This chapter provides an introduction to the clinical management of respiratory failure. Clinical management comprises both assessment and treatment, topics covered in more detail later in this book, and here the aim is to provide background knowledge on the definition of respiratory failure, and an understanding of the basic pathophysiological principles involved. The chapter concludes with some worked examples. After reading this chapter you should be able to:

- Define Type I and Type II respiratory failure.
- Understand the differences in pathogenesis between Type I and Type II respiratory failure.
- Describe the assessment and management of a patient with respiratory failure.

What is respiratory failure?

Respiratory failure may be defined as impaired pulmonary gas exchange leading to hypoxaemia (low blood oxygen tension) with or without hypercapnia (high blood carbon dioxide tension). The presence or absence of hypercapnia is used to classify respiratory failure into Type I and Type II, and this is important with regard to the likely underlying cause, and treatment, as we shall see. Type I respiratory failure is present when the partial pressure of arterial carbon dioxide (PaCO₂) is normal or low. Type II respiratory failure is present if the PaCO₂ is elevated. From this definition it will already be apparent that a key investigation in respiratory failure is blood gas analysis, both to make the diagnosis and to allow correct classification. Traditionally a partial pressure of arterial oxygen (PaO₂) <8 kPa indicates respiratory failure, but it is important to remember that PaO₂ is dependent on the fractional concentration of inspired oxygen (FiO₂) such that the 8 kPa cut-off is appropriate only for a patient breathing room air, at sea level. A normal PaO₂
under such circumstances is >12 kPa (somewhat less in older people) and the normal range for PaCO₂ is 4.5–6.0 kPa. We will describe in more detail later in this chapter how to identify whether a patient who is breathing supplemental oxygen has respiratory failure on the basis of blood gas analysis results.

What are the causes of respiratory failure?

The function of the respiratory system is gas exchange, but for this to be effective the individual components of the system must all be operating normally. The components are illustrated schematically in Figure 1.1, and include the conducting airways that transfer air from the outside to the gas exchanging airways, the gas-exchanging airways themselves, the respiratory muscle pump that drives air in and out of the lungs, the control system of that pump which includes the central and peripheral nervous systems, together with the pulmonary vasculature. Impairment of any one or a combination of these components might result in respiratory failure and, indeed, this provides one useful method of classifying the causes of respiratory failure as outlined in Table 1.1. One must accept, however, that this is an over-simplification and many disease processes may result in respiratory failure through a combination of mechanisms. Chronic obstructive pulmonary disease (COPD), for example, is associated with bronchoconstriction of the conducting airways, emphysema destroying the gas-exchange surface, a skeletal myopathy affecting the respiratory muscle pump and pulmonary hypertension.

Figure 1.1  Components of the respiratory system.
The pathophysiology of respiratory failure

Table 1.1 Causes of respiratory failure, classified by the predominant site of pathology in the respiratory system.

<table>
<thead>
<tr>
<th>Conducting airways</th>
<th>Gas-exchange airways</th>
<th>Respiratory muscle pump</th>
<th>Neuronal control</th>
<th>Pulmonary blood vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep apnoea</td>
<td>Pneumonia</td>
<td>Myopathy</td>
<td>Drugs</td>
<td>Pulmonary embolus</td>
</tr>
<tr>
<td>Upper airway obstruction</td>
<td>Acute respiratory distress syndrome (ARDS)</td>
<td>Chest wall disorders</td>
<td>Stroke</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (COPD)</td>
<td>Pulmonary fibrosis</td>
<td>Neuromuscular disease</td>
<td>Trauma</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>Cardiac failure</td>
<td></td>
<td>Motor neurone disease</td>
<td>Guillain–Barré syndrome</td>
</tr>
</tbody>
</table>

Figure 1.1 illustrates that for effective gas exchange oxygen must be transferred via the conducting airways to the gas-exchange portion of the lung, under the power of the respiratory muscle pump, which is itself controlled by the central nervous system, and into a functioning blood supply. Hypoxaemia may develop if any one or a combination of these components is damaged. In essence, there is therefore a disorder between the ventilation (gas delivery) and perfusion (blood delivery) in the lung. This is referred to as V/Q mismatch and implies that some gas-exchanging portions of the lung receive blood supply but no oxygen, and others receive oxygen and no blood supply. This explains why patients with pneumonia, for example, may be more breathless than those who have had pneumonectomy (lung removal). The pneumonectomy patient has no V/Q mismatch, whereas in pneumonia, for example, the consolidated and under-ventilated portion of the lung continues to receive blood supply, and indeed may receive more than usual as a result of the inflammatory reaction. In summary, Type I respiratory failure is usually the result of V/Q mismatch.

The situation for Type II respiratory failure is a little more complex. Carbon dioxide transfers much more easily across the alveolar–capillary barrier and excess carbon dioxide in the blood tends to represent alveolar under (hypo)ventilation. This may occur in the presence of respiratory disease but, unlike Type I respiratory failure, may also occur in lungs
that are completely normal and where respiratory failure results from failure of the respiratory muscle pump. When the pump itself is normal, but is subjected to excessive demands, Type II failure may also result and our patient with pneumonia and Type I failure may progress to Type II failure if treatment is not delivered effectively.

**The management of respiratory failure**

The management of respiratory failure comprises two main principles: treatment aimed at any specific underlying reversible cause, and interventions aimed at supporting respiratory function to give other therapies sufficient time to be effective (or when no specific underlying cause is identifiable).

Treatment of the underlying diseases leading to respiratory failure is beyond the scope of this chapter but include, for example, antibiotics in our patient with bacterial pneumonia, and steroids with nebulised bronchodilators in exacerbations of asthma and COPD. The supportive treatments available include oxygen, and respiratory support with continuous positive airway pressure (CPAP), non-invasive ventilation (NIV) or invasive ventilation. These will be discussed in more detail later in the book, and for now we will concern ourselves with the assessment of a patient known or thought to be in respiratory failure.

