CHAPTER 4
Respiratory failure

By the end of this chapter you will be able to:

- Understand basic pulmonary physiology
- Understand the mechanisms of respiratory failure
- Know when respiratory support is indicated
- Know which type of respiratory support to use
- Understand the effects of mechanical ventilation
- Apply this to your clinical practice

Basic pulmonary physiology
The main function of the respiratory system is to supply oxygenated blood and remove carbon dioxide. This process is achieved by:

- Ventilation: the delivery and removal of gas to and from the alveoli.
- Gas exchange: oxygen and carbon dioxide (CO₂) cross the alveolar–capillary wall by diffusion.
- Circulation: oxygen is transported from the lungs to the cells and carbon dioxide is transported from the cells to the lungs. The concept of oxygen delivery has been outlined in Chapter 2 and will not be discussed further here.

When it comes to respiratory failure, there are two types: failure to ventilate and failure to oxygenate. An understanding of basic pulmonary physiology is important in understanding why respiratory failure occurs.

Ventilation
During inspiration, the volume of the thoracic cavity increases, due to contraction of the diaphragm and movement of the ribs, and air is actively drawn into the lung. Beyond the terminal bronchioles is the respiratory zone, where the surface area of the lung is huge and diffusion of gas occurs. The lung is elastic and returns passively to its pre-inspiratory volume on expiration. The lung is also very compliant – a normal breath requires only 3 cmH₂O of pressure.

A normal breath (500 ml) is only a small proportion of total lung volume, shown diagrammatically in Fig. 4.1. Of each 500 ml inhaled, 150 ml stays in the anatomical deadspace and does not take part in gas exchange. Most of the rest of the gas which enters the respiratory zone takes part in alveolar ventilation, but around 5% does not due to normal ventilation–perfusion (V/Q) mismatch,
Respiratory failure

and this is called the alveolar deadspace. The anatomical plus alveolar deadspace is called the physiological deadspace. In health, the anatomical and physiological deadspaces are almost the same.

V/Q mismatch can increase in disease. If ventilation is reduced to a part of the lung and blood flow remains unchanged, alveolar O₂ will fall and CO₂ will rise in that area, approaching the values of venous blood. If blood flow is obstructed to a part of the lung and ventilation remains unchanged, alveolar O₂ will rise and CO₂ will fall in that area, approaching the values of inspired air. The V/Q ratio therefore lies along a continuum, ranging from zero (perfusion but no ventilation, i.e. shunt) to infinity (ventilation but no perfusion, i.e. increased deadspace).

When PaO₂ falls and PaCO₂ rises due to V/Q mismatch, normal people increase their overall alveolar ventilation to compensate. This corrects the hypercapnia but only partially the hypoxaemia due to the different shapes of the O₂ and CO₂ dissociation curves.

The alveolar–arterial (A-a) gradient is a measure of V/Q mismatch and is discussed later.

The mechanics of ventilation are complex. Surfactant plays an important role in the elastic properties of the lung (and is depleted in acute respiratory distress syndrome). The lungs tend to recoil while the thoracic cage tends to expand slightly. This creates a negative intrapleural pressure, which increases during

---

**Figure 4.1** Normal lung volumes. The closing volume (CV) is the volume at which the dependent airways begin to collapse, or close. It is normally about 10% of the vital capacity and increases to about 40% by the age of 65 years.
inspiration, because as the lung expands, its elastic recoil increases. Fig. 4.2 shows the pressure changes which occur in the alveolus during normal breathing.

Ventilation is controlled in the brainstem respiratory centres, with input from the cortex (voluntary control). The muscles which affect ventilation are the diaphragm, intercostals, abdominal muscles and the accessory muscles (e.g. sternomastoids). Ventilation is sensed by central and peripheral chemoreceptors, and other receptors in the lungs. Normally, PaCO₂ is the most important factor in the control of ventilation but the sensitivity to changes in PaCO₂ is reduced by sleep, older age and airway resistance (e.g. in chronic obstructive pulmonary disease (COPD)). Other factors which increase ventilation include hypoxaemia, low arterial pH and situations which increase oxygen demand (e.g. sepsis).

Oxygenation
Oxygen tension in the air is around 20 kPa (154 mmHg) at sea level, falling to around 0.5 kPa (3.8 mmHg) in the mitochondria. This gradient is known as the ‘oxygen cascade’ (illustrated in Fig. 4.3). Therefore, an interruption at any point along this cascade can cause hypoxia (e.g. high altitude, upper or lower airway obstruction, alveolar problems, abnormal haemoglobins, circulatory failure or mitochondrial poisoning).

If a patient is breathing 60% oxygen and his/her PaO₂ is 13 kPa (100 mmHg), it can be seen that there is a significant problem with gas exchange – the ‘normal’ value of 13 kPa is not normal at all in the context of a high inspired oxygen concentration (FiO₂). With normal lungs, the predicted PaO₂ is roughly 10 kPa (75 mmHg) below the FiO₂. Problems with gas exchange occur at the alveolar-arterial (A-a) step of the oxygen cascade (D to E in Fig. 4.3). Normal people have a small A-a difference because the bronchial veins of the lung and Thebesian veins of the heart carry unsaturated blood directly to the left ventricle, bypassing the alveoli. Large differences are always due to pathology.

