiring mechanical ventilation 48 hours or more following intubation. May occur in 9–27% of ventilated patients (Kalanuria et al., 2014)

The areas of lung below the bronchi are usually sterile despite the entry of pathogens into the airways by inhalation or aspiration of nasopharyngeal secretions. A number of defence mechanisms exist to protect the lower respiratory tract and prevent infections; these include: cough reflex, **mucociliary escalator**, alveolar macrophages, **immunoglobulins** (Ig) (IgA and IgG) and **cell-mediated** and **humoral immunity**. Loss of one or more of these defence mechanisms predisposes the lower respiratory tract to colonisation and subsequent infection. Those that are critically ill or have a long-term condition are more susceptible to pneumonia as their epithelial cells are much more receptive to binding

pathogens that cause pneumonia. Colonisation of the tracheobronchial tree is also enhanced in those that smoke, have diabetes or **chronic bronchitis**.

If a pathogen gains entry to the lower respiratory tract, especially the alveolar region, local host defences (**antibodies**, complement and cytokines) prepare the bacteria for ingestion by alveolar macrophages. Macrophages present the **antigens** to the adaptive immune system, thereby activating both cell-mediated and humoral immunity with the release of T and B cells. Macrophages also release inflammatory cytokines, e.g. **tumour necrosis factor**-alpha, interleukin (IL)-1, while mast cells and **fibroblasts** release **chemokines** and chemotactic signals that result in neutrophil recruitment from the lungs into the alveoli. Intense cytokine-mediated inflammation ensues, resulting in the destruction of bronchial mucous membranes and alveolocapillary membranes which leads to vascular **engorgement**, oedema and the production of **fibrinopurulent** exudate which infiltrates the **acini** and terminal bronchioles. Dyspnoea, V/Q mismatching and hypoxaemia result. Consolidation of lung tissue may occur if certain bacteria release toxins that further damage the lung tissue.

Typical pneumonia (acute bacterial)

Typical pneumonia is caused by bacteria, with the most common causative agent being *Streptococcus pneumoniae* (the pneumococcus). This type of pneumonia is often referred to as pneumococcal pneumonia and is a frequent cause of lobar pneumonia. Bronchopneumonia may be caused by one or more species of microorganism; infection usually begins in the bronchial mucosa and spreads to adjacent alveoli. **Legionnaires' disease** is a type of pneumonia caused by *Legionella pneumophila* (gram-negative bacteria), which thrive in warm, moist environments, e.g. air conditioning units, spas. The infection can cause severe congestion and consolidation and necrosis of lung tissue that potentially may have fatal consequences. Signs and symptoms associated with typical pneumonia include: sudden onset with pyrexia and chills, fatigue, dyspnoea, tachypnoea, tachycardia, productive cough and pleuritic pain.

Atypical pneumonia

Atypical pneumonia, or primary atypical pneumonia, can be caused by either viral or mycoplasmic pathogens and is associated with a patchy involvement of the lung that is predominantly confined to the alveolar septum or **interstitium** (support tissue). The term atypical refers to the lack of consolidation, absence of alveolar exudate, production of moderate amounts of white sputum and a slightly elevated white blood cell count. The most common causative agents of atypical pneumonia are *Chlamydia pneumoniae, Mycoplasma pneumoniae* and *Legionella pueumophila* (Arnold et al., 2016) and it is common in older children and young adults. Viruses responsible for causing atypical pneumonia include influenza types A and B, respiratory syncytial virus, adenovirus, rhinovirus, rubella and varicella viruses (Gu et al., 2017). Pathogens responsible for atypical pneumonia cause initial destruction of ciliated epithelium of the distal airway cellular material and impair respiratory defences. In doing so they predispose the respiratory tract to secondary bacterial infections. Signs and symptoms associated with atypical pneumonia are usually vague but can include a non-productive cough (absence of exudate in alveoli), mild fever, malaise, myalgia, headache, hoarseness and a sore throat.

Tuberculosis

Tuberculosis (TB) is an infection caused by *Mycobacterium tuberculosis* (MTB) (an acid-fast bacilli), usually affecting the lungs but it may invade other body systems, e.g. skin (cutaneous TB), kidneys

(Fogel, 2015). It is highly contagious and spread is airborne by means of droplet nuclei that are harboured in the respiratory secretions of persons with active tuberculosis (Zuma et al., 2013). TB is the ninth leading cause of death worldwide and it is the leading cause of death from a single infectious agent (WHO, 2017). Cruz-Knight and Blake-Gumbs (2013) state that approximately one-third of the world's population is latently infected with MTB. Whilst the incidence of TB is dropping globally at a rate of approximately 2% annually, the burden remains high with over 6 million new cases being diagnosed annually (WHO, 2017). Drug-resistant TB remains a threat; of the new cases reported in 2016, 600,000 were resistant to rifampicin (the most effective first-line drug) and, alarmingly, 490,000 of these cases were multidrug resistant (MDR-TB) (WHO, 2017).

As previously stated, MTB is spread from person-to-person via airborne droplets. Salgame et al. (2015) identify that a specific, complex interplay between host and pathogen with the environment determines the outcome of MTB infection, resulting in one of three possible outcomes: cure, latency or active disease. The virulence of the strain, intensity of exposure, size of bacterial inoculum and host factors (e.g. age, comorbidities) can contribute to the possible outcomes (Salgame et al., 2015). The majority of people mount an effective response with successful inhibition of the growth of MTB and the bacteria becomes dormant and inactive, i.e. latent (Thillai et al., 2014). Immunocompetent latent individuals infected with MTB do not present symptoms and do not transmit the disease to others (Fogel, 2015). Risk groups and factors for the development of the disease are presented in Box 14.1.

Box 14.1 Risk groups and factors for the development of tuberculosis

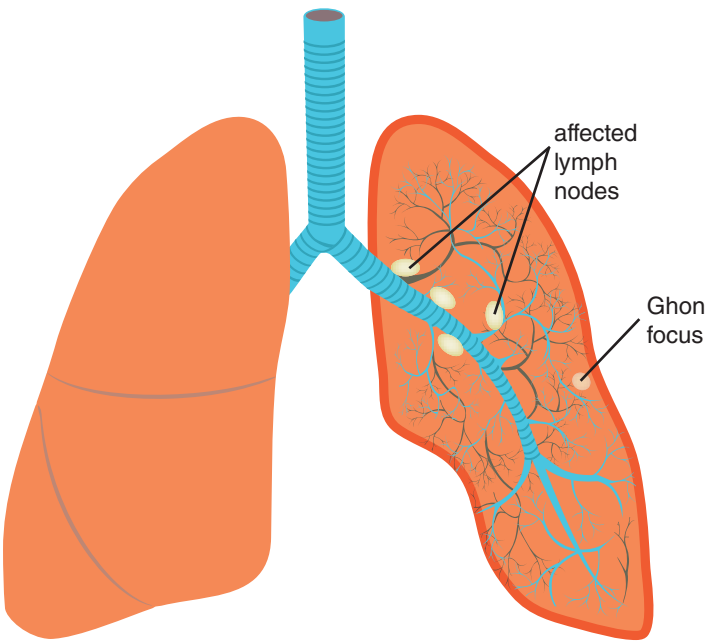
- Young adults – male > female
- People living in developing countries
- Poverty (higher level = higher risk)
- Health care workers who are exposed to disease on a frequent basis
- Those with compromised/weakened immune systems
- **Cancer**
- **Human immunodeficiency virus (HIV)**
- Smoking
- Host deficiency in IL-2-promoting T-helper 1 response (de Martino et al., 2014)
- Foreign-born individuals living in impoverished areas
- **Undernutrition**

Sources: Fogel, 2015; WHO, 2017

Once inhaled, MTB droplets pass down the bronchial tree and deposit in peripheral alveoli and cause non-specific pneumonitis (localised inflammation). Some MTB may migrate through the lymphatic system and lodge in the lymph nodes where they encounter lymphocytes and initiate an immune response. Activation of alveolar macrophages leads to bacilli being engulfed by **phagocytes**. Macrophages initiate a cell-mediated immune response and the infection is contained. Whilst the bacilli are phagocytosed and contained, they resist lysosomal killing and continue to multiply inside the alveolar macrophage. Macrophages degrade the bacilli and present the antigens to helper $CD4^+$ T lymphocytes. The sensitised T cells further stimulate the macrophages to increase the concentration of **lytic enzymes,** increasing the ability to destroy the bacilli. However, they also damage the lung tissue. In the immunocompetent person, this cell-mediated immune response leads to the development of a **granulomatous lesion** known as a **Ghon focus**. The Ghon focus contains tubercle bacilli, modified macrophages and other immune cells.

Infected tissue inside the Ghon focus dies and undergoes necrosis that subsequently produces a cheese-like material of dead cells known as caseous necrosis. Tubercle bacilli (free or inside macrophages) drain along lymph channels to the tracheobronchial lymph nodes of the affected lung and stimulate the formation of caseous **granulomas**. The primary lung lesion and lymph node granulomas are collectively known as the **Ghon complex** (Figure 14.1). As the Ghon complex heals it undergoes shrinkage, fibrous scarring and calcification. Tuberculosis may remain dormant for life; however, reactivation and progressive disease may occur when the immune system is compromised or impaired.

Signs and symptoms are not always initially apparent but may include: mild fever, cough with **purulent** sputum, fatigue and night sweats. As the disease progresses, dyspnoea, wheezing, **haemoptysis**, chest pain, weight loss and anorexia may become apparent.



Illustrated by Shaun Mercier © SAGE Publications

Figure 14.1 Ghon complex

Primary TB

Primary TB develops in previously unexposed, unsensitised people (Zuma et al., 2013). Most people with primary TB are asymptomatic and go on to develop latent TB whereby the cell-mediated response (T lymphocytes and macrophages) limits the spread as the organisms are surrounded by granulomas. In approximately 5% of people newly infected with MTB there will be an inadequate response that leads to progressive primary tuberculosis with the destruction of lung tissue and spread to multiple sites within the lung (Zuma et al., 2013). Most commonly affected are young children with immature immune systems, those with HIV infection or other **immunodeficiency** disorders, or those receiving immunosuppressive therapy.

Secondary TB

Secondary TB refers to the reinfection or reactivation of the disease in a person with some immunity. The tubercle ruptures and re-establishes an active infection, and bacteria can spread through the lungs via the

bronchioles. The disease tends initially to remain localised, often in apices of the lung. It tends to recur when there are impaired body defence mechanisms.

BRONCHIOLITIS

Bronchiolitis is the most common lower respiratory tract infection in the first year of life, affecting one in five children with 2–3% of these requiring hospitalisation (Ricci et al., 2015). It is caused by a range of viruses, including the respiratory syncytial virus, parainfluenza virus and adenoviruses (Meissner, 2016). However, **mycoplasmas** may also cause the disease. Children usually present with a **coryzal illness** (head cold, inflammation of nasal cavities) that progresses over 3–5 days to a troublesome cough, dyspnoea, tachypnoea, wheeze, crackles and difficulty feeding (Ricci et al., 2015). It is associated with an increased risk of chronic respiratory conditions such as asthma. However, it is unknown if it actually causes these conditions (NICE, 2017b).

The infection produces an inflammation and necrosis of the small bronchi and bronchioles accompanied by oedema, increased secretions and reflex **bronchospasm** that lead to obstruction (partial or complete). Partial obstruction of the lungs may cause hyperinflation and air trapping or alveolar collapse. In complete obstruction, air becomes trapped distal to the obstruction and may cause atelectasis or non-aeration, hypoxaemia and in severe cases hypercapnia.