**Assessment of a patient with respiratory failure**

Assessment comprises a clinical history (story from the patient and others, supplemented with information derived from direct questions), examination of the patient, and diagnostic investigations. The aim is to confirm the presence of respiratory failure, assess the severity, and establish an underlying diagnosis such that specific treatment can be given.

**History**

The principal symptoms of respiratory disease are breathlessness, cough, sputum production, wheeze and chest pain. We may add to these, those symptoms commonly associated with hypercapnia such as tiredness, morning headaches, ankle swelling, poor sleep quality and snoring.

When assessing breathlessness, a key feature is the speed of onset. The causes of respiratory failure listed in Table 1.1 vary considerably
in their speed of onset, and a schema for the onset of breathlessness is illustrated in Figure 1.2.

At the quickest, pneumothorax can occur over seconds. In contrast, the breathlessness associated with pulmonary hypertension, for example, may progress slowly over years.

In addition, one can consider the following aspects of the patient’s breathlessness:

- Are the symptoms constant or variable? Variation in symptoms is typical of diseases such as asthma where the obstruction to airflow is variable. In COPD, by contrast, much of the airflow limitation is fixed and therefore symptoms are typically more constant from day to day. In addition, it is important to assess whether the symptoms are worse after a period at work, and better when on holiday, suggesting a workplace exposure.

- Are the symptoms relieved or made worse by anything the patient does. For example, weakness of the respiratory muscles may be more noticeable when the patient is lying down, ‘orthopnoea’. Orthopnoea is also a feature of breathlessness in advanced heart failure.

- Is there or have there been any exposures to agents that are known to cause respiratory disease, in particular tobacco smoke, but including many others such as agents associated with asthma in the home and at work (for example animal dander), while environmental exposure to other agents such as asbestos can result in fibrosing (scarring) lung diseases.

- What are the associated symptoms? Cough and sputum, for example, may suggest COPD. Snoring may suggest sleep apnoea.
Finally, it should be emphasised that while the focus is on the cardiorespiratory system, a complete history should be obtained, and corroborated where necessary with information from others. There are many unusual causes of breathlessness and respiratory failure for which clues may be obtained in the history. One might consider, for example, information on pets at home informing on a diagnosis such as extrinsic allergic alveolitis, or a history of prior use of appetite suppressants resulting in pulmonary hypertension. Readers should refer to a standard text for further detail on the art of history taking (Douglas et al., 2005).

Examination

A complete examination should be performed, with an emphasis on the cardiorespiratory system. Again, the reader is referred to standard works which outline the principles of complete examination (Douglas et al., 2005).

Initially, the pattern, depth and rate of respiration can be observed. Likewise, the patient’s body habitus (general shape and size) can be examined prior to formal calculation of the body mass index (BMI, the weight in kg divided by the square of the height in m).

Peripheral signs of respiratory disease include tar staining of the fingers, digital clubbing (typically associated with lung fibrosis, lung cancer and chronic pulmonary infections such as bronchiectasis) and the coarse flapping tremor and bounding pulse of carbon dioxide retention (Type II respiratory failure).

In the head and neck it is important to assess for clinical signs of anaemia (conjunctival pallor), central cyanosis (a much better assessment than peripheral cyanosis in the assessment of respiratory failure), elevation of the jugular venous pressure, and the shape and size of the neck. Neuromuscular diseases are important causes of respiratory failure and therefore it is important to examine for evidence of muscle wasting and fasciculation. Similarly, sleep apnoea and obesity hypoventilation syndromes can present with respiratory failure, and in addition to a general impression of BMI and neck circumference, it is important to note features such as mouth breathing, and abnormalities of the pharynx such as tonsillar enlargement.

Examination of the chest includes inspection, palpation, percussion and auscultation. The chest is inspected for scars and deformities. Palpation is used to assess the position of the mediastinum (trachea and apex beat) and to assess the depth of respiration. Percussion and auscultation are used to localise and classify the site of lung disease. The
key question to ask when percussing is ‘Is this resonant or is this dull’, each time the chest is percussed, in comparison with the note in adjacent areas on that side of the chest, and on the contralateral side. The identification of hyper-resonant from resonant, and stony dull from dull is difficult. Similarly, when auscultating the key questions are ‘Are these breath sounds normal (vesicular), normal but reduced in volume, or different’. In addition, ask ‘Are there any added sounds?’ such as musical wheeze, or non-musical crackles and pleural rubs. Wheeze may be diffuse or localised, and monophonic (single note) or polyphonic (multiple notes). Disease such as asthma and COPD which cause widespread narrowing of many airways produce diffuse, polyphonic wheeze. Localised, monophonic wheeze suggests localised airflow obstruction. Bronchial breathing is quite different from normal vesicular sounds and has been characterised as occurring when inspiration and expiration are of equal volume and length, when there is a pause between inspiration and expiration, and when the sounds are ‘blowing’ in nature.

The clinical signs may then be put together and matched to various patterns of disease, as summarised in Table 1.2. These are stereotyped, and simplified, in the table, but serve to illustrate typical patterns of disease.

Table 1.2 Stereotypical patterns of diseases in respiratory failure.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Palpation (position of mediastinum)</th>
<th>Percussion</th>
<th>Auscultation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Not displaced</td>
<td>Resonant</td>
<td>Vesicular sounds, nil added</td>
</tr>
<tr>
<td>Large effusion</td>
<td>Displaced to the other side</td>
<td>('Stony') dull</td>
<td>Diminished vesicular, nil added</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>Displaced to the other side</td>
<td>('Hyper') resonant</td>
<td>Diminished vesicular, nil added</td>
</tr>
<tr>
<td>Collapse</td>
<td>Displaced to the same side</td>
<td>Dull</td>
<td>Diminished vesicular, nil added</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Not displaced</td>
<td>Dull</td>
<td>Bronchial sounds, with crackles</td>
</tr>
<tr>
<td>Asthma and chronic obstructive pulmonary disease</td>
<td>Not displaced</td>
<td>Resonant</td>
<td>Vesicular sounds, with wheeze</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Apex displaced</td>
<td>Resonant</td>
<td>Vesicular sounds, with crackles</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Not displaced</td>
<td>Resonant</td>
<td>Vesicular sounds, with crackles</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>Not displaced</td>
<td>Resonant</td>
<td>Vesicular sounds, nil added ?pleural rub</td>
</tr>
</tbody>
</table>
Diagnostic investigations

Standard investigations in the assessment of a patient with suspected respiratory failure includes the points discussed below.