In the example above, one can see the difference between FiO₂ and PaO₂ without a calculation. However, the difference between alveolar and arterial oxygen (the A-a gradient) can be measured using the alveolar gas equation.
Oxygen leaves the alveolus in exchange for carbon dioxide. Arterial and alveolar PCO2 are virtually the same. If we know the composition of inspired gas and the respiratory exchange ratio ($R$), then the alveolar oxygen concentration can be calculated. (The respiratory exchange ratio allows for metabolism by the tissues.) To convert FiO2 into the partial pressure of inspired O2, we have to adjust for barometric pressure, water vapour pressure and temperature. Assuming sea level (101 kPa or 760 mmHg), inspired air which is 100% humidified (water vapour pressure 6 kPa or 47 mmHg) and 37°C, the alveolar gas equation is as follows:

$$P_{A\,O_2} = F_{O_2} \left(P_B - P_{A\,H_2O}\right) - P_{A\,CO_2}/0.8$$

- $P_{A\,O_2}$: alveolar PO2
- $F_{O_2}$: fraction of inspired oxygen
- $P_B$: barometric pressure of 101 kPa
- $P_{A\,H_2O}$: alveolar partial pressure of water of 6 kPa
- $P_{A\,CO_2}$: alveolar PCO2
- 0.8: the respiratory exchange ratio (or respiratory quotient).

Once $P_{A\,O_2}$ has been estimated, the A-a gradient is calculated as $P_{A\,O_2} - PaO_2$. A normal A-a gradient is up to 2 kPa (15 mmHg) or 4 kPa (30 mmHg) in smokers and the elderly.
For example, a person breathing air with a PaO₂ of 12.0 kPa and a PaCO₂ of 5.0 kPa has an A-a gradient as follows:

\[
\text{PAO}_2 = F_iO_2 \times (P_B - PaH_2O) - PaCO_2/0.8 \\
\text{PAO}_2 = 0.21 \times 95 - 5/0.8
\]

When calculating the A-a gradient on air, 0.21 \times 95 is often shortened to 20.

\[
20 - 5/0.8 = 13.75
\]

The A-a gradient is therefore 13.75 \( - 12 = 1.75 \text{ kPa} \).

The calculation of the A-a gradient illustrates the importance of always documenting the inspired oxygen concentration on an arterial blood gas report, otherwise problems with oxygenation may not be detected. Some applications of the A-a gradient are illustrated in the case histories at the end of this chapter.

**The mechanisms of respiratory failure**

Respiratory failure is said to be present when there is PaO₂ of \(< 8.0 \text{ kPa} \) (60 mmHg), when breathing air at sea level without intracardiac shunting. It occurs with or without a high PaCO₂.

Traditionally, respiratory failure is divided into type 1 and type 2, but these are not practical terms and it is better to think instead of:

- Failure to ventilate
- Failure to oxygenate
- Failure to both ventilate and oxygenate.

**Failure to ventilate**

V/Q mismatch causes a high PaCO₂, as mentioned earlier. But hypercapnic respiratory failure occurs when the patient cannot compensate for a high PaCO₂ by increasing overall alveolar ventilation and this usually occurs in conditions which cause alveolar hypoventilation.

Fig. 2.8 illustrated how respiratory muscle load and respiratory muscle strength can be affected by disease and an imbalance leads to alveolar hypoventilation. To recap, respiratory muscle load is increased by increased resistance (e.g. upper or lower airway obstruction), reduced compliance (e.g. infection, oedema, rib fractures or obesity) and increased respiratory rate (RR). Respiratory muscle strength can be reduced by a problem in any part of the neuro-respiratory pathway: motor neurone disease, Guillain–Barré syndrome, myasthenia gravis or electrolyte abnormalities (low potassium, magnesium, phosphate or calcium). Drugs which act on the respiratory centre, such as morphine, reduce total ventilation.

Oxygen therapy corrects hypoxaemia which occurs as a result of V/Q mismatch or alveolar hypoventilation.
Failure to oxygenate
Although there are many potential causes of hypoxaemia, as illustrated by the oxygen cascade, the most common causes of failure to oxygenate are:
- V/Q mismatch
- Intrapulmonary shunt
- Diffusion problems.

V/Q mismatch
If the airways are impaired by the presence of secretions or narrowed by bronchoconstriction, that segment will be perfused but only partially ventilated. The resulting V/Q mismatch will result in hypoxaemia and hypercapnia. The patient will increase his/her overall alveolar ventilation to compensate. Giving supplemental oxygen will cause the PaO₂ to increase.

Intrapulmonary shunt
If the airways are totally filled with fluid or collapsed, that segment will be perfused but not ventilated at all (see Fig. 4.4). Mixed venous blood is shunted across it. Increasing the inspired oxygen in the presence of a moderate to severe shunt will not improve PaO₂. Intrapulmonary shunting as a cause of hypoxaemia is observed in pneumonia and atelectasis.

V/Q mismatch and intrapulmonary shunting can often be distinguished by the response of the patient to supplemental oxygen. With a large shunt, hypoxaemia cannot be abolished even by giving the patient high-concentration oxygen. Small reductions in inspired oxygen may lead to a large reduction in PaO₂ because of the relatively steep part of the oxygen dissociation curve (see Fig. 2.11).

Figure 4.4 V/Q mismatch vs shunt.
Diffusion problems
Some conditions affect the blood–gas barrier (e.g. fibrosis), which is normally extremely thin, leading to ineffective diffusion of gas. The response to supplemental oxygen reduces with increasing severity of disease.

With V/Q mismatch, intrapulmonary shunt and diffusion problems, there is adequate ventilation but inadequate gas exchange and therefore a low PaO2 with a normal or low PaCO2 is seen.

Failure to both ventilate and oxygenate
Post-operative respiratory failure is an example of a situation where problems with gas exchange are accompanied by hypoventilation, leading to hypoxaemia (despite oxygen therapy) as well as hypercapnia. In post-operative respiratory failure, the hypoxaemia is caused by infection and atelectasis due to a combination of supine position, the effects of general anaesthesia and pain. A reduction in functional residual capacity below closing volume also contributes leading to airway collapse in the dependent parts of the lung (see Fig. 4.1). The hypercapnia is caused by excessive load from reduced compliance and increased minute volume in combination with opiates which depress ventilation. At-risk patients are those with pre-existing lung disease, who are obese or who have upper abdominal or thoracic surgery. Box 4.1 outlines the measures to prevent post-operative respiratory failure.