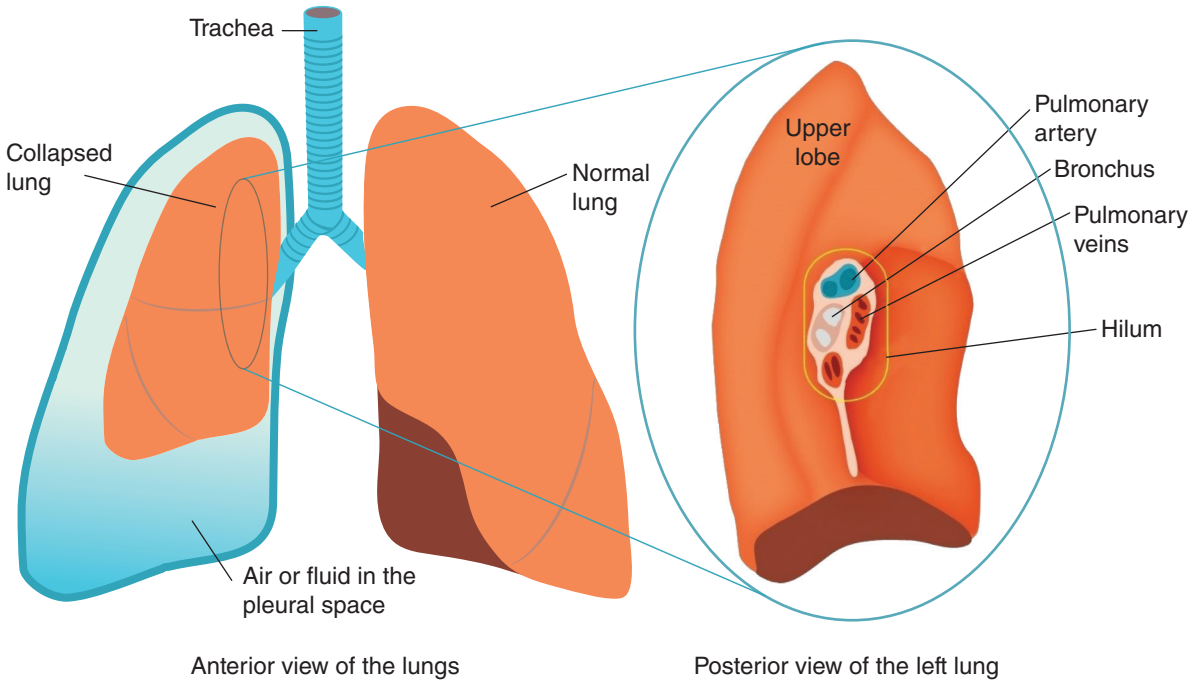
DISORDERS OF THE PLEURA

The pleura is a thin double-layered serous membrane that surrounds the lungs consisting of the parietal pleura (attached to the inside of the thoracic cavity) and the visceral pleura (attached to the surface of the lungs). Between the two layers is the pleural cavity, filled with pleural fluid that allows the layers to move freely over each other, preventing friction when breathing (Boore et al., 2016). The pleura and pleural fluid create a pressure gradient that assists with lung inflation. Anything that interferes with the pleura can have a negative impact on the ability to breathe properly and maintain effective gaseous exchange. The two disorders we are going to discuss in this chapter are **pneumothorax** and **pleural effusion**.

Pneumothorax

A pneumothorax refers to the presence of air in the pleural cavity caused by rupture of either the parietal or visceral pleura. Separation of the parietal and visceral pleural disrupts the negative pressure and changes the balance between elastic recoil forces of the lung and chest wall. A pneumothorax can cause either partial or complete collapse of the affected lung, which recoils towards the hilum (Figure 14.2). There are various types of pneumothorax: open/traumatic, closed/**spontaneous** and **tension**.

- *Spontaneous*: occurs when an air-filled bleb or blister on the surface of the lung ruptures (Weldon and Williams, 2012). Blebs are usually situated at the apices of the lungs. Following rupture of the bleb, atmospheric air from the airways enters the pleural cavity and changes the pressure gradient. Alveolar pressure is greater than pleural pressure so air flows from the alveoli to the pleural space; air takes up space, thereby restricting lung expansion and causing the lung to collapse. Spontaneous pneumothoraces can be further subdivided into primary and secondary (Weldon and Williams, 2012).



Illustrated by Shaun Mercier © SAGE Publications

Figure 14.2 Pneumothorax

- Primary spontaneous – spontaneous rupture of blebs that occur unexpectedly in healthy individuals (predominantly males) between the ages of 20 and 40 years. Tall, thin people are at higher risk as it is suggested that pleural pressure from top to bottom of the lung is greater and thus may contribute to the development of blebs (Weldon and Williams, 2012). Smoking is also a contributory factor as it is thought to cause inflammation of the small airways.
- Secondary spontaneous – occurs as a complication associated with underlying lung disease and tends to be more serious. Various types of lung disease may be associated with secondary spontaneous pneumothorax, including asthma, tuberculosis, cystic fibrosis and sarcoidosis.

- *Traumatic*: may be caused by either penetrating or non-penetrating chest injuries. The most common cause is fractured or dislocated ribs that subsequently puncture the pleura.
- *Tension*: occurs when intrapleural pressure exceeds atmospheric pressure (Walden and Williams, 2012). Air enters the pleural cavity on inhalation but cannot leave on exhalation, resulting in a rapid increase in pressure within the chest, making it a life-threatening condition. Due to the increased pressure, compression of the unaffected lung and mediastinal shift to the opposite side occurs, leading to compression of the vena cava. This reduces venous return to the heart and results in reduced cardiac output.

Signs and symptoms associated with a pneumothorax include **dyspnoea**, cough and chest pain. **Atelectasis** also manifests and there will be reduced air entry and breath sounds on the affected lung(s). There may also be unequal, asymmetrical chest rise and fall and mediastinal shift depending on the severity of pneumothorax; this may cause tracheal deviation. Over time, **hypoxia** results and initiates a sympathetic nervous system response, leading to tachycardia, pallor and anxiety; decreased venous return will lead to hypotension.

Pleural effusion

Pleural effusion refers to an abnormal collection of fluid in the pleural cavity (Saguil et al., 2014). Whilst a small amount of fluid is usually present to allow for lubrication of the pleural membrane, a pleural effusion occurs when there are large amounts of fluid in the pleural cavity. This excess fluid firstly increases the pressure within the pleural cavity and then causes separation of the pleural membranes. This prevents cohesion during inspiration, thereby preventing expansion of the lung, leading to atelectasis. Atelectasis on the affected side and shift of the mediastinal contents towards the unaffected lung limit expansion and gaseous exchange. Venous return in the inferior vena cava and cardiac filling become impaired due to increased pressure in the mediastinum when the pleural effusion is large. There are a number of types of pleural effusions that are characterised by the presence of substances in them: **hydrothorax** (serous fluid, transudative or exudative), **empyema** (pus), **chylothorax** (chyle) and **haemothorax** (blood) (Weldon and Williams, 2012):

- *Hydrothorax*: refers to the collection of serous fluid in the pleural cavity caused by increased **hydrostatic pressure** or decreased **osmotic pressure** in blood vessels, leading to a shift of fluid out of blood vessels into the potential space in the pleural cavity. May occur secondary to cardiac failure, liver or kidney disease.
- *Empyema*: refers to infection in the pleural cavity, resulting in pus (purulent fluid containing glucose, proteins, leukocytes and debris from dead cells and tissue) accumulation. It usually occurs as a result of infection, usually pneumonia.
- *Chylothorax*: refers to the presence of lymphatic fluid in the pleural space secondary to leakage from the thoracic duct or one of its main tributaries due to trauma, **malignant infiltration** that prevents the transport of chyle from thoracic duct to central circulation or inflammation.
- *Haemothorax*: refers to the presence of blood in the pleural cavity due to chest trauma, tumours, aortic **aneurysm** rupture or chest **surgery**.

Signs and symptoms associated with pleural effusion will vary according to the cause (Weldon and Williams, 2012). However, as previously noted, lung expansion on the affected side will be decreased proportionally to the amount of fluid collected in the pleural cavity. Dyspnoea is the most common symptom associated with it; the person may also complain of chest discomfort/pleural pain. There will also be decreased breath sounds on auscultation and dullness on percussion. If the person has an empyema, they may also present with fever, tachycardia and cough.

PULMONARY DISORDERS

Atelectasis

The term atelectasis is derived from the Greek words *ateles* and *ektasis*, which mean incomplete expansion or collapse resulting in reduced or absent gas exchange. Atelectasis may affect all or part of a lung. There are three different types of atelectasis: compression atelectasis, **absorption** atelectasis and surfactant impairment (Table 14.4). It may be present at birth (primary atelectasis) or develop later in life (acquired atelectasis).

Signs and symptoms associated with atelectasis include dyspnoea, **tachypnoea**, cyanosis, signs of hypoxaemia (e.g. altered **consciousness** levels), tachycardia, reduced chest expansion and absence of breath sounds on the affected side.

Obstructive lung disorders

This is a group of disorders caused by an obstruction or limitation to airflow characterised by a reduction in expiratory airflow and respiratory symptoms. The main disorders of obstructive lung disease are **asthma**, chronic bronchitis and **emphysema**.

Table 14.4 Different types of atelectasis

Type	Cause
Compression atelectasis	External pressure exerted by tumour, fluid or air in pleural space, or by abdominal distension, causing alveolar collapse
Absorption atelectasis	Removal of air from obstructed/hypoventilated alveoli, inhalation of: **anaesthetic** agents, concentrated O_2
Surfactant impairment	Decreased production or inactivation of surfactant due to premature birth, **acute respiratory distress syndrome (ARDS),** anaesthetics, mechanical ventilation

Bronchial asthma

Bronchial asthma is a chronic inflammatory disease and the most prevalent chronic respiratory disease. The World Health Organisation (WHO, 2018a) states that between 100 million and 150 million people worldwide suffer from asthma and this number continues to grow. Asthma is linked to genetic and environmental factors and it is classified as atopic/allergic (triggered by allergic **sensitisation**) or non-atopic/non-allergic. The Global Initiative for Asthma defines asthma as a disease characterised by chronic airway inflammation with a history of wheeze, shortness of breath, chest tightness and cough (GINA, 2018). This can be due to inflammation, oedema and mucus production (Papi et al., 2018).

Asthma is associated with the release of inflammatory mediators from mast cells in the airways and this leads to a response clinically manifested as expiratory wheeze, experience of chest tightness, dyspnoea, tachypnoea and cough. In atopic (allergic) asthma the inflammatory response is triggered by allergens and is often associated with other allergic conditions such as **eczema**, rhinitis or food allergy and a positive family history of the disease (Papi et al., 2018). Non-atopic (non-allergic) asthma occurs in people with no history of allergy and often develops in middle age. In both types, bronchospasm is triggered by exposure to a stimulant such as viral respiratory infection, smoke, exercise and cold air.