Blood gas analysis

Blood gas analysis is performed to confirm the presence of respiratory failure, inform on the likely timescale of development, and differentiate Type I from Type II disease. Pulse oximetry, which estimates oxygen saturation but gives no information on carbon dioxide, in addition to having limitations in many situations including reduced cardiac output, is often used as a screening tool. Blood gas analysis may be performed on capillary or arterial samples as described later in this book. One simplified approach to blood gas analysis is given below, and summarised in Figure 1.3.

1. Is the patient acidotic or alkalotic, or is the pH normal? An abnormal pH suggests either that the problem is new, or that a longer standing problem has become decompensated. In either event, an abnormal pH generally indicates a greater urgency for treatment.

2. When the pH is abnormal, if the direction of change of the carbon dioxide explains the abnormality seen in pH then this is a primary respiratory problem. For example, a low pH and a high carbon dioxide indicate primary respiratory acidosis.

3. Conversely, when the pH is abnormal and the direction of change is not explained by the carbon dioxide, but is explained by the direction of change in bicarbonate, then this is a primary metabolic problem. This would occur, for example, when a low pH is accompanied by a reduced bicarbonate concentration, indicating metabolic acidosis.

4. Is there a partial compensatory change in the other parameter (bicarbonate if pH explained by carbon dioxide, carbon dioxide if the pH explained by bicarbonate)?

5. If the pH is normal, is this a fully compensated acid–base disturbance manifested by abnormalities of both carbon dioxide and bicarbonate?

6. Finally, ask what is the PaO₂ and how does this relate to the FiO₂? It is possible to assess the presence of respiratory failure when patients are breathing oxygen, by calculating the A-a gradient.

\[
A-a\ \text{gradient} = \text{PAO}_2 - (\text{PaO}_2 + \text{PaCO}_2/0.8)
\]
**PAO₂**, or the alveolar PO₂, is calculated by expressing the FiO₂ as a percentage of 100 kPa (atmospheric pressure) − 7 kPa water vapour pressure. The normal A-a gradient is less than 3 kPa. Thus, for example, a patient who has a PaO₂ of 15 kPa and PaCO₂ of 4 kPa when breathing 60% oxygen has an A-a gradient of:

\[
(60/100 \times (100 - 7)) - (15 + 4/0.8) = 55.8 - 20 = 35.8 \text{ kPa}
\]

This is abnormal and therefore indicates the presence of respiratory failure. A simplified approach, used in the definition of acute lung injury and the acute respiratory distress syndrome, is to calculate the PaO₂/FiO₂ ratio. The definition of acute lung injury includes PaO₂/FiO₂ < 27 kPa (200 mmHg).

**Figure 1.3** Flow chart showing a simplified approach to the assessment of blood gases.
Full blood count

Anaemia is a cause of breathlessness, and respiratory failure can be associated with the development of polycythaemia which may require specific treatment.

Lung function tests

Spirometry (forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC)) will differentiate obstructive from restrictive diseases, a crucial distinction in respiratory medicine that is discussed further below. Static lung volumes such as total lung capacity give additional information on conditions associated with scarring and gas trapping. Assessing the carbon monoxide transfer factor (a proxy for the ability of oxygen to cross the alveolar–capillary barrier) can aid differentiation of restrictive defects due to lung diseases (such as pulmonary fibrosis, where the barrier is thickened) from extra-thoracic restriction in, for example, neuromuscular disease where the problem is one of mismatched demand and ability of the respiratory muscle pump to achieve adequate gas exchange.

The distinction between obstructive and restrictive patterns on spirometry is important in establishing a differential diagnosis. These are best considered by reference to a flow-volume loop, which will be provided by many spirometry services. A hypothetical normal flow volume loop, and those that may be obtained in obstructive and restrictive diseases are illustrated in Figure 1.4. Note that flow is plotted on the y-axis, and a positive flow indicates expiration, a negative flow is inspiration. The x-axis represents lung volume, with total lung capacity at the origin, and distance travelled along the x-axis indicating the vital capacity (VC, total amount of air that can be moved in and out of the lung). The total lung capacity is made up of VC and residual volume, the volume of air that remains in the chest after a maximal expiration. In the normal loop (a), starting from a maximal inspiration where the axes cross, the maximum (peak) expiratory flow rate is achieved rapidly, before it tails off more gradually to the end of expiration. This expiratory limb, above the axis, is roughly triangular in shape. The inspiratory limb is below the x-axis. It takes longer to reach the maximal inspiratory flow, which is lower in magnitude than the maximal expiratory flow, and the shape of this curve is roughly semi-circular.
In diseases characterised by obstruction to the flow of air (Figure 1.4b), and therefore those typically affecting the bronchial tree such as asthma and COPD, the peak expiratory flow rate is reduced and in early expiration, collapse of the airways results in a rapid reduction in expiratory flow rate and a characteristic ‘scalloped’ shape to the curve. Note that vital capacity, the distance on the y-axis, is not reduced and therefore expressing FEV₁/FVC in an obstructive condition results in a lower than normal value. In restrictive lung diseases, the total lung capacity has been affected and is reduced considerably as shown in Figure 1.4c where the distance on the y-axis is reduced. Compare the patient’s trace to the normal trace shown in dotted lines. However, the relative flow rates throughout inspiration and expiration are not altered, and the shape of the trace is a miniaturised version of the normal trace. Expressing FEV₁/FVC here, in a restrictive condition, will result in a normal ratio as both FEV₁ and FVC have been reduced. Restrictive conditions can be caused by lung pathology such as the fibrotic lung diseases, but a restrictive pattern may also result when the respiratory muscle pump is unable to meet the demands placed on it, for example in the case of respiratory muscle weakness, or gross obesity. Fortunately it is possible to distinguish lung (‘thoracic’) from other (‘extra-thoracic’) restriction, by reference to the measurement of gas transfer, as described above. Readers requiring further detail are referred to a standard work on pulmonary function testing (Ruppel, 2003).