Respiratory support
Ideally, patients with acute respiratory failure which does not rapidly reverse with medical therapy should be admitted to a respiratory care unit or other level 2–3 facility. Hypoxaemia is the most life-threatening facet of respiratory failure. The goal of treatment is to ensure adequate oxygen delivery to the tissues which is generally achieved with a PaO2 of at least 8.0 kPa (60 mmHg) or SpO2 of at least 93%. However, patients with chronic respiratory failure require different therapeutic targets than patients with previously normal lungs. One would not necessarily aim for normal values in these patients.

Box 4.1 Preventing post-operative respiratory failure
- Identify high-risk patients pre-operatively: pre-existing lung disease, upper abdominal or thoracic surgery, smokers (impaired ciliary transport), obesity
- Use regional analgesia if possible
- Early post-operative chest physiotherapy
- Humidified oxygen
- Avoid use of drugs which may depress ventilation
- Early identification of pneumonia
- Early use of CPAP
Apart from oxygen therapy (see Chapter 2) and treatment of the underlying cause, various forms of respiratory support are used in the treatment of respiratory failure. There are two main types of respiratory support: non-invasive and invasive. Non-invasive respiratory support consists of either bilevel positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP), administered via a tight-fitting mask. Invasive respiratory support, on the other hand, requires endotracheal intubation and comes in several different modes.

‘Respiratory support’ does not necessarily mean mechanical ventilation. For example, CPAP is not ventilation, as will be explained later. The ABCDE (airway, breathing, circulation, disability, examination and planning) approach is still important, and should be used to assess and manage any patient with respiratory failure (see Box 4.2).

Respiratory support is indicated when:
- There is a failure to oxygenate or ventilate despite medical therapy
- There is unacceptable respiratory fatigue
- There are non-respiratory indications for tracheal intubation and ventilation (e.g. the need for airway protection).

Once a decision has been made that a patient needs respiratory support, the next question is, which type? Failure to ventilate is treated by manoeuvres

**Box 4.2 Approach to the patient with respiratory failure**

**Action**

A  Assess and treat any upper airway obstruction  
   Administer oxygen

B  **Look** at the chest: assess rate, depth and symmetry  
   Measure SpO₂  
   Quickly listen with a stethoscope (for air entry, wheeze, crackles)  
   You may need to use a bag and mask if the patient has inadequate ventilation  
   Treat wheeze, pneumothorax, fluid, collapse, infection etc  
   Is a physiotherapist needed?

C  Fluid challenge(s) or rehydration may be needed  
   Vasoactive drugs may be needed if severe sepsis is also present (see Chapter 6)

D  Assess conscious level as this affects treatment options

E  Are ABCD stable? If not, go back to the top and call for help  
   Arterial blood gases  
   Gather more information (e.g. usual lung function)  
   Decide if and what type of respiratory support is needed  
   Make ICU and cardio-pulmonary resuscitation (CPR) decisions now  
   Do not move an unstable patient without the right monitoring equipment and staff  
   Call a senior colleague (if not already called)
designed to increase alveolar minute ventilation by increasing the depth and rate of breathing. Failure to oxygenate, however, is treated by restoring and maintaining lung volumes using alveolar recruitment manoeuvres such as the application of a positive end-expiratory pressure (PEEP or CPAP). Fig. 4.5 summarises the different types of respiratory support.

There is considerable evidence available as to what works best in different clinical situations [1]. This information is important. For example, there is no evidence that ‘trying’ non-invasive ventilation (NIV) in a young person with life-threatening asthma is of any benefit. The first-line methods of respiratory support for different conditions are shown in Fig. 4.6.

Figure 4.5 Different types of respiratory support. BiPAP: bilevel positive pressure ventilation; IPPV: intermittent positive pressure ventilation; CPAP: continuous positive airway pressure; SIMV: synchronised intermittent mandatory ventilation; PSV: pressure support ventilation.

<table>
<thead>
<tr>
<th>Tracheal intubation</th>
<th>Non-invasive ventilation (NIV/BiPAP)</th>
<th>Non-invasive CPAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>COPD with respiratory acidosis causing pH 7.25–7.35</td>
<td>Acute cardiogenic pulmonary oedema</td>
</tr>
<tr>
<td>ARDS (acute respiratory distress syndrome)</td>
<td>Decompensated sleep apnoea</td>
<td>Hypoxaemia in chest trauma/atelectasis</td>
</tr>
<tr>
<td>Severe respiratory acidosis causing pH &lt;7.25</td>
<td>Acute on chronic hypercapnic respiratory failure due to chest wall deformity or neuromuscular disease</td>
<td></td>
</tr>
<tr>
<td>Any cause with impaired conscious level</td>
<td>Pneumonia*</td>
<td></td>
</tr>
</tbody>
</table>

*If NIV or CPAP is used as a trial of treatment in pneumonia in patients without COPD or post-operative respiratory failure, this should be done on an ICU with close monitoring and rapid access to intubation. Patients with excessive secretions may also require tracheal intubation.

Figure 4.6 First-line methods of respiratory support for different conditions.
Non-invasive respiratory support

Non-invasive respiratory support will be more familiar to people who do not work on an intensive care unit (ICU). BiPAP and CPAP are the two main types of non-invasive respiratory support. Non-invasive BiPAP is also referred to as NIV. The ventilator cycles between two different pressures triggered by the patient’s own breathing, the higher inspiratory positive airway pressure (IPAP) and the lower expiratory positive airway pressure (EPAP). In CPAP a single positive pressure is applied throughout the patient’s respiratory cycle. The difference between non-invasive BiPAP and CPAP is shown in Fig. 4.7.