ACTIVITY 14.1: APPLY

Living with asthma

As a person-centred practitioner, it is important to understand the lived experience of asthma in order that you can support people in their illness. Watch the following video to help you gain some insight into that lived experience and reflect on how it may help you in your practice. If you are using the eBook just click on the play button. Alternatively go to
https://study.sagepub.com/essentialpatho/videos

ASTHMA (3:38)

Allergic (atopic) asthma

The allergic (atopic) form of asthma is associated with exposure to a stimulant, usually an allergen, that induces a type 1 **hypersensitivity** response (see Chapter 7). The mechanisms of response can be described in two distinct phases: the early phase and the late or delayed phase. During the early phase

response following antigen exposure to the bronchial mucosa, dendritic cells activate T-helper-2 cells to produce interleukins (ILs) IL-5, IL-4, IL-13.

IL-5 activates eosinophils and IL-4 and IL-13 stimulate B lymphocytes to produce immunoglobulin E (IgE) (Russell and Brightling, 2017). IL-13 also stimulates mucus production and eosinophil recruitment to the lung mucosa. IgE antibodies attach to the receptors on the mast cell surface, causing them to degranulate their contents. The inflammatory mediators histamine, **bradykinins**, interleukins, tumour necrosis factor, prostaglandins and **leukotrienes** are released, causing vasodilation and altered capillary permeability and resulting in mucosal oedema and smooth muscle contraction with subsequent bronchospasm and mucous secretion (Figure 14.3), narrowing the airways and obstructing airflow. Eosinophil products cause damage directly to the lung epithelial tissue and may also cause **bronchoconstriction** through the release of leukotrienes (Diver et al., 2018).

The late phase response occurs 4–8 hours after the early phase and involves the recruitment of more eosinophils, neutrophils and lymphocytes to the lung tissue, which increases and sustains the inflammatory response. Recurrent episodes of inflammation lead to injury to the epithelium and the formation of scar tissue (Kudo et al., 2013). Ciliated epithelial cells are damaged and mucous accumulates in the lumen of the airways. Long-term airway damage leads to airway remodelling that results in goblet cell **hyperplasia**, epithelial damage and cilia dysfunction with increased smooth muscle mass and increased vascularity. This leads to a thickening of the airway wall and narrowing of the airway lumen (Brightling et al., 2012). This, along with an increased production of mucus, can lead to smaller airways becoming completely blocked (Russell and Brightling, 2017).

Non-allergic (non-atopic) asthma

Asthma can be triggered by non-allergic stimulants, for example exercise, drug-induced or respiratory infection. Exercise can induce bronchoconstriction and is thought to be due to heat loss, **dehydration** and increased **osmolarity** of the respiratory mucosa, triggering bronchospasm (Smoliga et al., 2016). Drug-induced asthma is mainly associated with aspirin ingestion and can lead to bronchospasm, rhinorrhoea (when the nasal cavity is filled with large amounts of mucus), rash and itching. It is thought to involve abnormal pathways in prostaglandin metabolism and release of leukotrienes, causing bronchoconstriction (Rajan et al., 2015). Respiratory tract infection (RTI), particularly viral infection, causes epithelial damage and stimulates IgE antibodies against the virus (Wos et al., 2008). It has been suggested that there is an increased risk for asthma development associated with recurrent RTIs in childhood (Del Giacco et al., 2017). RTIs also increase hyper-responsiveness of the airways to other triggers. Airway hyper-responsiveness is a feature of asthma where airway smooth muscle is hypercontractile, resulting in airway narrowing. This can result from direct or indirect stimuli; the degree of hyper-responsiveness is determined by the number of mast cells affected (Diver et al., 2018).

Bronchoconstriction, inflammation and secretions lead to airway obstruction. Constriction of the smooth muscle in the walls of the airways narrows the lumen and increases resistance to airflow, particularly on expiration (Figure 14.4). Normally during expiration, the elastic recoil of the lungs decreases the diameter of the airways but air can still flow out. Where there is high airway resistance the airways collapse just before expiration, trapping air in the alveoli and causing hyperinflation; this leads to non-uniform ventilation. Alveolar gas pressure increases and perfusion decreases, leading to ventilation–perfusion (V/Q) mismatching. Hypoxaemia results. However, due to hyperventilation, CO_2 levels initially remain normal or may fall with associated respiratory alkalosis. Continued hyperinflation reduces the effectiveness of the respiratory muscles, leading to hypoventilation and reduced tidal volumes that subsequently result in systemic hypoxaemia, hypercapnia and respiratory acidosis.

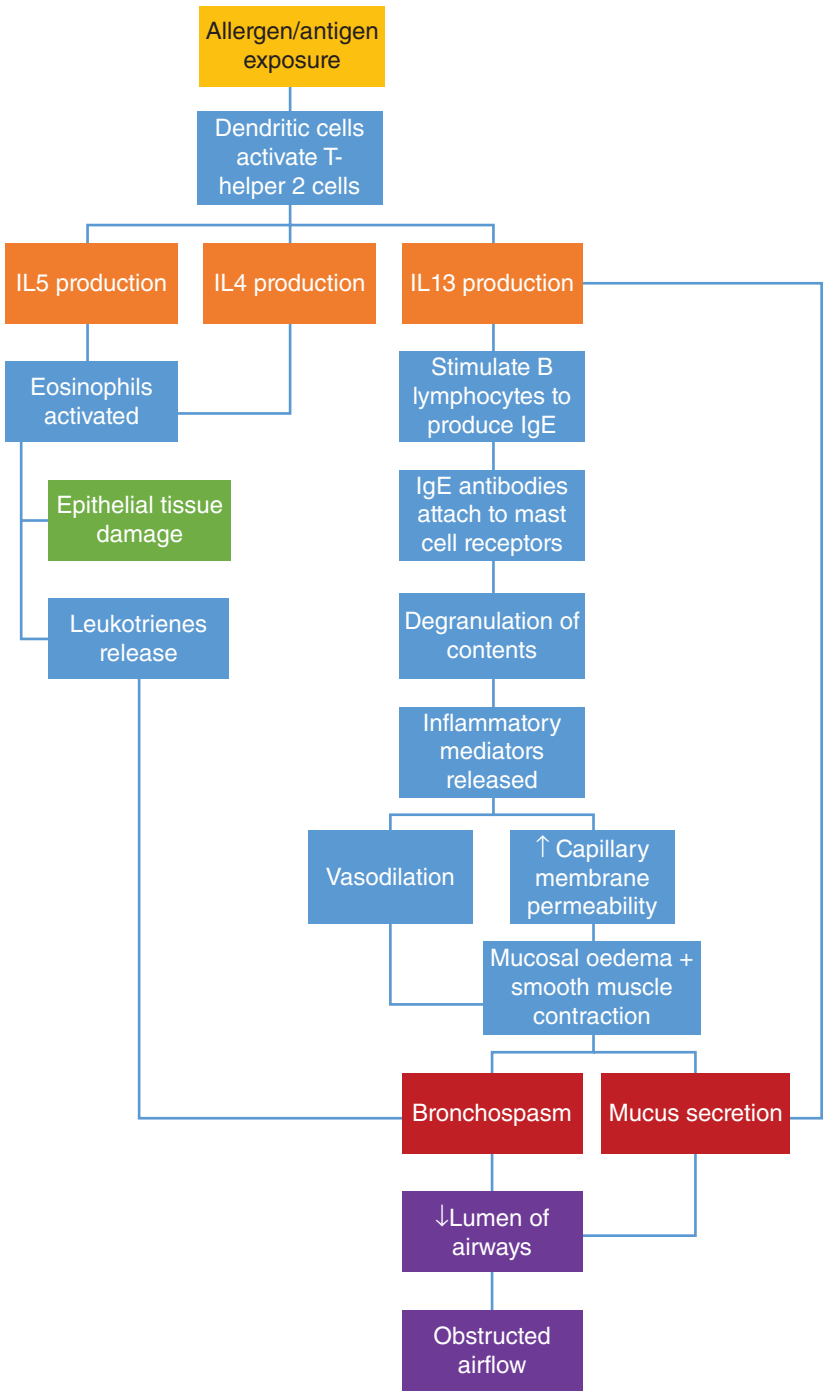
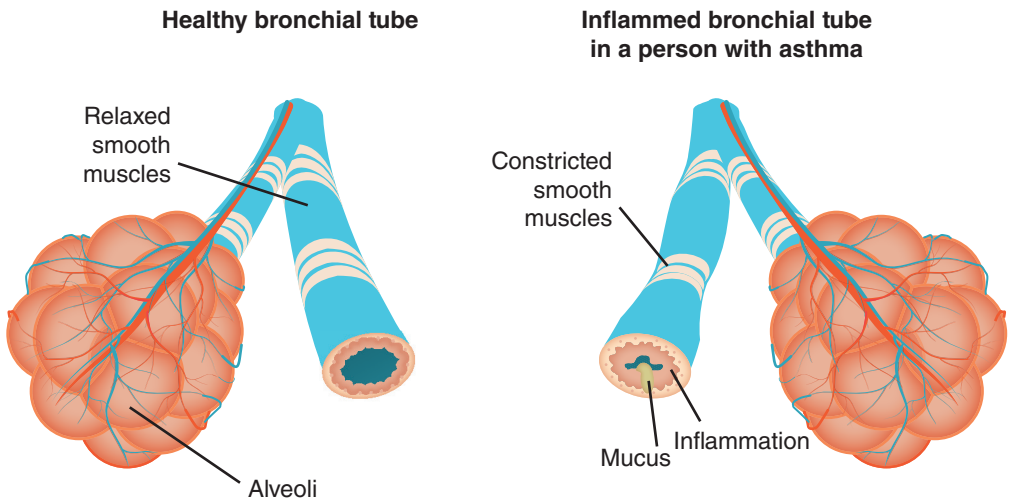


Figure 14.3 Pathophysiology of asthma



Illustrated by Shaun Mercier © SAGE Publications

Figure 14.4 Normal bronchial tube and the bronchial tube in asthma

APPLY

Asthma

Signs and symptoms

A person with asthma is often asymptomatic in between attacks and the severity of an attack will determine the physical effects. A mild attack shows signs of expiratory wheezing, dyspnoea, tachypnoea and the person may complain of chest tightness and fatigue. A more severe attack is associated with dyspnoea, use of the sternocleidomastoid and scalene accessory muscles, and inspiratory as well as expiratory wheeze. Oxygen saturations may fall below 90% and arterial blood gases indicate hypoxaemia and later hypercapnia.

Status asthmaticus occurs where bronchospasm has not responded to bronchodilators and or anti-inflammatory drugs. Hypoxaemia worsens, and hypercapnia leads to respiratory acidosis. The person may appear cyanotic and there may be very little airflow and ventilation, requiring emergency medical intervention and mechanical ventilation.

Diagnosis

Diagnosis is based on history, including family history of asthma or allergens, and history of recurrent episodes of cough and wheezing or shortness of breath. Pulmonary function tests are an important part of diagnosis and management, using spirometry. A forced expiratory volume test measures the amount of air that can be forcibly expired in one second (FEV_1) and peak expiratory flow rate (PEFR), measured in litres per second, is the fastest rate air can flow out on expiration. These tests provide an indication of expiration ability and airway obstruction. Forced vital capacity (FVC) is the amount of air exhaled forcefully and quickly after inhaling as much as you can. A FEV_1/FVC ratio of less than 70% is a positive test for obstructive airway disease.