A simplified strategy for the interpretation of lung function tests might therefore be as follows, assuming that the test is of an acceptable technical quality.
1. Examine the FEV₁ and FVC, expressed as a percentage of predicted for that patient’s age, sex, height and race; <80% predicted is considered abnormal.

2. If the FEV₁ or FVC are abnormal, examine the FEV₁/FVC ratio. For reasons described above, in relation to the flow volume loop, a ratio >0.7 implies a restrictive disease (either thoracic or extra-thoracic), while a ratio <0.7 implies an obstructive disease. The ratio is not generally helpful if both FEV₁ and FVC are normal (>80%).

3. If there is evidence of airflow obstruction, consider whether there is additional supporting evidence such as the shape of the flow-volume loop, which can be reflected mathematically by examining the flow-rate at between 25% and 75% of VC, the FEF25–75, which would be significantly reduced.

4. In airflow obstruction, a bronchodilator reversibility test is sometimes performed in which spirometry is repeated before and after administration of a bronchodilator such as salbutamol. Classically, COPD is characterised by fixed airflow obstruction, and asthma by reversible airflow obstruction, although these concepts are currently being challenged (Calverley et al., 2003). The cut-off for reversibility is also controversial but might typically be around 200 ml or 15% change in absolute FEV₁.

5. If there is evidence of restriction, consider whether there is additional supporting evidence such as reduced total lung capacity.

6. In a restrictive disease, examining the gas transfer can differentiate between thoracic and extra-thoracic restriction.

**Chest X-ray**

Chest X-rays are performed to assess the appearance of the underlying lungs. One simplified strategy for interpretation of a chest X-ray is given below.

1. Check that this is the correct X-ray film (name and date).

2. Assess if the film is technically adequate (that is, exclude rotation by looking at the ends of the clavicles in relation to the vertebral spinous processes, ensure there is adequate penetration such that the vertebral bodies are just visible behind the heart, ensure there has been an adequate inspiration and that all the lung fields have been included on the film). A film that is generally too white is described as under-penetrated (the X-ray dose was too low) and a film that is too black is over-penetrated (the X-ray dose was too high).
3. Assess whether the film has been taken in the antero-posterior (AP) or postero-anterior (PA) direction (which is important, for example, on the ability to comment on heart size) and whether the X-ray was taken with the patient erect or supine.
4. Systematically examine the lung fields, soft tissues and bones for abnormalities. In general, the lungs should be of approximately equal density from top to bottom and left to right.
5. Describe the shape, size, density, location and distribution of any abnormalities.
6. Check whether there are any old X-ray films available for comparison.

**Specialist investigations**

The investigations described above will be important in most patients presenting with respiratory failure. Many patients, as we shall see in the worked examples below, require more specialised tests, the detailed description of which is outwith the scope of this chapter. However, these may include:

- Further **lung imaging** – for example with a high-resolution chest computed tomography (CT) scan of the chest.
- More complex **lung function assessment** – for example testing the strength of respiratory muscles, with mouth (inspiratory) pressure.
- **Sleep study** to investigate the possibility of diagnoses such as the obstructive sleep apnoea syndrome (OSAS).
- **Trans-thoracic echocardiography** to inform on cardiac function, perhaps progressing in selected patients to further tests such as serum brain natriuretic protein (BNP) assay (which is elevated in heart failure), or cardiac catheterisation and assessment of pulmonary artery pressure.

**Summary**

Respiratory failure may be defined as impaired pulmonary gas exchange leading to hypoxaemia with or without hypercapnia. Type I respiratory failure is present when the partial pressure of arterial carbon dioxide (PaCO₂) is normal or low. Type II respiratory failure is present if the PaCO₂ is elevated. Impairment of any one or a combination of the conducting airways, the gas-exchanging airways, the respiratory muscle pump and the control system of that pump, together
with the pulmonary vasculature may result in respiratory failure. The assessment of a patient with suspected respiratory failure includes the history, examination, and diagnostic investigations. The aim is to confirm the presence of respiratory failure, assess the severity, and establish an underlying diagnosis such that specific treatment can be given. The management of respiratory failure comprises two main principles: treatment aimed at any specific underlying reversible cause, and interventions aimed at supporting respiratory function to give other therapies sufficient time to be effective or when no such specific cause has been identified. Such principles of investigation and management are discussed in more detail in the subsequent chapters.

This chapter concludes with some worked examples of patients with respiratory failure, illustrating how the principles of assessment described above may be applied in clinical practice.

**Case studies**

**Case study 1.1**

A 63-year-old woman makes an appointment to see you, her primary care provider, as she has noticed increasing breathlessness when out shopping over the past few months.

**What are the important points you will wish to address in the history?**

The key to assessing breathlessness is to establish the speed of onset, and any associated symptoms. Here the onset is over months, which changes the likely diagnosis in comparison with breathlessness that has occurred over a few hours. On direct questioning, she also has a daily cough productive of white sputum, and wheeze but no chest pain. She does not complain of ankle swelling, or morning headaches. She is a little tired but says that her sleep quality is good. She does not think that she snores. The breathlessness is not variable, or worse in any particular position. She can lie flat without breathlessness. She started smoking aged 14, up to 20 cigarettes per day, and stopped at age 54. She had hay fever as a child. There do not seem to be any current environmental factors affecting her disease.