Non-invasive respiratory support is contraindicated in:

- Recent facial or upper airway surgery, facial burns or trauma
- Vomiting
- Recent upper gastrointestinal surgery or bowel obstruction
- Inability to protect own airway
- Copious respiratory secretions
- Other organ system failure (e.g. haemodynamic instability)
- Severe confusion/agitation.

However, non-invasive BiPAP is sometimes used in drowsy or confused patients if it is decided that the patient is not suitable for tracheal intubation because of severe chronic lung disease.

Non-invasive BiPAP

Non-invasive ventilators have a simpler design compared with the ventilators on an ICU. This is because most were originally designed for home use. The

![Figure 4.7](image-url) The difference between (a) non-invasive BiPAP and (b) CPAP. With non-invasive BiPAP, mechanical ventilation is superimposed on spontaneous breathing (see also Fig. 4.12).
disadvantage of this is that some are not adequately equipped in terms of monitoring and alarms when used in hospital.

The operator has to choose the appropriate type and size of mask and set basic ventilator controls: supplementary oxygen flow rate, IPAP, EPAP, backup respiratory rate (RR) and inspiratory time or inspiration to expiration (I:E) ratio.

Non-invasive BiPAP is used in certain patients with a mild-to-moderate acute respiratory acidosis (see Fig. 4.6). In an acute exacerbation of COPD, it is usual to begin with an IPAP of 15 cmH2O and an EPAP of 5 cmH2O. The levels are then adjusted based on patient comfort, tidal volume achieved (if measured) and arterial blood gases.

The main indications for non-invasive BiPAP in the acute setting are:
- Exacerbation of COPD (pH low due to acute respiratory acidosis)
- Weaning from invasive ventilation.

There is a large body of evidence supporting non-invasive BiPAP in acute exacerbations of COPD (see Mini-tutorial: NIV for exacerbations of COPD). Non-invasive BiPAP can also be used as a step-down treatment in patients who have been intubated and ventilated on ICU. Weaning problems occur in at least 60% patients with COPD and this is a major cause of prolonged ICU stay. A randomised multi-centre trial has shown that non-invasive BiPAP is more successful in weaning than a conventional approach in patients with COPD [2]. Patients who failed a T-piece trial (breathing spontaneously with no support) 48 h after intubation were randomly assigned to receive either non-invasive BiPAP immediately after extubation or conventional weaning (a gradual reduction in ventilator support). The non-invasive BiPAP group took a shorter time to wean, had shorter ICU stays, a lower incidence of hospital-acquired pneumonia and increased 60-day survival. Other studies have reported similar findings.

Early trials of non-invasive BiPAP for pneumonia were discouraging, but a later prospective randomised trial of non-invasive BiPAP in community-acquired pneumonia (56 patients) showed a significant fall in RR and the need for intubation [3]. However, half of the patients in this study had COPD and it was carried out in an ICU. Previously well patients who require ventilation for pneumonia should be referred to an ICU as they are likely to need tracheal intubation.

Non-invasive CPAP
Non-invasive CPAP was first introduced in the 1980s as a therapy for obstructive sleep apnoea (OSA). A tight-fitting face or nasal mask delivers a single positive pressure throughout the patient’s respiratory cycle. In OSA, CPAP prevents pharyngeal collapse. CPAP can also be delivered through an endotracheal tube or tracheostomy tube in spontaneously breathing patients and is used this way during weaning from the ventilator.

The main indications for non-invasive CPAP in the acute setting are:
- To deliver increased oxygen in pneumonia or post-operative respiratory failure associated with atelectasis
- Acute cardiogenic pulmonary oedema.
Mini-tutorial: NIV for exacerbations of COPD

An exacerbation of COPD requiring admission to hospital carries a 6–26% mortality [5]. One study found a 5-year survival of 45% after discharge and this reduced to 28% with further admissions [6]. Invasive ventilation for an exacerbation of COPD has an even higher mortality [7]. Ventilator-associated pneumonia is common and increases mortality still further. Non-invasive BiPAP is associated with less complications than tracheal intubation (see Fig. 4.8).

Most studies of non-invasive BiPAP in acute exacerbations of COPD have been performed in critical care areas. There have been at least half a dozen prospective randomised-controlled trials of non-invasive BiPAP vs standard care in acute exacerbations of COPD. The studies performed in ICUs showed a reduction in intubation rates and some also showed reduced mortality when compared to conventional medical therapy. None have directly compared non-invasive BiPAP with tracheal intubation. A multi-centre randomised-controlled trial of non-invasive BiPAP in general respiratory wards showed both a reduced need for intubation and reduced hospital mortality [8]. Patients with a pH below 7.3 on enrolment had a significantly higher failure rate and in-hospital mortality than those with an initial pH over 7.3, whether they received non-invasive BiPAP or not. It is therefore recommended that patients with a pH below 7.3 are monitored in a facility with ready access to tracheal intubation.

Non-invasive BiPAP should be commenced as soon as the pH falls below 7.35 because the further the degree of acidosis, the less the chances of improvement. It should be used as an adjunct to full medical therapy which treats the underlying cause of acute respiratory failure. In a 1-year prevalence study of nearly 1000 patients admitted with an exacerbation of COPD in one city, around 1 in 5 were acidic on arrival in the Emergency Department, but 20% of these had a normal pH by the time they were admitted to a ward [9]. This included patients with an initial pH of <7.25, and suggests that non-invasive BiPAP should be commenced after medical therapy and controlled oxygen has been administered.