Source: NICE, 2017a

Treatment

Self-management and education play a key role in the approach to asthma management. Avoidance of known triggers and risk factors should reduce the frequency and risk of asthmatic attacks. Pharmacological therapy needs to be monitored and adjusted to find the minimum effective dose for the individual. A short-acting inhaled beta-2 agonist is used to relax bronchial smooth muscle and is used in people with low risk for exacerbations and who have symptoms less than twice per month (GINA, 2018). A regular low-dose inhaled **corticosteroid** to reduce inflammation and improve symptom control is used in combination with the short-acting beta-2 agonist. A long-acting beta-2 agonist can be used where symptoms are not well controlled (GINA, 2018).

Severe or uncontrolled asthma is where there is poor symptom control and frequent severe exacerbations (Chung et al., 2014). IgE monoclonal antibodies have been used to treat moderate to severe allergic asthma (Olin and Wechsler, 2014). Omalizumab was the first monoclonal antibody used for severe asthma and it works by binding to IgE to prevent it from attaching to the receptor on the surface of the mast cell, basophils and dendritic cells (Diver et al., 2018).

APPLY

Asthma and long-term treatment

Referring back to the Bodie family, Derek Jones has had mild persistent asthma since childhood. Among children, asthma prevalence is higher in boys than girls and atopic asthma is common in adults with childhood onset asthma (Del Giacco et al., 2017). Derek is taking a beta-2 agonist and a low dose corticosteroid inhaler. This is considered standard treatment and should be effective in symptom control and reducing risk of exacerbations.

Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease (COPD) refers to a group of respiratory disorders that are characterised by persistent respiratory symptoms and airflow limitation due to abnormalities caused by exposure to noxious particles or gases (GOLD, 2016). It is a progressive disease and is associated with risk factors, in particular tobacco smoking, and exposure to respiratory irritants such as dust, chemicals and environmental pollution (Kim and Criner, 2013). COPD is the fourth leading cause of death in the world, accounting for 6% of all deaths globally. It is a major cause of **morbidity** and mortality and is in most cases a preventable disease (GBD [2015 Chronic Respiratory Disease Collaborators], 2017). There are two types of obstructive airway disease associated with COPD: emphysema, and chronic bronchitis. Whilst the two conditions have many similarities, they also display distinct differences. Table 14.5 identifies the characteristics of emphysema and chronic bronchitis.

Table 14.5 Characteristics of emphysema and chronic bronchitis

Feature	Emphysema	Chronic bronchitis
Health history	Generally healthy, but smoker	Recurrent chest infections Exacerbation of symptoms by irritants and cold air, smoker
Cough/sputum	Minor	Significant/copious, purulent
Physical examination and general appearance	Cachetic, history of weight loss and protein calorie **malnutrition**	Tendency towards **obesity**, cyanotic, polycythaemia, oedematous, distended neck veins
Dyspnoea	Slowly progressive	Variable, often late in illness
Breath sounds	Quiet or diminished	Scattered wheezing, ronchi, rales
Chest appearance	Increase in anteroposterior diameter, barrel chest, prominent accessory muscles of respiration, limited diaphragmatic excursion	Slight to marked increase in anteroposterior diameter, **pulmonary hypertension**
ABGs	Near normal, ↓PaO_2, normal or ↓$PaCO_2$, hypercapnia (late stages)	↓PaO_2, ↑$PaCO_2$
Chest X-ray	Hyperinflation, flat diaphragm, widened intercostal margins	Congested lung fields, cardiac enlargement

Chronic bronchitis

The Global Initiative for Chronic Obstructive Lung Disease defines chronic bronchitis as a persistent cough and sputum production for at least 3 months per year for two consecutive years (GOLD, 2016). Exposure to respiratory irritants such as tobacco smoke or acute and chronic respiratory infections causes airway inflammation and the overproduction of mucus by **goblet cells** and hypersecretion from increased degranulation by neutrophil-mediated elastase (Kim and Criner, 2013). There is difficulty in clearing mucus due to poor ciliary function and ineffective cough. This causes narrowing of the lumen of the airway and obstruction to airflow. Initially, the larger airways are affected but with disease **progression** all airways are involved.

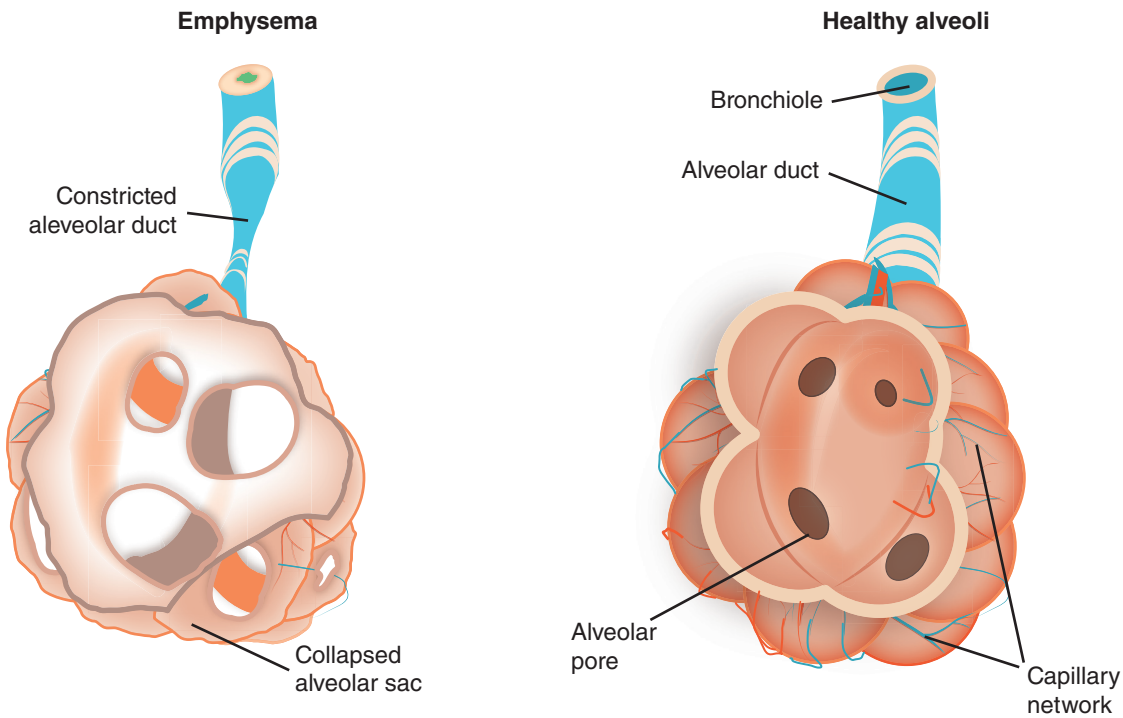
Inflammatory mechanisms responsible for mucus overproduction are attributed to Th1 cells (T-helper cells type 1) and specifically the subset Th17 cells (Kim and Criner, 2013). Interleukin 6 (IL-6) and interleukin 17 (IL-17) induce the production of proteins called mucins by lung epithelial cells which contribute to thick mucus production and the formation of mucus plugs, blocking the airway lumen. Impaired **mucociliary clearance** due to dysfunction and loss of cilia leads to the consolidation of mucus in the lungs.

Inflammatory infiltration of neutrophils, lymphocytes and macrophages in the bronchial wall leads to oedema of the bronchial mucosa and eventually fibrosis. These changes extend to the alveoli and further contribute to airway obstruction. Bacterial and viral infections are common and lead to exacerbations of COPD and amplification of alveolar injury (Tuder and Petrache, 2012). The narrowed airways increase resistance to airflow and cause obstruction, resulting in ventilation–perfusion mismatch with hypoxaemia and hypercapnia. Pulmonary blood vessels constrict in response to hypoxaemia, leading to pulmonary hypertension (Portillo et al., 2015) which can eventually lead to right-sided **heart failure**.

The classic signs of chronic bronchitis are a productive cough and prolonged expiration. Dyspnoea occurs late in the disease progression and cyanosis is often present as a result of hypoxaemia. The person usually has a history of smoking.

Emphysema

Emphysema is an obstructive airway disease characterised by destructive changes of the alveolar walls and irreversible enlargement of the alveolar sacs with loss of surface area for gas exchange (Tuder and Petrache, 2012) (Figure 14.5). The main characteristic of emphysema is the destruction of lung tissue rather than mucus production and inflammation as in chronic bronchitis. Abnormal, permanent enlargement of gas-exchange airways accompanied by destruction of alveolar walls without obvious fibrosis of the small airways contributes to airflow obstruction.



Illustrated by Shaun Mercier © SAGE Publications

Figure 14.5 Structural alveolar changes in emphysema

The distribution of damage to terminal respiratory units (acini) within the respiratory lobule and the extent of alveolar wall damage are used as a basis for the classification of emphysema. **Centriacinar** and **panacinar** emphysema are the most common forms of emphysema:

- *Centriacinar emphysema*: refers to the central or proximal parts of the acini and is associated with smokers. It is often seen in COPD.
- *Panacinar emphysema*: involves the acini at the terminal alveoli and is associated with alpha(α)-1-antitrypsin deficiency, an **autosomal recessive** inherited disorder. This enzyme inhibits the action of **proteolytic enzymes** released by neutrophils during inflammation. Absence of alpha-1-antitrypsin increases the risk of developing emphysema (Baraldo et al., 2015), particularly if the person smokes, as proteolytic enzymes are not inhibited and contribute to the damage of acini.

Prolonged exposure to a respiratory irritant such as tobacco smoke stimulates the inflammatory response and infiltration of inflammatory cells such as neutrophils and inflammatory mediators (i.e. leukotrienes, IL-8 and tumour necrosis factor [TNF]) in the lung tissue (Goldklang and Stockley, 2016). Proteases (enzymes that break down proteins) are released and there is inadequate production of protective antiproteases to counteract the action of the proteases, resulting in the breakdown of **elastin** and destruction of alveolar walls.

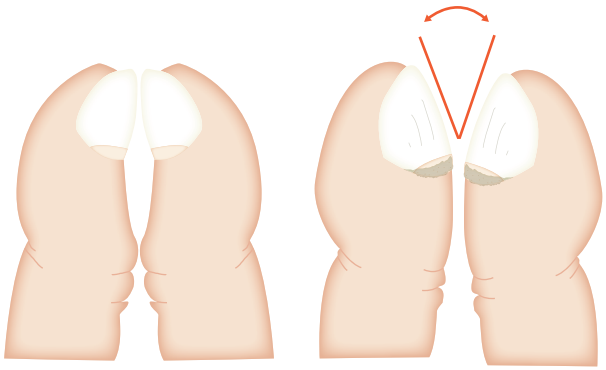
The destruction of alveoli results in large air spaces known as **bullae**; these are not effective in gaseous exchange, leading to ventilation–perfusion mismatch and hypoxia. The loss of the elastic recoil makes expiration difficult and leads to air-trapping in the alveoli (Gelb et al., 2015). This causes hyperexpansion of the chest and increases the work of breathing. Destruction of pulmonary capillaries leads to pulmonary hypertension and **cor pulmonale** (enlargement of the right side of the heart secondary to lungs or pulmonary blood vessel disease) with right-sided heart failure.

People with emphysema have a history of increasing dyspnoea, particularly on exertion. Use of accessory muscles is evident and expiration is prolonged through pursed lips in an effort to exhale as much air as possible before the alveoli and small airways collapse. They may or may not have a cough and a wheeze. Hyperinflation of the lungs produces an increase in the anteroposterior dimensions of the chest, resulting in a barrel-shaped chest typical of a person with emphysema which further contributes to dyspnoea and activity limitation (Langer et al., 2014). The person with emphysema will often have a history of smoking.