**What do you think the most likely cause of her breathlessness is, and how will you establish this?**

The slow progression of symptoms that do not vary, and a supporting significant exposure to tobacco smoke, make COPD the most likely diagnosis. Smoking exposure can be quantified by calculating the ‘pack-years’ smoked. This is calculated by dividing the number of cigarettes smoked per day by 20, and multiplying this by the number of years smoked. To develop COPD, it would be unusual to have less than 20 pack-years exposure and this woman has 40 pack-years. The hay fever as a child does raise the possibility that this may be asthma, as asthma is...
associated with other atopic diseases including hay fever. Although clinical examination is important and the finding of wheeze on examination may help, the diagnosis of COPD can only be confirmed by performing spirometry. The differentiation from asthma can be challenging and may require a formal reversibility test in response to nebulised bronchodilators or steroids, or daily peak-flow monitoring to assess for any day-to-day variation in symptoms.

**You have spirometry available in the surgery and her results are as follows:** \( FEV_1 \) 0.63 l or 33% predicted, \( FVC \) 2.01 l or 87% predicted, and \( FEV_1/FVC \) ratio 0.31. **Interpret these results.**

Assuming the spirometry is technically adequate, the \( FEV_1 \) is low and \( FVC \) is normal (>80%), with a \( FEV_1/FVC \) ratio <0.7 suggesting an obstructive process. If a flow volume loop was available it may show the characteristic ‘scallop’ shape. After nebulised salbutamol, her \( FEV_1 \) increased to 0.66 l but as this is <200 ml and 15%, the disease is not considered ‘reversible’ and COPD is the most likely diagnosis. Criteria, and indeed the concept of reversibility remains a subject of debate.

**What other tests are indicated?**

The degree of impairment of \( FEV_1 \) is used to classify the severity of COPD in current international guidelines (National Institute for Clinical Excellence, 2004; Global Initiative for Chronic Obstructive Lung Disease, 2007). With an \( FEV_1 \) of 33%, this woman has severe COPD and it would be appropriate to perform oxygen saturations (to exclude respiratory failure), a full blood count (to exclude anaemia) and a chest X-ray (to exclude other complicating diagnoses, and which may show features compatible with COPD). Her haemoglobin concentration was normal, and her chest X-ray is shown in Figure 1.5.

**Interpret the X-ray.**

Figure 1.5 is a PA erect film of reasonable technical quality. The lungs are hyper-expanded in keeping with a diagnosis of COPD, there are no focal lung lesions, and the bones and soft tissues appear normal.
Case study 1.1  (Continued)

Her oxygen saturation breathing room air was 92%. What would you do next?

An oxygen saturation of 92% equates, approximately, to an arterial oxygen tension of 8 kPa. The patient may therefore have respiratory failure, but this needs to be confirmed with blood gas analysis, which will also inform on the carbon dioxide levels and allow differentiation of Type I respiratory failure from Type II respiratory failure.

She was referred to her local oxygen assessment service and the following blood gas results were returned. What is your interpretation of these?

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.368</td>
</tr>
<tr>
<td>PaO₂ (11–15 kPa)</td>
<td>7.71 kPa</td>
</tr>
<tr>
<td>PaCO₂ (4.5–6.0 kPa)</td>
<td>8.0 kPa</td>
</tr>
<tr>
<td>HCO₃⁻ (24–30 mmol/l)</td>
<td>32.3 mmol/l</td>
</tr>
<tr>
<td>FiO₂</td>
<td>0.21</td>
</tr>
</tbody>
</table>

The pH is normal so by definition she is neither acidotic nor alkalotic, however both the HCO₃⁻ and PaCO₂ are abnormal in keeping with a fully compensated and therefore chronic acid–base disturbance. It is not possible, theoretically, to say whether this is a primary respiratory acidosis with complete metabolic compensation, or a primary metabolic alkalosis with complete respiratory compensation. However, the latter does not occur, so this is indeed a fully compensated respiratory acidosis. The PaO₂ is <8 kPa breathing room air, so she has respiratory failure, and the PaCO₂ is elevated defining this as Type II respiratory failure.

What are the principles of management?

Recall that the management of respiratory failure comprises two main principles: treatment aimed at any specific underlying reversible cause, and interventions aimed at supporting respiratory function. Therefore, her COPD therapy should be optimised by a specialist in this condition. If, after this, she remains hypoxic then current guidelines support the use of domiciliary oxygen therapy for patients with COPD who have a PaO₂ < 7.3 kPa breathing room air, twice, when clinically stable. This criteria is raised to <8 kPa where there is clinical evidence of right heart failure. Oxygen is titrated to correct the PaO₂ to >8 kPa and evidence suggests that it should be used for at least 15 hours in every 24-hour period (Nocturnal Oxygen Therapy Trial Group, 1980; Medical Research Council Working Party, 1981). If she is active, she may also benefit from a portable (ambulatory) supply. Assessments will need to be performed to ensure that increasing her FiO₂ does not result in a rise in PaCO₂ of >1 kPa or fall in pH (decompensation). Acutely, for example at an exacerbation, an inability to achieve adequate oxygenation without a rise in PaCO₂ and fall in pH would be an indication for non-invasive ventilation. The benefits of domiciliary non-invasive ventilation for newly diagnosed chronic Type II respiratory failure in COPD are less clear and this subject remains controversial.
Case study 1.2

As a member of staff working in emergency medicine, you are asked to see a 24-year-old man who has walked into the emergency department, complaining of breathlessness, a cough productive of green sputum, right-sided pleuritic chest pains and fever.

What are the important points you will wish to address in the history?