Patients on non-invasive BiPAP require close supervision because sudden deterioration can occur at any time. Simple measures, such as adjusting the mask to reduce excessive air leaks can make a difference to the success or otherwise of treatment. Basic vital signs frequently measured give an indication of whether or not non-invasive BiPAP is being effective. If non-invasive BiPAP does not improve respiratory acidosis in the first 2 h, tracheal intubation should be considered.

Predictors of failure of non-invasive BiPAP in an acute exacerbation of COPD are:
- No improvement within 2 h
- High APACHE II score (Acute Physiological and Chronic Health Evaluation)
- Pneumonia
- Very underweight patient
- Neurological compromise
- pH <7.3 prior to starting NIV.

The updated UK guidelines on non-invasive BiPAP for exacerbations of COPD can be found on the British Thoracic Society website [4].
Chapter 4

CPAP is employed in patients with acute respiratory failure to correct hypoxaemia. In the spontaneously breathing patient, the application of CPAP provides positive end-expiratory pressure (PEEP) that can reverse or prevent atelectasis, improve functional residual capacity and oxygenation. These improvements may prevent the need for tracheal intubation and can sometimes reduce the work of breathing. However, in patients with problems causing alveolar hypoventilation, mechanical ventilation rather than CPAP is more appropriate.

The inspiratory flow in a CPAP circuit needs to be high enough to match the patient’s peak inspiratory flow rate. If this is not achieved, the patient will breathe against a closed valve with the risk that the generation of significant negative intrapleural pressure will lead to the development of pulmonary oedema. Look at the expiratory valve on a CPAP circuit in use. The valve should remain slightly open during inspiration (see Fig. 4.9).

Meta-analysis shows that non-invasive CPAP reduces the need for tracheal intubation in patients with acute cardiogenic pulmonary oedema (numbers needed to treat = 4) with a trend towards a reduction, but no significant difference in mortality [10].
In acute cardiogenic pulmonary oedema, CPAP ‘squeezes’ fluid out of the alveoli into the circulation. There is a decline in the level of shunt because of redistribution of lung water from the alveolar space to the perivascular cuffs.

CPAP also has cardiovascular effects:

- **Left ventricular function** is improved because afterload is reduced (leading to an increase in stroke volume (SV)). This occurs because the increased intrathoracic pressure has a squeezing effect on the left ventricle. There is a subsequent reduction in the pressure gradient between the ventricle and the aorta which has the effect of reducing the work required during contraction (the definition of afterload) (see Fig. 4.10).
- Relief of respiratory distress leads to haemodynamic improvement and reversal of hypertension and tachycardia – probably through reduced sympathoadrenergic stimulation.

Non-invasive CPAP in acute cardiogenic pulmonary oedema is indicated when the patient has failed to respond to full medical therapy and there is an acute respiratory acidosis or hypoxaemia despite high-concentration oxygen therapy. However, patients who do not respond quickly to non-invasive CPAP should be referred for tracheal intubation.

**Invasive respiratory support**

In the past ‘iron lungs’ were used to apply an intermittent negative pressure to the thorax, thus inflating the lungs, but manual intermittent positive pressure
ventilation (IPPV) was introduced during a large polio epidemic in Copenhagen in 1952. Mortality rates were lower than with previously used techniques. This heralded the introduction of ICUs.

ICU ventilators are set to deliver either a certain volume or a certain pressure when inflating the lungs. This is termed ‘volume-control’ or ‘pressure-control’ ventilation. These different modes of ventilation have their own advantages and disadvantages (see Fig. 4.11).

In volume-controlled ventilation, inhalation proceeds until a preset tidal volume is delivered and this is followed by passive exhalation. The set tidal volume is calculated from flow over a time period. A feature of this mode is that gas is often delivered at a constant inspiratory flow rate, resulting in peak pressures applied to the airways higher than that required for lung distension. Since the volume delivered is constant, airway pressures vary with changing pulmonary compliance and airway resistance. A major disadvantage is that excessive airway pressure may be generated, resulting in barotrauma, and so a pressure limit should be set by the operator.

In pressure-controlled ventilation a constant inspiratory pressure is applied and the pressure difference between the ventilator and lungs results in inflation until that pressure is attained. Passive exhalation follows. The volume delivered is dependent on pulmonary and thoracic compliance. A major advantage of pressure control is use of a decelerating inspiratory flow pattern, in which inspiratory flow tapers off as the lung inflates. This usually results in a more homogenous gas distribution throughout the lungs. A disadvantage is that dynamic changes in pulmonary mechanics may result in varying tidal volumes.

Sophisticated ventilators have been manufactured which incorporate the advantages of both modes and also interact with patients. ICU ventilators can switch between modes, so they can adapt to clinical circumstances and also facilitate weaning from the ventilator as the patient recovers. Ventilator modes are often described by what initiates the breath (trigger variable), what controls gas delivery during the breath (target or limit variable) and what terminates the breath (cycle variable). Hence, for example, BiPAP is machine or patient triggered, pressure targeted and time cycled.

<table>
<thead>
<tr>
<th>Volume control</th>
<th>Pressure control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td></td>
</tr>
<tr>
<td>Delivers a set tidal volume no matter what pressure this requires.</td>
<td>If airway pressures are high, only small tidal volumes will be delivered.</td>
</tr>
<tr>
<td>This can cause excessively high peak pressures and barotrauma</td>
<td>Not good if lung compliance keeps changing</td>
</tr>
<tr>
<td>Leaks</td>
<td></td>
</tr>
<tr>
<td>Poor compensation</td>
<td>Compensates for leaks well (e.g. poor fitting mask or circuit fault)</td>
</tr>
<tr>
<td>PEEP</td>
<td></td>
</tr>
<tr>
<td>Some flow/volume control ventilators cannot apply PEEP</td>
<td>PEEP easily added</td>
</tr>
</tbody>
</table>

**Figure 4.11** Advantages and disadvantages of volume vs pressure control. PEEP: positive end-expiratory pressure.
The most commonly used ventilator modes on ICU are:

- **BiPAP**
- **SIMV** (synchronised intermittent mandatory ventilation)
- **pressure support ventilation (PSV)** also known as assisted spontaneous breaths (ASB)
- **CPAP**.