Bronchiectasis

Bronchiectasis is characterised by the permanent dilation of the bronchi caused by destruction of the bronchial wall and elastic supporting tissue. There may be a genetic predisposition, or it may occur in conjunction with another respiratory disease such as cystic fibrosis and tuberculosis and a compromised host defence to infection (King, 2018). Bronchiectasis is associated with recurrent infection of the lower respiratory tract, which leads to a persistent inflammatory response and permanent dilation of the medium-sized bronchi and bronchioles (Chen et al., 2018). Chronic inflammation causes destruction of the central bronchial wall with collapse of the peripheral bronchi and bronchioles. Loss of ciliated columnar epithelium and production of copious secretions lead to obstruction of airflow (Pasteur et al., 2010). The microorganisms that cause infection in bronchiectasis are present in the **microbiome** of the upper respiratory tract and include *Streptococcus pneumoniae, Haemophilus influenzae* and *Pseudomonas aeruginosa* (King, 2018).

A chronic productive cough with copious foul-smelling sputum is characteristic of bronchiectasis as a result of these pathophysiological changes. The person may have a fever, dyspnoea, wheezing and haemoptysis. Systemic manifestations include night sweats, **anaemia** and weight loss (due to the increased work of breathing and associated energy expenditure). In severe cases, clubbing may be present in the fingertips. Clubbing is enlargement of the distal segment of the digit (fingers or toes). It is thought that **vascular endothelial growth factor (VEGF)** (a platelet-derived factor) is an important component in its development (Rajagopalan and Schwartz, 2018). Hypoxia stimulates the release of VEGF that induces vascular hyperplasia, oedema and **proliferation** of fibroblasts/**osteoblasts** at a peripheral level in the nail (Rajagopalan and Schwartz, 2018). Large **megakaryocyte** fragments enter the systemic circulation and affect distal sites, releasing growth factors including VEGF. Platelets in the vasculature of the fingertips release platelet-derived growth factor that subsequently stimulates growth, increased vascular permeability and monocyte and neutrophil **chemotaxis**, leading to the proliferation of vascular smooth muscle cells and fibroblasts (Figure 14.6). It is associated with disorders such as bronchiectasis and **cystic fibrosis** and the severity of clubbing reflects the severity of the respiratory disease.



Illustrated by Shaun Mercier © SAGE Publications

Figure 14.6 Finger clubbing

Cystic Fibrosis (CF)

Cystic fibrosis is an inherited autosomal recessive disorder of the exocrine glands and is a major cause of severe respiratory disease in children and young adults. It affects 70,000 people worldwide and improved survival has led to increasing numbers reaching adulthood, with average survival to 40 years (Elborn et al., 2016).

Cystic fibrosis is a genetic disorder arising from a **mutation** on the cystic fibrosis transmembrane conductance regulator (*CFTCR*) gene on **chromosome** 7, resulting in a defective CFTCR protein (Stolz et al., 2015). This protein normally functions as a chloride channel in the epithelial cells lining the airways, the bile duct, the pancreas and the vas deferens. The defective protein means that chloride transport is impaired and both secretion and reabsorption can be affected. In the lung, the transport of chloride into the airway lumen is impaired which leads to increased absorption of sodium and water into the circulation, resulting in the secretion of thick tenacious mucus and dehydration of the mucociliary layer with a subsequent reduction in ciliary mobility and an ineffective clearing of mucus. The build-up of mucus obstructs the airways and provides a medium for recurrent pulmonary infection. Neutrophils release tissue-damaging proteases and oxidants that induce airway cells to destroy immunoglobulin G (IgG) and produce interleukin 8 (IL-8), which attracts more neutrophils and stimulates mucus secretion. Airway obstruction from mucus plugs and chronic inflammation and infection results in respiratory signs and symptoms.

Respiratory symptoms of CF include a persistent cough and the production of thick sputum and recurrent respiratory infections. Dyspnoea, tachypnoea and wheeze may be present. Over time, structural changes in the bronchial wall lead to bronchiectasis, and later signs of barrel chest and digital clubbing may be present. Chronic recurrent infection is common and microorganisms such as *Staphylococcus aureus* and *Haemophilus influenzae* are common in younger children (King, 2018). *Pseudomonas aeruginosa* colonises the lungs and leads to a decline in lung function (Harun et al., 2016).

Other manifestations of CF result from the impaired chloride transport in the sweat glands and the exocrine glands of the pancreas. In the sweat glands, the reabsorption of chloride and the subsequent reabsorption of sodium into the ducts of the glands fail, leading to a high concentration of sodium chloride in the sweat of the person with CF. The pancreatic and biliary ducts are affected by impaired sodium, chloride and potassium resorption, resulting in thick mucus production which blocks the pancreatic ducts. This in turn blocks the flow of digestive enzymes, leading to **malabsorption** of proteins, fats, carbohydrates and vitamins. Degenerative and fibrotic changes occur in the pancreas and gastrointestinal tract and diabetes can develop from the destruction of beta cells in the pancreas.

Diagnosis is based on clinical signs and diagnostic tests. Newborn screening includes a sweat chloride test to detect sodium and chloride levels in the sweat in excess of 60 mEq/l and blood tests for **immunoreactive trypsinogen** (IRT) (Farrell et al., 2017). IRT is a pancreatic enzyme precursor and it is elevated in infants and children with CF. Genetic testing for mutations in the *CFTR* gene can also be carried out (Farrell et al., 2017).

Interstitial lung disease

Interstitial lung disease (ILD) refers to a group of diffuse parenchymal lung disorders associated with substantial morbidity and mortality (Antoniou et al., 2014). They exert their effects on the **collagen** and elastic **connective tissue** found in the interstitium of the alveolar walls (Behr, 2012). ILD may occur in isolation or it may coexist alongside systemic disease (Behr, 2012); diminished lung compliance resulting in 'stiff' lungs that are difficult to inflate is the definitive hallmark of the condition. Increased work of breathing ensues as greater pressures need to be generated to inflate the lungs. Impaired gas exchange and hypoxaemia result due to damage of the alveolar epithelium and interstitial vasculature. As the disease progresses, respiratory failure may develop and may be associated with pulmonary hypertension or cor pulmonale.

ILD is initiated by some form of injury to the alveolar epithelium that causes an inflammatory response involving both the alveoli and the interstitium. Persistent injury leads to an accumulation of inflammatory and immune cells that cause damage to the lung tissue and development of fibrous scar tissue. Further development of fibrosis occurs as alveolar macrophages secrete a range of fibrogenic factors (e.g. fibroblast growth factor, platelet-derived growth factor) that attract fibroblasts and encourage their multiplication. Destruction of type I alveolar cells alongside an increase in type II alveolar cells chemotactically attracts further macrophages, cytokines and growth factors that further contribute to fibrotic changes.

Two of the most common ILDs are **idiopathic pulmonary fibrosis** (IPF) and sarcoidosis, therefore we will discuss both these disorders as they are frequently encountered in the people we care for.

Idiopathic pulmonary fibrosis

Idiopathic pulmonary fibrosis (IPF) is the most common disorder diagnosed among people with ILD; Antoniou et al. (2014) report that it is the most lethal disorder amongst ILDs. IPF is a chronic, progressive ILD of unknown aetiology that is difficult to diagnose and usually requires collaborative expertise to do so (NICE, 2017d). NICE (2017d) identifies clinical features that should be considered so that an early diagnosis can be made (Box 14.2). Two-thirds of those affected are people over the age of 60 years at the time of presentation. It affects men more than women. Risk factors for the disease include smoking and some occupations (e.g. farming, hairdressing, stone cutting and metal cutting) (Behr, 2012).

Box 14.2 Clinical features of IPF

- Age over 45 years
- Persistent breathlessness on exertion
- Persistent cough
- Bilateral inspiratory crackles when listening to the chest
- Clubbing of the fingers
- Normal spirometry or impaired spirometry, usually with a restrictive pattern but sometimes with an obstructive pattern

People presenting with IPF experience symptoms of breathlessness/dyspnoea initially on exertion and a cough (productive or non-productive); over time they will develop decreased lung function, cyanosis and cor pulmonale and have a reduced quality of life and ultimately death.

The rate of disease progression can vary greatly from person to person; the median survival time of someone with IPF is approximately 3 years from time of diagnosis, however 20% of people may live for more than 5 years (NICE, 2017d). Meyer (2014) acknowledges that ILD with extensive fibrosis is difficult to treat but appropriate therapies, including immunosuppressive anti-inflammatory therapies, oxygen therapy and pulmonary rehabilitation, can have a positive impact on quality of life and symptom palliation.

ACTIVITY 14.2: APPLY

Living with pulmonary fibrosis

As a person-centred practitioner, it is important to understand the lived experience of pulmonary fibrosis in order that you can support people in their illness. Watch the following video to help you gain some insight into that lived experience and reflect on how it may help you in your practice. If you are using the eBook just click on the play button. Alternatively go to **https://study.sagepub.com/essentialpatho/videos**

INTERSTITIAL PULMONARY FIBROSIS (1:53)

Sarcoidosis

Sarcoidosis is a systemic granulomatous disease process that may impact on any organ (in particular the lung) and can mimic other disease processes, especially malignancy or infection, making it difficult to diagnose (Parker et al., 2016). The disease usually affects people younger than 40 years but can occur in older people, affecting more females than males. The aetiology of sarcoidosis remains unclear. However, it is thought it may be linked to defective **human leucocyte antigen (HLA)** genes located in the **major histocompatibility complex (MHC)** (Baughman et al., 2011). The pathogenesis of sarcoidosis seems to involve the interplay of antigen, HLA class II molecules and T-cell receptors, with specific combinations of these three facets required for sarcoidosis to develop (Baughman et al., 2011). Sarcoidosis most likely requires exposure to one or more exogenous antigens. Infectious agents have long been suspected as possible causes of sarcoidosis; although it is unclear at present what these are specifically, it is thought that mycobacteria or *Propionibacterium acnes* may contribute to the disease (Baughman et al., 2011). Baughman et al. (2011) believe that the triggering antigen may vary depending on ethnicity, geographic location and individual genetic background.

The immune response is focused on the alveoli and is characterised by chronic inflammation, starting with polarisation of T lymphocytes to a Th1 phenotype, followed by cellular recruitment, especially macrophages and lymphocytes, that multiply and differentiate with the subsequent formation of the sarcoid granulomas (Baughman et al., 2011). The sarcoid granulomas do not show evidence of necrosis, however Chen et al. (2010) demonstrated that granulomas in sarcoidosis are characterised by extensive deposition of **serum amyloid**, a protein capable of starting an immune response and triggering cytokine release.