Again, the key to assessing breathlessness is to establish the speed of onset, and any associated symptoms. In this case the onset is much more acute, over a few days, and he is previously fit and active, with a physical job as a builder. The cough, phlegm and fever suggest infection of the airways (bronchitis) or lung parenchyma (pneumonia) but the chest pain suggests the latter as there is peripheral, pleural irritation and this is localising to the right side. ‘Pleuritic’ pain is typically worse on inspiration and may ‘catch’ the patient if they are asked to take a deep breath in. As always, it is important to be thorough and, for example, his job as a builder may result in exposure to various occupational dusts that could cause diseases of the lung.

On examination, his temperature is 38.3°C, his heart rate is 100/minute, and his blood pressure is 100/60 mmHg. His respiratory rate is 20/minute and his oxygen saturation is 94% breathing room air. Interpret these vital signs, and outline your immediate plan.

These signs are consistent with a diagnosis of pneumonia: the patient is pyrexial, tachycardic, has borderline hypotension, tachypnoea and hypoxia. He needs a rapid but complete physical assessment, and urgent investigations and treatment. Oxygen therapy should be given to maintain a target saturation of around 95%, and in the absence of signs of heart failure it would be sensible to commence intravenous fluids to support his cardiovascular system, aiming to see a reduction in heart rate and increase in blood pressure.

On examination of the chest, expansion is greater on the left than the right, the mediastinum is not displaced, the left side is more resonant than the right, and while breath sounds on the left are normal those on the right sound blowing and there are coarse crackles present. Interpret the clinical findings.

These findings are consistent with right sided consolidation and a diagnosis of pneumonia. In pneumonia the lung parenchyma fills with an inflammatory reaction (becomes ‘consolidated’) and this accounts for the reduction in expansion on that side because not as much air is moving in and out. However, there is no mediastinal shift as there is no overall change in volume of the lung. The reduction in percussion note, termed ‘dull’, is because the underlying lung is now airless, and the ‘blowing’ breath sounds are typical of ‘bronchial breathing’ where the consolidated lung is transmitting the sounds of airflow in the larger airways to the surface of the lung. Bronchial breathing is also characterised by an audible pause between inspiration and expiration (this does not normally occur), and inspiration and expiration being of equal length (normally expiration is longer). Bronchial breathing is characteristic of pneumonia, and coarse crackles are also often heard.
Case study 1.2  (Continued)

What investigations would you perform to confirm this, and to assess the severity of the disease process?

This patient should have a full blood count, urea and electrolyte assay, liver function tests, C-reactive protein and blood cultures. An arterial blood gas should be performed. He should have a chest X-ray and an electrocardiogram (ECG). Urine should be collected for urinalysis and detection of pneumococcal and legionella antigens. Sputum should be sent for microscopy, culture and sensitivity. The aim of these tests is to confirm the clinical suspicion of pneumonia, to attempt to identify the causative organism, and to assess the severity of the disease. National and international guidelines for the treatment of pneumonia also exist (British Thoracic Society, 2004; Infectious Disease Society of America, 2007) and these include severity scales. The simplest to use is the CURB-65 (Lim et al., 2003):

Score one point for each of the following:

**CONFUSION** (abbreviated mental test score <8)
**UREA** >7 mmol/l
**RESPIRATORY RATE** >30/min
**BLOOD PRESSURE** <90 systolic and/or <60 diastolic
>65 years old.

Mortality is related to the score such that:

<table>
<thead>
<tr>
<th>Score</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.7%</td>
</tr>
<tr>
<td>1</td>
<td>3.2%</td>
</tr>
<tr>
<td>2</td>
<td>13.0%</td>
</tr>
<tr>
<td>3</td>
<td>17.0%</td>
</tr>
<tr>
<td>4</td>
<td>41.5%</td>
</tr>
<tr>
<td>5</td>
<td>57.0%</td>
</tr>
</tbody>
</table>

In this example, a points is scored for Blood Pressure but not Confusion, Urea (if normal), Respiratory Rate or Age and the total score is therefore 1 representing a low risk of death.

**Interpret the chest X-ray.**

Figure 1.6 is an erect PA chest X-ray that is adequately penetrated and not rotated, but it is not perfect as it is not possible to see the lung apices. There are ECG electrodes visible in an arc around the left chest wall, and a left-sided nipple ring. The most obvious area of abnormality is an area of dense, confluent shadowing in the right lower zone. This has a horizontal upper border (representing the horizontal fissure). The right heart border is obscured suggesting that the process is anterior and in contact with the heart border, and there are air bronchograms visible. This is the appearance of a right middle lobe pneumonia. Air bronchograms are also typical of pneumonia. They appear as branching black lines within the consolidated white lung, and represent patent larger airways entering an area of alveoli that are consolidated.
Arterial blood gas analysis is given below. Interpret the blood gas results. Why is he breathless?

- pH 7.40
- \( \text{PaO}_2 \) (11–15 kPa) 8.2 kPa
- \( \text{PaCO}_2 \) (4.5–6.0 kPa) 3.8 kPa
- \( \text{HCO}_3^- \) (24–30 mmol/l) 22.0 mmol/l
- \( \text{FiO}_2 \) 0.50

The pH is normal so by definition he is neither acidotic nor alkalotic, but both the \( \text{HCO}_3^- \) and \( \text{PaCO}_2 \) are abnormal suggesting a fully compensated acid–base disturbance. This could be a primary respiratory alkalosis with metabolic compensation, or a primary metabolic acidosis with respiratory compensation. Either can occur in pneumonia, as systemic infection can result in a metabolic (lactic) acidosis, and respiratory alkalosis may be seen if ventilatory drive is increased in an attempt to maintain blood oxygen tensions. The \( \text{PaO}_2 \) is >8 kPa but the patient is breathing supplemental oxygen, so an assessment of respiratory failure will need to consider the A-a gradient. This is calculated using the formula given below:

\[
\text{A-a gradient} = \text{PAO}_2 - (\text{PaO}_2 + \text{PaCO}_2/0.8)
\]

and \( \text{PAO}_2 \), or the alveolar \( \text{PO}_2 \), is calculated by expressing the \( \text{FiO}_2 \) as a % of 100 kPa (atmospheric pressure) – 7 kPa water vapour pressure. Therefore:

\[
\text{A-a} = (50/100 (100 – 7)) - (8.2 + (3.8/0.8)) = 33.55 \text{ kPa}
\]