In the ICU setting, BiPAP is considered to be a single mode of ventilation that covers the entire spectrum of mechanical ventilation to spontaneous breathing. When the patient has no spontaneous breaths the ventilator acts as a pressure-controlled ventilator. When the patient has spontaneous breaths, the ventilator synchronises intermittently with the patient's breathing and spontaneous breaths can occur during any phase of the respiratory cycle without increasing airway pressure above the set maximum level, as can occur with conventional pressure-controlled ventilation (so-called ‘fighting’ the ventilator). When the patient is able to breathe more adequately, pressure support is used to augment every spontaneous breath.

The waveforms of these different ventilator modes are shown in Fig. 4.12.

The operator of an ICU ventilator can adjust the following main variables: FiO₂, the inspiratory pressure, expiratory pressure (PEEP), backup RR, inspiratory time or I:E ratio and alarm limits (e.g. minimum and maximum tidal volumes).

**PEEP**

PEEP prevents the collapse of alveoli and this has several benefits:

- Improvement of V/Q matching
- Reduced lung injury from shear stresses caused by repeated opening and closing
- Prevention of surfactant breakdown in collapsing alveoli leading to improved lung compliance.

Lung disease is usually heterogeneous so recruitment of alveoli in one part of the lung may cause over-distension in another. PEEP also increases mean intrathoracic pressure which can reduce cardiac output (CO). PEEP is normally set to 5 cmH₂O and increased if required. ‘Best PEEP’ for a particular patient can be elucidated from a ventilator’s pressure-volume loop display.

**The effects of mechanical ventilation**

During IPPV there is reversal of the thoracic pump – the normal negative intrathoracic pressure during spontaneous inspiration which draws blood into the chest from the vena cavae, a significant aspect of venous return. With IPPV, venous return decreases during inspiration, and if PEEP is added venous return could be impeded throughout the respiratory cycle. This can cause hypotension. The degree of impairment of venous return is directly proportional to the mean intrathoracic pressure. So changes in ventilatory pattern, not just pressures, can cause cardiovascular changes.

At high lung volumes the heart may be directly compressed by lung expansion. This prevents adequate filling of the cardiac chambers. Ventricular
Chapter 4

contractility is also affected. Elevated intrathoracic pressures directly reduce the left and right ventricular ejection pressure which is the difference between the pressure inside and outside the ventricular wall during systole. As a result, SV is reduced for a given end-diastolic volume.

IPPV can also reduce renal, hepatic and splanchnic blood flow.

These physiological changes during IPPV can be precipitously revealed when intubating critically ill patients. Marked hypotension and cardiovascular collapse can occur as a result of uncorrected volume depletion prior to tracheal intubation. This is compounded by the administration of anaesthetic drugs which cause vasodilatation and reduce circulating catecholamine levels as the patient loses consciousness.

The effects of mechanical ventilation are not as severe when the patient is awake and breathing spontaneously.

Although mechanical ventilation can be life saving for people with respiratory failure, poorly applied ventilation techniques can not only cause cardiovascular

---

**Figure 4.12** Waveforms of different ventilator modes. (a) BiPAP in a paralysed patient (i.e. no spontaneous breaths); (b) SIMV. There are spontaneous breaths between mechanical breaths. The ventilator synchronises mechanical breaths so that the lungs are not inflated during inspiration; (c) Augmented PSV (pressure support ventilation). The ventilator assists every spontaneous breath; (d) CPAP. Spontaneous ventilation plus a continuous positive airway pressure.
compromise but can also damage lung tissue and lead to ventilator-induced lung injury (VILI). In particular, large tidal volumes and extreme cyclical inflation and deflation have been shown to worsen outcome in acute lung injury (see Chapter 6).

**Mini-tutorial: tracheal intubation in acute severe asthma**

Tracheal intubation and ventilation can be a life-saving intervention. If indicated, it is important that it is performed sooner rather than later in acute severe asthma (when there is no response to maximum medical therapy). However, 10-min preparation beforehand is time well spent, particularly in those who are most unstable, as cardiovascular collapse can occur due to uncorrected volume depletion, the abolition of catecholamine responses and vasodilatation when anaesthetic drugs are given. Patients should be volume loaded prior to induction of anaesthesia and a vasopressor (e.g. ephedrine) kept ready to treat hypotension. Anaesthetic drugs are given cautiously to minimise any vasodilatory effect and drugs that cause histamine release are avoided if possible. In severe life-threatening asthma, maximum medical therapy might mean intravenous (i.v.) salbutamol, magnesium sulphate, hydrocortisone and nebulised or subcutaneous adrenaline [11]. Therapy should be started while preparations to intubate are underway. Following tracheal intubation, the patient is ventilated with a long expiratory time and this may mean only 6–8 breaths/min is possible. ‘Permissive hypercapnia’ is the term used when the PaCO₂ is allowed to rise in such situations, in order to prevent ‘stacking’. This is when the next positive pressure is delivered before there has been enough time for expiration to occur (prolonged in severe lower airway obstruction). The lung volume slowly expands, reducing venous return and leading to a progressive fall in CO and BP. This is corrected by disconnecting the ventilator and allowing passive expiration to occur (which can take several seconds). The updated UK asthma guidelines can be found on the British Thoracic Society web site [12].

An algorithm outlining the management of respiratory failure is shown in Fig. 4.13.