Signs and symptoms are variable, progression of the disease is unpredictable and any organ can be affected although mostly lungs, eyes and skin are involved. People may present with respiratory symptoms such as dyspnoea, non-productive cough and chest pain. They may also complain of fever, diaphoresis, anorexia, weight loss, fatigue and myalgia. The presence of skin plaques and **papules** is noted when there is skin

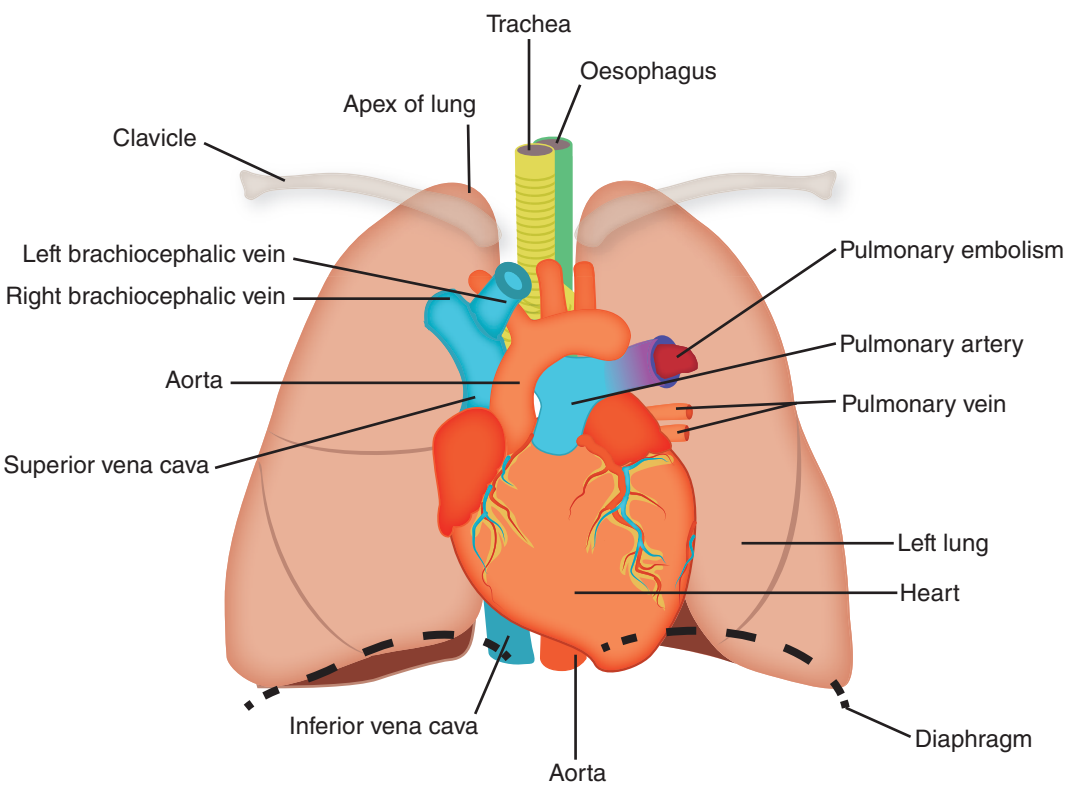
involvement; involvement of the eyes leads to inflammation of the middle layer of the eye, i.e. **uveitis**. The person may experience periods of progressive chronicity, activity interspersed with periods of **remission**.

DISORDERS OF PULMONARY CIRCULATION

Disruption to blood flow through the lungs can be caused by the occlusion of blood vessels, increased pulmonary vascular resistance and destruction of the vascular bed that can lead to ventilation/perfusion mismatching. The effects of disrupted blood flow can range from mildly dysfunctional to severe and life-threatening. Two major problems associated with disruption in pulmonary blood flow are **pulmonary embolism** and pulmonary hypertension, both of which will be discussed.

Pulmonary embolism

Pulmonary embolism (PE) occurs when a blood-borne substance lodges in a branch of the pulmonary artery, occluding pulmonary vasculature (Figure 14.7). PE can originate from numerous sources, including **deep vein thrombosis** (DVT) (commonly in the lower extremities), tumours, fat (e.g. from a **fracture**), amniotic fluid, foreign bodies, air and **sepsis** (NICE, 2018). The most common source of PE is DVT; thrombus formation in the venous system occurs as a result of venous stasis, trauma (endothelial injury) and hypercoagulability. Collectively, these factors are known as Virchow's triad (Merli et al., 2018). Risk factors for the development of PE are presented in Table 14.6.



Illustrated by Shaun Mercier © SAGE Publications

Figure 14.7 Pulmonary embolism

Table 14.6 Risk factors for the development of pulmonary embolism

Stasis of blood flow	Prolonged immobilisation Long aeroplane or other journeys Diagnosis of DVT Varicose veins
Endothelial injury	Surgery within last 2 months Fractures Hypertension Contact with substances that promote coagulation: e.g. implants, medical devices, cell membranes (platelets, monocytes in chronic inflammation)
Hypercoagulability	Advancing age Obesity Malignancy Genetic factors: factor V Leiden, prothrombin gene mutations, inherited coagulation disorders Hormones: pregnancy, use of oral contraceptive pill, hormone replacement therapy

In PE, the lung tissue is ventilated but not perfused, causing a V/Q mismatch that creates intrapulmonary dead space, resulting in impaired gas exchange and loss of alveolar surfactant. Over a period of several hours the alveoli collapse, resulting in worsening hypoxaemia. There is a reduction in blood flow to a cross-sectional area of the pulmonary bed that leads to the elevation of pulmonary arterial pressure and decreased cardiac output. The affected area of the lung is no longer perfused and may infarct, although this only happens on rare occasions as oxygen continues to be supplied by bronchial circulation and the airways (Merli et al., 2018).

Signs and symptoms of PE depend on the size and location of the obstruction. If the embolus is small and lodged in peripheries of the pulmonary artery, it may go unnoticed and be clinically silent, particularly in the elderly or acutely ill. If the embolus is moderate in size, the person may complain of chest pain, dyspnoea and a sense of apprehension. In some cases, they may present with haemoptysis or **syncope**. Persons with a large embolus usually present with a sudden collapse or crushing substernal chest pain; they may be cyanotic, tachycardic, hypotensive and diaphoretic; they may also have distension of the jugular vein. PEs are potentially life-threatening if they completely occlude the pulmonary vasculature as this can lead to right ventricular failure, cardiac arrest and ultimately death.

Pulmonary hypertension

Pulmonary hypertension is defined as an increase in mean pulmonary arterial pressure (PAPm) greater than 25 mmHg at rest as assessed by right heart catheterisation (Galiè et al., 2016). It is a relatively common complication of chronic obstructive pulmonary disease and diffuse pulmonary lung disease (including ILD) that may have serious implications for the function of the right ventricle (Tseng et al., 2018). Pulmonary hypertension causes profound functional limitations and results in a poor quality of life (Babu et al., 2016). It can be categorised into five groups (Galiè et al., 2016):

1. Pulmonary arterial hypertension
2. Pulmonary hypertension due to left heart disease

3. Pulmonary hypertension due to lung disease with or without hypoxia
4. Chronic thromboembolic pulmonary hypertension
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms.

ACTIVITY 14.3: GO DEEPER

Classification of pulmonary hypertension

To find out more about the five groups of pulmonary hypertension, read the 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. The article is openly available online but if you are using the eBook just click on the icon to access it.

ARTICLE: PULMONARY HYPERTENSION

The pathophysiology of pulmonary hypertension focuses on endothelial dysfunction and the interplay between the overproduction of powerful vasoconstrictors (e.g. thromboxane, endothelin) and the underproduction of the vasodilators (e.g. prostacyclin and **nitric oxide**). Remodelling (fibrosis and thickening) of the vessel walls occurs due to the release of growth vascular factors and subsequent narrowing of the lumen and abnormal vasoconstriction (Gao and Raj, 2017). Resistance to pulmonary blood flow ensues, thereby increasing pressure within the pulmonary arteries and right ventricle; there is a reduction in lung volumes and gas exchange is impaired. Right ventricular workload is increased as pressure and resistance continue to rise, resulting in right ventricular **hypertrophy** followed by right-sided heart failure.

Signs and symptoms of pulmonary hypertension are non-specific and are mainly related to the progression of right-sided heart failure (Galiè et al., 2016). Initially symptoms are induced by exertion and include dyspnoea, shortness of breath, fatigue, weakness, **angina** and syncope. On occasion, the person may present with a dry cough and exercise-induced **nausea** and **vomiting** (Galiè et al., 2016). As the disease progresses and reaches advanced stages, symptoms begin to occur at rest, with increased right ventricle dysfunction, abdominal distension and ankle oedema more likely to develop.

ACUTE RESPIRATORY DISORDERS

Acute respiratory disorders refer to disruptions in gaseous exchange that are life-threatening with a high morbidity and mortality rate. Acute respiratory disorders include **acute lung injury (ALI)**, acute respiratory distress syndrome (ARDS) and acute respiratory failure.

Acute lung injury and acute respiratory distress syndrome

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are manifestations of an inflammatory response of the lung to an insult either directly or indirectly (Ragaller and Richter, 2010). ALI and ARDS are characterised by severe hypoxaemia, hypercapnia, diffuse infiltrate on chest X-ray and substantial reduction in lung compliance. ALI can be defined as an acute lung disease with bilateral pulmonary infiltrate consistent with oedema and with no evidence of left atrial hypertension (Ragaller and Richter, 2010).

ARDS can be defined as an acute inflammatory lung injury associated with increased pulmonary vascular permeability, increased lung weight and loss of aerated tissue (Bellani et al., 2016). The conditions are differentiated by the difference in the extent of hypoxaemia determined by the ratio of partial pressure of oxygen in arterial blood (PaO_2) to the fraction of inspired oxygen (FiO_2) (Saguil and Fargo, 2012). ALI and ARDS can be caused by a variety of insults, including aspiration of gastric contents, trauma, sepsis, **acute pancreatitis**, **disseminated intravascular coagulation** and reactions to drugs/toxins.

The pathophysiology of ALI and ARDS is unclear although both local and systemic inflammatory responses occur. Mattihay et al. (2012) suggest that dysregulation of the inflammatory response, the accumulation of neutrophils, uncontrolled activation of coagulation pathways and altered permeability of the endothelium and disruption of endothelial barriers play a role in their development. Activation and migration of neutrophils across the alveolar epithelial surfaces result in the release of cytokines, proteases and **reactive oxygen species** that cause increased permeability and damage to alveolar type I and type II cells. Increased permeability allows the movement of fluid, plasma protein and blood cells from the vascular compartment to move into the interstitium and alveoli of the lung. Pulmonary oedema, hyaline membrane formation and the loss of alveolar surfactant decrease lung compliance, increasing intrapulmonary shunting of blood (V/Q mismatching), impairing gas exchange and resulting in hypoxaemia. At the bedside, ALI and ARDS culminate in life-threatening hypoxia, hypercapnia, acidosis and pulmonary hypertension, and require a fast and goal-oriented therapy without further lung damage (Ragaller and Richter, 2010).

Acute respiratory failure

Respiratory failure refers to the failure of the respiratory system to oxygenate the body or to eliminate carbon dioxide from the body. It may be due to acute disorders or trauma or can develop as a result of the course of a chronic disease. Respiratory failure is divided into two types: hypoxaemic respiratory failure (type I) and hypercapnic/hypoxaemic respiratory failure (type II) (Saguil and Fargo, 2012).

- *Type I (hypoxaemic)*: characterised by low O_2 and normal or low PCO_2, often due to a dysfunction of gaseous exchange. Two major factors contribute to a decrease in oxygen level: V/Q mismatching and impaired diffusion. V/Q mismatching occurs when areas of the lungs are perfused but not ventilated, or ventilated but not perfused. This could be due to hypoventilation or decreased cardiac output. Impaired diffusion refers to the disruption in gaseous exchange between the alveoli and pulmonary circulation due to permeability of the alveolar surface or an increase in the distance for diffusion.
- *Type II (hypercapnic)*: characterised by low O_2 with high PCO_2, often caused by a dysfunction of alveolar ventilation. Type II respiratory failure is usually caused by conditions that occur outside of the respiratory system, including depression of the central nervous system (drug/alcohol induced, brain injury); conditions that affect nerve supply to the respiratory system (**Guillain-Barré syndrome**, spinal cord injury); disorders of the respiratory muscles (muscular dystrophy); or thoracic cage disorders (**scoliosis**).