The A-a gradient here is 33.55 kPa, and therefore elevated. The \( \text{PaCO}_2 \) is low defining this as Type I respiratory failure. The patient is breathless because his right middle lobe is full of pus, however this alone is an insufficient explanation as patients can tolerate lobectomy very well. A better explanation would be V/Q mismatch, such that the affected part of the lung, not taking part in gas exchange, is preferentially receiving the blood supply as a result of inflammatory vasodilation.
Case study 1.2  (Continued)

How should he be managed?

Once again, the management principles are to treat the underlying cause and to support respiratory function until clinical improvement. The patient will require intravenous antibiotics for the right middle lobe pneumonia, and intravenous fluids to support his cardiovascular system. Regarding the respiratory failure, he is at present maintaining his PaO$_2$ > 8 kPa and therefore it would be appropriate to continue the 50% oxygen. An alternative would be to apply continuous positive airway pressure (CPAP) which is an effective treatment for Type I respiratory failure and may allow reduction in FiO$_2$ and increase in PaO$_2$.

Case study 1.3

A 74-year-old man is referred by his GP to the respiratory outpatient department for assessment of breathlessness. He has been getting progressively breathless for years, and it is now occurring on minimal exertion. It also occurs when lying down, and he has occasionally woken up from sleep feeling breathless, with the production of pink, frothy sputum. At other times he has a cough productive of some green phlegm, but this has not changed recently. He does not have any chest pain or wheeze. He has a past medical history of atrial fibrillation, ischaemic heart disease (including a non-ST elevation myocardial infarction 3 years ago) and late-onset diabetes mellitus. He stopped smoking 10 years ago but smoked 30 cigarettes per day for 40 years. He is a retired mechanic. On direct questioning he has gained 2 kg in weight over the past week and snores loudly.

Interpret the history.

This case is complex, and it is likely that his breathlessness is multi-factorial. The history of ischaemic heart disease, orthopnoea, paroxysmal nocturnal dyspnoea and weight gain suggest decompensated cardiac failure. However, with a significant smoking history (60 pack-years) and chronic sputum production he may also have COPD. His previous occupation as a mechanic may have resulted in exposure to asbestos. In addition, a history of snoring could suggest OSAS.

On examination, he was obese (BMI 30 kg/m$^2$) and breathless at rest. He was aopyrexial. His heart rate was 90/minute and irregularly irregular. His blood pressure was 134/76 lying. His respiratory rate was 26/minute and his saturation was 90% breathing room air. Positive findings on examination of the cardiovascular system included a pan-systolic murmur, pitting oedema on the thigh, and bilateral expiratory polyphonic wheeze. Do the examination findings modify the differential diagnosis?

No, this is still likely to be multi-factorial. There is evidence to support diagnoses of both cardiac failure, and COPD, and in addition there is a heart valve lesion. The patient’s high BMI increases the likelihood of diagnosing sleep apnoea.
What investigations should be ordered and why?

When breathlessness is likely to be multi-factorial, it is often necessary to perform a variety of tests. Initially, some simple investigations would be appropriate which might include a full blood count (to exclude anaemia), arterial blood gas analysis (as he is hypoxic on air and possibly has respiratory failure), ECG (to examine the heart rhythm), chest X-ray, lung function tests and echocardiogram (given the murmur and peripheral oedema which raise the possibility of cardiac dysfunction). Depending on the results of these it may be necessary to perform more detailed studies.

The initial investigations show that the haemoglobin is normal. The ECG confirmed atrial fibrillation with a rate of 80/minute. The echocardiogram reported an ejection fraction of 45% with mild mitral regurgitation. The arterial blood gas, lung function tests and chest X-ray are shown below. Interpret these results.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.350</td>
</tr>
<tr>
<td>PaO₂ (11–15 kPa)</td>
<td>6.47 kPa</td>
</tr>
<tr>
<td>PaCO₂ (4.5–6.0 kPa)</td>
<td>8.34 kPa</td>
</tr>
<tr>
<td>HCO₃⁻ (24–30 mmol/l)</td>
<td>28.9 mmol/l</td>
</tr>
<tr>
<td>FiO₂</td>
<td>0.21</td>
</tr>
<tr>
<td>FEV₁</td>
<td>1.30 l (60.3% predicted)</td>
</tr>
<tr>
<td>FVC</td>
<td>2.61 l (91.9% predicted)</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>49.66%</td>
</tr>
<tr>
<td>Lung volumes</td>
<td>Not reported</td>
</tr>
<tr>
<td>TLCO</td>
<td>3.64 mmol/min/kPa (55.0% predicted)</td>
</tr>
<tr>
<td>KCO</td>
<td>0.93 mmol/min/kPa/l (78.4% predicted)</td>
</tr>
</tbody>
</table>

The blood gas results indicate fully compensated Type II respiratory failure (normal pH but raised PaCO₂ and raised bicarbonate; PaO₂ < 8 kPa on air). The lung function tests demonstrate an obstructive pathology (FEV₁/FVC < 0.7 or 70%), but the correction of transfer factor also suggests a degree of extrathoracic restriction. The chest X-ray (Figure 1.7) is a PA erect film that is somewhat under-penetrated (too white) and was reported by the radiologist as showing cardiomegaly (the heart size is greater than 50% the distance across the lungs at that point), bilateral calcified pleural plaques (one is clearly visible one-third of the way down the pleural border on the left, for example) and pleural thickening consistent with the patient’s asbestos exposure.