**Key points: respiratory failure**

- Respiratory failure is characterised by a failure to ventilate or a failure to oxygenate or both.
- Treatment consists of oxygen therapy and treatment of the underlying cause.
- If there is no improvement, respiratory support is indicated and the type of respiratory support depends on the clinical situation.
- Respiratory support can be non-invasive (via a tight-fitting mask) or invasive (tracheal intubation).
- ICU ventilators utilise several different ventilator modes depending on the clinical situation.
- Invasive mechanical ventilation is associated with cardiovascular effects and VILI.
Self-assessment: case histories

1 A previously well 30-year-old woman is admitted in a coma from a drug overdose and responds only to painful stimuli. Arterial blood gases on air show: pH 7.24, PaCO₂ 8.32 kPa (64 mmHg), st bicarbonate 29 mmol/l, base excess (BE) -3, PaO₂ 7.8 kPa (60 mmHg). The Emergency Department doctor diagnoses drug intoxication with aspiration pneumonia because of the hypoxaemia. What is your assessment?

2 Twenty-four hours later you are asked to assess the same patient for discharge as the hospital is in need of beds. She is alert and orientated, and her repeat arterial blood gases on air show: pH 7.6, PaCO₂ 3.1 kPa (24 mmHg), st bicarbonate 22 mmol/l, BE -3, PaO₂ 9.1 kPa (70 mmHg). Should you discharge this patient?

3 A 24-year-old woman is admitted with acute severe asthma. Her vital signs are as follows: BP 100/60 mmHg, pulse 130/min, RR 40/min with poor respiratory effort, temperature 37°C and she is drowsy. Her arterial blood gases on 15 l/min oxygen via reservoir bag mask show: pH 7.15, PaCO₂
Respiratory failure

9.0 kPa (70 mmHg), st bicarbonate 22 mmol/l, BE −3, PaO₂ 7 kPa (54 mmHg). What is your management?

Later on, in ICU the same patient develops hypotension (60/30 mmHg). The patient is sedated and paralysed, and the ventilator is set to 12 breaths/min. The inspiratory to expiratory ratio is 1:4, tidal volumes are 600 ml and peak airway pressures are 45 cmH₂O. What are the possible causes of the hypotension and what is your management?

A 50-year-old man is admitted with an exacerbation of his COPD. His arterial blood gases on a 28% Venturi mask show: pH 7.3, PaCO₂ 8.0 kPa (62 mmHg), st bicarbonate 29 mmol/l, BE +3, PaO₂ 7 kPa (54 mmHg). What is your management?

A 40-year-old man with no past medical history is admitted with severe pneumonia. His vital signs are: BP 120/70 mmHg, pulse 110/min, RR 40/min, temperature 38°C and he is alert. His arterial blood gases on 15 l/min oxygen via reservoir bag mask show: pH 7.31, PaCO₂ 4.0 kPa (31 mmHg), PaO₂ 6 kPa (46 mmHg), st bicarbonate 14 mmol/l, BE −7. What should you do?

A 50-year-old woman is admitted with breathlessness. On examination she has a BP of 80 mmHg systolic which can only be measured by palpation. Her pulse is 110/min, RR 36/min and she is alert. Her chest sounds clear. The ECG shows sinus tachycardia with T-wave inversion in leads V₁–V₆ and her chest X-ray is normal. Arterial blood gases on 15 l/min oxygen via reservoir bag mask show: pH 7.25, PaCO₂ 3.0 kPa (23 mmHg), st bicarbonate 10 mmol/l, BE −12, PaO₂ 12 kPa (92 mmHg). What is the diagnosis and what is your management?

A 70-year-old man with COPD is admitted in extremis. He has been more breathless for a few days. He responds to painful stimuli only, his BP is 130/60 mmHg, pulse 120/min and arterial blood gases on air show: pH 7.1, PaCO₂ 14.0 kPa (108 mmHg), st bicarbonate 20 mmol/l, BE −5, PaO₂ 6 kPa (46 mmHg). What is your management?

**Self-assessment: discussion**

1 There is a low pH (acidaemia) due to a high PaCO₂ – a respiratory acidosis. The st bicarbonate is normal/high as expected. The PaO₂ is low. In this
situation, the PaO$_2$ could be low because of upper airway obstruction, aspiration pneumonia or hypoventilation caused by the drug overdose. The patient can be assessed clinically for signs of airway obstruction and the A-a gradient can be calculated to distinguish between a problem with gas exchange or hypoventilation. PAO$_2 = 0.21 \times 95 - 8.32/0.8 = 9.6$ kPa. The A-a gradient is therefore $9.6 - 7.8 = 1.8$ kPa which is normal. This suggests hypoventilation rather than pneumonia is the cause of the low PaO$_2$. The management in this case still starts with ABC.

2 There is a high pH (alkalaemia) due to a low PaCO$_2$. The st bicarbonate is normal/low as expected. The PaO$_2$ has improved from before, but is still below the expected value. The A-a gradient can be calculated. PAO$_2 = 0.21 \times 95 - 3.1/0.8 = 16.1$ kPa. The A-a gradient is therefore $16.1 - 9.1 = 7$ kPa which is abnormal. This could be explained by the development of aspiration pneumonia and requires further evaluation. The patient should not be discharged.