Signs and symptoms of acute respiratory failure are associated with hypoxaemia or hypercapnia and the clinical manifestations that occur because of this.

CHAPTER SUMMARY

In this chapter you will have learned about disorders of the respiratory system across the life span and how they impact not only physiologically but also how they influence health-related quality of life. To be an effective person-centred practitioner, you need to be relational when considering these disorders; being compassionate and working with someone's belief system and values will enable you to care for them within the context of their culture and social structure.

KEY POINTS

- Hypoventilation refers to inadequate alveolar ventilation compared to the metabolic demands of the body. It occurs when the minute volume is reduced and is caused by changes in the mechanics of breathing or due to changes in the neurological control of breathing.
- Hyperventilation refers to increased alveolar ventilation that exceeds the metabolic demands of the body. It occurs when the excretion rate of CO_2 exceeds that which is produced by cellular metabolism.
- Hypoxia refers to a reduction in tissue oxygenation and can result from pulmonary alterations, or other abnormalities that are not related to pulmonary function, e.g. decreased cardiac output. Hypoxaemia refers to a reduction of oxygen in arterial blood and is caused by pulmonary dysfunction and may lead to hypoxia.
- Hypercapnia refers to an increase in CO_2 content of arterial blood and is usually caused by disorders that lead to hypoventilation or V/Q mismatching.
- Respiratory disease can be categorised into three phases: respiratory impairment, respiratory insufficiency and respiratory failure.
- Respiratory tract infections (RTIs) refer to infectious diseases that can affect any part of the respiratory tract; they tend to be discussed in terms of upper respiratory tract infections (URTIs), i.e. infection of nose, oropharynx or larynx, or lower respiratory tract infections (LRTIs), i.e. lower airways and lungs.
- Infections of the upper respiratory tract include: the common cold, influenza, rhinitis, sinusitis and otitis media. Infections of the lower respiratory tract include: bronchiolitis, pneumonia and tuberculosis.
- Pneumonia refers to infection of the pulmonary parenchyma, i.e. bronchioles and alveoli. It occurs when the normal defence mechanisms are bypassed and a pathogen gains access to the lower respiratory tract, causing an extensive inflammatory response. Pneumonias can be classified in a number of ways based on the pathogen (typical or atypical) or the area of infection (lobar pneumonia or bronchopneumonia). Pneumonias may also be classified according to the setting in which they occur and referred to as community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), health care-associated pneumonia (HCAP) or ventilator-associated pneumonia (VAP).
- Tuberculosis (TB) is an infection caused by *Mycobacterium tuberculosis* (MTB) (an acid-fast bacilli), usually affecting the lungs but it may invade other body systems. It is highly contagious and the spread is airborne by means of droplet nuclei that are harboured in the respiratory secretions of persons with active tuberculosis. It is the ninth leading cause of death worldwide and is the leading cause of death from a single infectious agent.
- A pneumothorax refers to the presence of air in the pleural cavity caused by rupture of either the parietal or visceral pleura. A pneumothorax can cause either partial or complete collapse of the affected lung.
- Pleural effusion refers to an abnormal collection of fluid in the pleural cavity. Types of pleural effusions are characterised by the presence of substances in them: hydrothorax (serous fluid, transudative or exudative), empyema (pus), chylothorax (chyle) and haemothorax (blood).

- Obstructive lung disorders are a group of diseases caused by obstruction or limitation to airflow. The main disorders of obstructive lung disease are asthma, chronic bronchitis and emphysema.
- Chronic obstructive pulmonary disease (COPD) is an umbrella term for a group of disorders that cause airway obstruction, particularly chronic bronchitis and emphysema. Tobacco smoke is a primary risk factor for COPD.
- Bronchiectasis is characterised by the permanent dilation of the bronchi caused by destruction of the bronchial wall and elastic supporting tissue.
- Cystic fibrosis is an autosomal recessive disorder of defective chloride transport, resulting in thick mucus production in the airways and the glandular ducts.
- Interstitial lung disease (ILD) refers to a group of diffuse parenchymal lung disorders that exert their effects on the collagen and elastic connective tissue found in the interstitium of the alveolar walls. Two of the most common ILD are idiopathic pulmonary fibrosis and sarcoidosis.
- Pulmonary embolism (PE) occurs when a blood-borne substance lodges in a branch of the pulmonary artery occluding pulmonary vasculature.
- Pulmonary hypertension is defined as an increase in mean pulmonary arterial pressure (PAPm) greater than 25 mmHg at rest as assessed by right heart catheterisation.
- Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are manifestations of an inflammatory response of the lung to an insult either directly or indirectly. They are characterised by severe hypoxaemia, hypercapnia, diffuse infiltrate on chest X-ray and substantial reduction in lung compliance.
- Respiratory failure refers to the failure of the respiratory system to oxygenate the body or to eliminate carbon dioxide from the body. It can be divided into two types: hypoxaemic respiratory failure (type I) and hypercapnic/hypoxaemic respiratory failure (type II).

REVISE

TEST YOUR KNOWLEDGE

In this chapter you will have learned about a variety of disorders of oxygenation and carbon dioxide elimination; these can be complex and in order to check your understanding, the following questions will help you confirm your knowledge and application.

Answers are available online. If you are using the eBook just click on the answers icon below. Alternatively go to **https://study.sagepub.com/essentialpatho/answers**

1. Identify and briefly explain the different types of hypoxia.
2. Identify and briefly explain the defence mechanisms of the respiratory tract function.
3. Briefly discuss the pathophysiology of pneumonia, indicating the different types.
4. Identify the risk groups and factors for developing tuberculosis.

5 What are the signs and symptoms of tuberculosis?

6 Briefly explain what a pleural effusion is and identify the different types.

7 What are the different types of atelectasis?

8 Explain the inflammatory response in atopic asthma.

9 Describe the physiological mechanism of 'air trapping'.

10 Explain the inflammatory mechanisms responsible for mucous overproduction in chronic bronchitis.

11 Describe the types of emphysema.

12 Explain the physiological mechanisms that lead to thick mucus secretions in cystic fibrosis.

13 Identify the sources that can cause pulmonary embolism.

14 Differentiate between Type I and Type II respiratory failure.

REVISE

ACE YOUR ASSESSMENT

- Further revision and learning opportunities are available online
- Test yourself away from the book with **Extra multiple choice questions**
- Learn and revise terminology with **Interactive flashcards**

If you are using the eBook access each resource by clicking on the respective icon. Alternatively go to **https://study.sagepub.com/essentialpatho/chapter14**

CHAPTER 14 ANSWERS

EXTRA QUESTIONS

FLASHCARDS

REFERENCES

Antoniou, K.A., Margaritopoulous, G.A., Tomasetti, S., Bonella, F., Costabel, U. and Poletti, V. (2014) Interstitial lung disease. *European Respiratory Review*, *23* (131): 40–54.

Arnold, F.W., Summersgill, J.T. and Ramirez, J.A. (2016) Role of atypical pathogens in the etiology of community-acquired pneumonia. *Seminars in Respiratory and Critical Care Medicine*, *37* (6): 819–28.

Babu, A.S., Padmakumar, R., Maiya, A.G., Mohapatra, A.K. and Kamath, R.L. (2016) Effects of exercise training on exercise capacity in pulmonary arterial hypertension: a systematic review of clinical trials. *Heart, Lung and Circulation*, *25* (4): 333–41.

Baraldo, S., Turato, G., Lunardi, F., Bazzan, E., Schiavon, M., Ferrarotti, I. et al. (2015) Immune activation in α1-antitrypsin-deficiency emphysema: beyond the protease–antiprotease paradigm. *American Journal of Respiratory and Critical Care Medicine*, *191* (4): 402–9.

Baughman, R.P., Culver, D.A. and Judson, M.A. (2011) A concise review of pulmonary sarcoidosis. *American Journal of Respiratory and Critical Care Medicine*, *183* (5): 573–81.

Behr, K. (2012) Approach to diagnosis of interstitial lung disease. *Clinics in Chest Medicine*, *33* (1): 1–10.

Bellani, G., Laffey, J.G., Pham, T., Fan, E., Brochard, L., Esteban, A. et al. (2016) Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*, *316* (8): 788–800.

Bjornson, C.L. and Johnson, D.W. (2013) Croup in children. *CMAJ: Canadian Medical Association Journal*, *185* (15): 1317–23.

Boore, J., Cook, N. and Shepherd, A. (2016) *Essentials of Anatomy and Physiology for Nursing Practice*. London: Sage.

Brightling, C.E., Gupta, S., Gonem, S. and Siddigui, S. (2012) Lung damage and airway remodeling in severe asthma. *Clinical and Experimental Allergy*, *42* (5): 638–49.

Chen, E.S., Song, Z., Willett, M.H., Heine, S., Yung, R.C., Liu, M.C., Groshon, S.D. et al. (2010) Serum amyloid A regulates granulomatous inflammation in sarcoidosis through Toll-like receptor-2. *American Journal of Respiatory and Critical Care Medicine*, *181*: 360–73.

Chen, Z.G., Li, Y.Y., Wang, Z.N., Li, M., Lim, H.F. et al (2018) Aberrant epithelial remodeling with impairment of cilic architecture in non-cystic fibrosis bronchiectasis. *Journal of Thoracic Disease*, *10* (3): 1753–64.

Chung, K.F., Wenzel, S.E., Brozek, J.L., Li, M., Lim, H.F., Zhou Y.Q. et al. (2014) International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *European Respiratory Journal*, *43*: 343–73.

Cruz-Knight, W. and Blake-Gumbs, L. (2013) Tuberculosis: an overview. *Primary Care*, *40* (3): 743–56.

De Martino, M., Galli, L. and Chiappini, E. (2014) Reflections of the immunology of tuberculosis: will we ever unravel the skein? *BMC: Infectious Diseases*, *14* (Suppl 1) [online] doi: 10.1186/1471-2334-14-S1-S1].

Del Giacco, S.R., Bakirtas, A., Be, L.E., Custovic, A., Diamant, Z., Hamelmann, E. et al. (2017) Allergy in severe asthma. *Allergy*,: *72*: 207–20.

Diao, M., Shen, X., Cheng, J., Chai, J., Feng, R., Zhang, P. et al. (2018) How patients' experiences of respiratory tract infections affect healthcare-seeking and antibiotic use: insights from a cross-sectional survey in rural Anhui, China. *BMJ Open*, *8* (2) [online] doi: 10.1136/bmjopen-2017-019492.

Diver, S., Russell, R.J. and Brightling, C.E. (2018) New and emerging drug treatments for asthma. *Clinical and Experimental Allergy*, *48* (3): 241–52.

Elborn, J.S., Bell, S.C., Madge, S.L., Burgel, P.R., Castellani, C., Conway, S. et al. (2016) Report of the European Respiratory Society/European Cystic Fibrosis Society task force on the care of adults with cystic fibrosis. *European Respiratory Journal*, *47* (2): 420–8.

Farrell, P.M., White, T.B., Ren, C.L., Hempstead, S.E., Accurso, F., Derichs, N. et al. (2017) Diagnosis of cystic fibrosis: consensus guidelines from the cystic fibrosis foundation. *Journal of Paediatrics*, *181* (Suppl): S4–S15.