What further investigations may now assist?

This case illustrates the important points that breathlessness may sometimes be multi-factorial, requiring multiple investigations, and that investigations can sometimes give results that conflict with the clinical picture.

Regarding cardiac function, the relatively normal echocardiogram is inconsistent with the clinical findings of oedema, and the patient is known to have ischaemic heart disease. It is often technically difficult to perform echocardiography in subjects with COPD as the chest may be hyper-expanded. It would therefore be important to examine the echocardiography report for comments about the confidence of the results. In addition, given the clinical discrepancy, one may also wish to seek additional evidence of heart failure and for this reason a serum BNP (brain natriuretic peptide) assay could be requested. BNP is released by the ventricles of the heart
when they are stretched, as occurs in heart failure. Like all tests, however, the sensitivity and specificity are not perfect.

Regarding the lung function, a reversibility test was performed and this showed no significant response in FEV₁ and therefore these results are consistent with a degree of COPD. However, the FEV₁ is 60% predicted, suggesting that the disease is of only moderate severity and it would therefore be most unusual for COPD alone to result in hypercapnic respiratory failure without additional diagnoses being present. The history of snoring suggested sleep apnoea and a sleep study subsequently confirmed the OSAS. Finally, while the extra-thoracic restriction may just have reflected his increased BMI, the asbestos exposure and pleural thickening visible on the chest X-ray raised the possibility of more extensive pleural disease. This was investigated further with a high resolution CT scan of the chest that confirmed significant, circumferential pleural thickening.

**Why was this patient breathless and how should he be treated?**

The features contributing to this patient’s breathlessness include raised BMI, moderate COPD, possible cardiac dysfunction, extensive pleural thickening secondary to asbestos exposure and OSAS. Management is therefore aimed at optimising all these diagnoses but the presence of Type II respiratory failure suggests the need for ventilatory support. Simple OSAS may be treated effectively with nasal CPAP but in this case where there is co-existent cardiac and respiratory disease, and Type II respiratory failure, it is preferable to establish the patient on non-invasive ventilation. Despite extensive encouragement and training this patient tolerated non-invasive ventilation poorly and the decision was made not to persist with the treatment. Application of 24% oxygen did not result in decompensation and he was eventually discharged home with long-term oxygen therapy, to use for at least 15 hours per 24-hour period, including the overnight period when desaturations are more likely.
Case study 1.4

A 32-year-old woman with a congenital kyphoscoliosis is referred to the respiratory outpatient department because of progressive breathlessness. She is 26 weeks’ pregnant and, prior to the pregnancy, was not limited by dyspnoea.

Outline your initial approach to her management.

As with all these cases, the initial approach comprises a complete history and examination, followed by appropriate general and specific investigations.

On specific questioning the breathlessness had been slowly progressive from the tenth week of her pregnancy. The severity did not vary aside from this gradual progression, though it was worse on lying down and easier when standing. She had never smoked and there were no apparent occupational or environmental exposures to potential toxins. There were no associated symptoms.

On examination the kyphoscoliosis and gravid uterus were apparent. With the exception of reduced oxygen saturation while breathing room air, at 93%, examination of the cardiorespiratory system was otherwise normal. In particular, her conjunctivae were not pale and there was no peripheral oedema or signs to suggest deep vein thrombosis.

Suggest a differential diagnosis and plan of investigation.

The differential diagnosis here remains wide, and in addition to the conditions described above one must also consider conditions connected with the patient’s pregnancy and kyphoscoliosis. Patients with severe kyphoscoliosis can develop respiratory failure, especially nocturnal hypventilation, that can be remarkably asymptomatic. It is possible that her pregnant uterus is now further compromising her respiratory function. However, pregnancy can also be associated with anaemia, and an increased risk of thrombo-embolic disease, and such diagnoses must also be considered.

Appropriate initial investigations would therefore include full blood count, blood gas analysis, chest radiograph (with shielding of the fetus) and spirometry.

Blood gas analysis revealed a normal pH, PaO₂ of 10.2 kPa and PaCO₂ of 5.8 kPa while breathing room air. The spirometry is given below. Her haemoglobin, and chest X-ray, except for the kyphoscoliosis, were normal. Interpret the results.

<table>
<thead>
<tr>
<th>FEV₁</th>
<th>0.77 l (34% predicted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>0.87 l (33% predicted)</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>88.51%</td>
</tr>
</tbody>
</table>

The normal full blood count excludes anaemia, and the normal X-ray a range of intrinsic lung diseases. Her blood gases demonstrate hypercapnia which, as the pH is normal, must be chronic. The spirometry is consistent with a restrictive process and, in the absence of evidence suggesting intrinsic lung disease the most likely explanation is indeed a worsening of kyphoscoliosis-associated respiratory impairment due to the pregnant uterus. This would also be in keeping with the history of a positional worsening of symptoms.
Case study 1.4  (Continued)

How could this be confirmed?

A sleep study would confirm nocturnal hypoventilation, which is the commonest respiratory complication of kyphoscoliosis. In this case, the sleep study did indeed confirm significant desaturations and the patient was managed successfully with non-invasive ventilation through to an elective caesarean section performed at 36 weeks’ gestation. Non-invasive ventilation was continued for a further 1 week post partum. Four months later her spirometry was as below, and she had returned to her baseline functional capacity.

| FEV₁ | 0.80 l (35% predicted) |
| FVC  | 1.00 l (38% predicted)  |
| FEV₁/FVC | 80.00%       |

Interpret the spirometry.

Although improved following delivery, the spirometry remains abnormal and is still consistent with a restrictive process. Assessment of gas transfer would be useful to confirm that this is indeed extra-thoracic restriction. A repeat sleep study would also be appropriate and, if nocturnal desaturations are still present, nocturnal non-invasive ventilation should be continued to prevent the long-term complication of cor pulmonale.

References