3 There is a low pH (acidaemia) due to a high PaCO$_2$ – a respiratory acidosis. The st bicarbonate is normal/high as expected. The PaO$_2$ is very low when compared with the F$_{2}$O$_2$ of approximately 0.8 (or 80%). Nine per cent of people with an attack of acute severe asthma have respiratory failure. One per cent patients with asthma have a fatal or near-fatal attack each year [11,12]. Previous life-threatening attacks increase the risk of death from asthma. You should have recognised, from the seriously abnormal vital signs, that this is a case of life-threatening asthma. Appropriate management therefore would be to call for help immediately, then assess and manage the airway, give the highest-concentration oxygen possible, assess and manage breathing (nebulised and/or i.v. bronchodilators and exclude pneumothorax), assess and manage circulation (give generous i.v. fluid – see Mini-tutorial: tracheal intubation in acute severe asthma) and move on to disability and examination once ABC are stable or help arrives. Unless there is a dramatic improvement, this patient requires the ICU team and tracheal intubation.

4 See the Mini-tutorial: tracheal intubation in acute severe asthma. However, apart from stacking, tension pneumothorax and hypovolaemia are other possible causes. Normally, ventilators are set so that peak airway pressures do not exceed 35–40 cmH$_2$O. This is slightly complicated by the fact that peak pressures in acute severe asthma do not necessarily reflect alveolar pressures but the ventilator pressures needed to overcome airway obstruction. PEEP is routinely added on ICU ventilators, but is not usually of benefit in acute severe asthma as patients already have significant intrinsic or auto-PEEP. In summary, an expert should supervise the ventilator requirements of any patient with acute severe asthma!

5 There is a low pH (acidaemia) due to a high PaCO$_2$ – a respiratory acidosis. The st bicarbonate is normal/high as expected. The PaO$_2$ is low. Apart from ABC, prompt medical management of his exacerbation of COPD may improve things. The oxygen could be increased to 35% and information about the patient’s usual lung function sought. A chest X-ray should be
Respiratory failure

6 There is a low pH (acidaemia) due to a low st bicarbonate. The expected PaCO₂ should be lower, indicating a 'hidden' respiratory acidosis—he is tiring. This patient has serious abnormal vital signs and marked hypoxaemia despite a high concentration of oxygen. He may well be alert and talking, but he requires immediate assessment by the intensive care team. Generous fluid should be given for the metabolic acidosis, which is due to severe sepsis. Although some may be tempted to try non-invasive CPAP first, this will not alleviate respiratory fatigue and should not be performed outside an ICU in a situation like this. This patient is likely to require tracheal intubation soon.

7 There is a low pH (acidaemia) due to a high PaCO₂—a respiratory acidosis. The st bicarbonate is normal/high as expected. The PaO₂ is low. Postoperative respiratory failure is caused by atelectasis due to a combination of recumbency, general anaesthesia and pain which prevents deep breathing and cough. Opioid analgesia also depresses respiration and cough. Retained secretions and even lobar collapse can occur. Management in this case should emphasise good pain relief (consider epidural analgesia) and urgent physiotherapy. The oxygen concentration should be increased and humidified. Antibiotics and sputum culture are required. If there is no improvement, the ICU team should be contacted. Non-invasive CPAP may be tried, but may not help when there is a significant problem with ventilation. Each patient is assessed on an individual basis.

8 There is a low pH (acidaemia) due to a high PaCO₂—a respiratory acidosis. The st bicarbonate is normal and the PaO₂ is low. There is evidence of ventilatory failure (high PaCO₂ and increased RR) as a result of increasing respiratory muscle weakness (falling FVC). Closer examination may reveal a patient who is using accessory respiratory muscles and has a cough which is bovine in nature. Neurological examination may reveal poor bulbar function. Monitoring oxygen saturations and arterial blood gases in this condition are of little help in deciding when to institute respiratory support because abnormal arterial blood gases follow ventilatory failure rather than precede it. This is why the FVC is closely monitored. The usual cut-off is 15 ml/kg, below which tracheal intubation and ventilation are recommended. Up to one-third of patients with Guillain–Barré syndrome admitted to hospital require mechanical ventilation [13]. Autonomic neuropathy can accompany the syndrome, leading to tachycardia and hypotension which also require close observation especially during tracheal intubation which can precipitate asystole from profound vagal stimulation.

9 This patient is in shock. There is a low pH (acidaemia) due to a low st bicarbonate—a metabolic acidosis. The PaCO₂ is low as expected. The PaO₂ is also
low compared with the FiO₂. The A-a gradient is as follows: PAO₂ = 0.8 × 95 - 3.0/0.8 = 72.25 kPa. A-a gradient = 72.25 - 12 = 60.25 kPa. What would cause such a significant problem with gas exchange, BP and the ECG changes with a normal chest X-ray? The answer is a massive pulmonary embolism. Treatment (after ABC) in this case includes i.v. thrombolysis which should be considered in pulmonary embolism causing shock and is as effective as surgical embolectomy. Recent literature suggests thrombolysis is safe and effective in ‘sub-massive’ pulmonary embolism as well [14].

There is a low pH (acidaemia) due to a high PaCO₂ – a respiratory acidosis. The bicarbonate should be normal/high but it is low, indicating a ‘hidden’ metabolic acidosis as well, probably due to hypoperfusion (from dehydration). The PaO₂ is also low. His airway should be assessed and he requires oxygen to get his PaO₂ to around 8 kPa (60 mmHg). His breathing should be assessed next and medical therapy commenced. Non-invasive ventilation is usually contraindicated in patients with severe respiratory acidosis or who are unconscious. However, before proceeding to tracheal intubation, further information should be sought as to the severity of the patient’s chronic lung disease. Has a discussion already taken place about tracheal intubation and ventilation between the patient and his specialist? Do the next of kin have information (e.g. an advanced directive) about what the patient would want in these circumstances? Sometimes, NIV is used as a ‘second best’ but more appropriate treatment. Each patient should be assessed individually by an experienced doctor.

References

8. The YONIV Trial, Plant PK, Owen JL and Elliot MW. A multi-centre randomised controlled trial of the early use of non-invasive ventilation for acute exacerbations of


**Further resource**