Fogel, N. (2015) Tuberculosis: a disease without boundaries. *Tuberculosis*, *95* (5): 527–31.

Galiè, N., Humbert, M., Vachiery, J-L., Gibbs, S., Lang, I., Torbicki, A. et al. (2016) 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the Association for European Paediatric

and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *European Heart Journal*, *37* (1): 67–119.

Gao, Y. and Raj, J.U. (2017) Pathophysiology of pulmonary hypertension. *Colloquium Series on Integrated Systems Physiology: From Molecule to Function*, *9* (6): i–104. doi.org/10.4199/C00158ED1V01Y201710ISP078. Available at: www.morganclaypool.com/doi/10.4199/C00158ED1V01Y201710ISP078 (accessed 10 August 2018).

GBD (2015 Chronic Respiratory Disease Collaborators) (2017) Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet Respiratory Medicine*, *5* (9): 691–706.

Gelb, A.F., Yamamoto, A., Verbeken, E.K. and Nadal, J.A. (2015) Unravelling the pathophysiology of the asthma-COPD overlap syndrome. *Chest*, *148* (2): 313–20.

GINA (2018) GINA 2018 Report, Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma. [online]. Available at: https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/ (accessed 6 August 2018).

GOLD (2016) Global Strategy for the Diagnosis, Management and Prevention of COPD. Global Initiative for Chronic Obstructive Lung Disease. [online]. Available at: https://goldcopd.org/ (accessed 8 August 2018).

Goldklang, M. and Stockley, R. (2016) Pathophysiology of emphysema and implications. *Chronic Obstructive Pulmonary Diseases*, *3* (1): 454–8.

Gu, K., van Caeseele, P., Dust, K. and Ho, J. (2017) Atypical pneumonia due to human bacovirus in an immunocompromised patient. *CMAJ: Canadian Medical Association Journal*, *189* (19): E697–E699.

Harun, S.N., Wainwright, K. and Henning, S. (2016) A systematic review of studies examining the rate of lung function decline in patients with cystic fibrosis. *Paediatric Respiratory Reviews*, *20*: 55–66.

Hemilä, H. and Chalker, E. (2017) Zinc for preventing and treating the common cold. *Cochrane Database of Systematic Reviews*, *9*. [online]. Available at: www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012808/ (accessed 6 August 2018).

Hull, J.D., Barton, I.P., Torgersen, J. and McNeil, C.M. (2013) A survey of the experiences and impact of acute upper respiratory tract infections on people in six countries in the 2011/2012 common cold and flu season. *Open Journal of Respiratory Disease*, *3*: 175–87.

Johnson, D.W. (2014) Croup. *BMJ: Clinical Evidence*, published online 29 September 2014. Available at: www.ncbi.nlm.nih.gov/pubmed/25263284 (accessed 6 August 2018).

Kalanuria, A.A., Zai, W. and Mirski, M. (2014) Ventilator-associated pneumonia in the ICU. *Critical Care*, *18*: 208.

Kim, V. and Criner, J.G. (2013) Chronic bronchitis and chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*, *187* (3): 228–37.

King, P.T. (2018) The role of the immune response in the pathogenesis of bronchiectasis. *BioMed Research International*, *2018* (6802637): 1–12. [online]. Available at: www.hindawi.com/journals/bmri/2018/6802637/ (accessed 10 August 2018).

Kudo, M., Ishigatsubo, Y. and Aoki, I. (2013) Pathology of asthma. *Frontiers in Microbiology*, *4* (263): 1–16.

Labella, A.M. and Merel, S.E. (2013) Influenza. *Medical Clinics of North America*, *97* (4): 621–45.

Langer, D., Ciavaglia, C.E., Neder, J.A., Webb, K.A. and O'Donnell, D.E. (2014) Lung hyperinflation in chronic obstructive pulmonary disease: mechanisms, clinical implications and treatment. *Expert Review of Respiratory Medicine*, *8* (6): 731–49.

Mattihay, M.A., Ware, L.B. and Zimmerman, G.A. (2012) The acute respiratory distress syndrome. *Journal of Clinical Investigation*, *122* (8): 2731–40.

Meissner, H.C. (2016) Viral bronchiolitis in children. *New England Journal of Medicine*, *374* (1): 62–72.

Merli, G., Eraso, L.H., Galanis, T. and Ouma, G. (2018) Pulmonary embolism. *BMJ Best Practice*. Available at: https://bestpractice.bmj.com/topics/en-gb/116#referencePop1 (accessed 10 August 2018).

Meyer, K.C. (2014) Diagnosis and management of interstitial lung disease. *Translational Respiratory Medicine*, *2*: 4. doi: 10.1186/2213-0802-2-4.

NICE (2017a) Asthma: diagnosis, monitoring and chronic asthma management. NICE guideline [NG80]. National Institute for Health and Care Excellence. Available at: www.nice.org.uk/guidance/ng80 (accessed 9 August 2018).

NICE (2017b) Bronchiolitis in children: diagnosis and management. NICE guideline [NG9]. National Institute of Health and Care Excellence. Available at: www.nice.org.uk/guidance/ng9 date (accessed 8 August 2018).

NICE (2017c) Croup. Clinical Knowledge Summaries. National Institute of Health and Care Excellence. Available at: https://cks.nice.org.uk/croup (accessed 6 August 2018).

NICE (2017d) Idiopathic pulmonary fibrosis in adults: diagnosis and management. Clinical guidance [CG163]. National Institute of Health and Care Excellence. Available at: www.nice.org.uk/guidance/cg163 (accessed 8 August 2018).

NICE (2018) Venous thromboembolism in over 16s. Reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. NICE guideline [NG89] Volume 1: Methods, evidence and recommendations. National Institute for Health and Care Excellence. Available at: www.nice.org.uk/guidance/ng89/evidence/full-guideline-volume-1-pdf-4787002765 (accessed 9 August 2018).

Olin, J.T. and Wechsler, M.E. (2014) Asthma: pathogenesis and novel drugs for treatment. *British Medical Journal*, *349*: g5517. Available at: https://doi.org/10.1136/bmj.g5517 (accessed 6 August 2018).

Papi, A., Brightling, C.E., Pedersen, S.E. and Reddel, H.K. (2018) Asthma. *The Lancet*, *391*: 783–800.

Parker, C., Allen, K. and Browning, S. (2016) Can a leopard change its spots? Metastatic breast cancer or sarcoidosis. *American Journal of Respiratory and Critical Care Medicine*, *193*: A5051. Available at: www.atsjournals.org/doi/pdf/10.1164/ajrccm-conference.2016.193.1_MeetingAbstracts.A5051 (accessed 8 August 2018).

Pasteur, M.C., Bilton, D. and Hill, A.T. (2010) British Thoracic Guideline for non-CF bronchiectasis. *Thorax*, *65*: 11–58.

Patel, P.P., Jacob, C., Thind, G.S., Loehrke, M. and Stryker, H. (2018) Croup in adults: all bite and no bark? *American Journal of Respiratory and Critical Care Medicine*, *197*: A6748. Available at: www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2018.197.1_MeetingAbstracts.A6748 (accessed 7 August 2018).

Portillo, K., Torralba, Y., Blanco, I., Burgos, F., Rodriguez-Roisin, R., Rios, J. et al. (2015) Pulmonary haemodynamic profile in chronic obstructive pulmonary disease. *International Journal of Chronic Obstructive Pulmonary Disease*, *10*: 1313–20.

Ragaller, M. and Richter, T. (2010) Acute lung injury and acute respiratory distress syndrome. *Journal of Emergencies, Trauma and Shock*, *3* (1): 43–51.

Rajagopalan, M. and Schwartz, R.A. (2018) Assessment of clubbing. *BMJ Best Practice*. Available at: https://bestpractice.bmj.com/topics/en-gb/623#referencePop2 (accessed 16 August 2018).

Rajan, J.P., Wineinger, N.E., Stevenson, D.D. and White, A.A. (2015) Prevalence of aspirin-exacerbated respiratory disease among asthmatic patients: a meta-analysis of the literature. *Journal of Allergy and Clinical Immunology*, *135* (3): 676–81.

Ricci, V., Delgado, V., Murphy, S.M. and Cunningham, S. (2015) Bronchiolitis in children: summary of NICE Guidance. *BMJ*, *350*: h2305.

Russell, R.J. and Brightling, C. (2017) Pathogenesis of asthma: implications for precision medicine. *Clinical Science (London)*, *131*: 1723–35.

Saguil, A. and Fargo, M. (2012) Acute respiratory distress syndrome: diagnosis and management. *American Family Physician*, *84* (4): 352–8.

Saguil, A., Wyrick, K. and Hallgren, J. (2014) Diagnostic approach to pleural effusion. *American Family Physician*, *90* (2): 99–104.

Salgame, P., Geadas, C., Collins, L., Jones-López, E. and Ellner, J.J. (2015) Latent tuberculosis infection: revisiting and revising concepts. *Tuberculosis*, *95* (4): 373–84.

Smoliga, J.M., Weiss, P. and Rundell, K.W. (2016) Exercise induced bronchoconstriction in adults: evidence based diagnosis and management. *British Medical Journal*, *352*: h6951.

Stolz, D.A., Meyerhols, M.J. and Welsh, M.J. (2015) Origins of cystic fibrosis lung disease. *New England Journal of Medicine*, *372* (4): 351–62.

Thillai, M., Pollock, K., Pareek, M. and Lalvani, A. (2014) Interferon-gamma release assays for tuberculosis: current and future application. *Expert Review of Respiratory Medicine*, *8* (1): 67–78.

Tseng, S., Stanziola, A.A., Sultan, S., Henry, K., Saggar, R. and Saggar, R. (2018) Pulmonary hypertension related to chronic obstructive pulmonary disease and diffuse parenchymal lung disease: a focus of right ventricle (dys)function. *Heart Failure Clinics*, *14* (3): 403–11.

Tuder, R.M. and Petrache, I. (2012) Pathogenesis of chronic obstructive pulmonary disease. *Journal of Clinical Investigation*, *122* (8): 2749–55.

Weldon, E. and Williams, J. (2012) Pleural disease in the emergency room. *Emergency Medicinal Clinics of North America*, *30*: 475–99.

World Health Organisation (WHO) (2017) Global Tuberculosis Report 2017. Geneva: WHO. Available at: http://apps.who.int/medicinedocs/en/m/abstract/Js23360en (accessed 8 August 2018).

World Health Organisation (WHO) (2018a) Bronchial asthma. Factsheet No. 206. [online]. Available at: www.who.int/mediacentre/factsheets/fs206/en/ (accessed 16 August 2018).

World Health Organisation (WHO) (2018b) Influenza (seasonal). Factsheet. [online]. Available at: www.who.int/en/news-room/fact-sheets/detail/influenza-(seasonal) (accessed 7 August 2018).

Wos, M., Sanak, M., Soja, J., Olechnowicz, H., Busse, W.W. and Szczeklik, A. (2008) The presence of rhinovirus in lower airways of patients with bronchial asthma. *American Journal of Respiratory and Critical Care Medicine*, *177* (10): 1082–9.

Zoorob, T., Sidani, M. and Murray, J. (2011) Croup. *American Family Physician*, *83* (9): 1067–73.

Zuma, A., Raviglione, H., Hafner, R. and van Reyn, C.F. (2013) Tuberculosis. *New England Journal of Medicine*, *368* (8): 745–55.