Respiratory failure occurs when the respiratory system is no longer able to meet the metabolic demands of the body. The major function of the lung is to get oxygen into the body and drive carbon dioxide out.

**Getting oxygen in**

It happens in two steps. The first step is to bring oxygen from atmosphere to alveoli and the second step to transfer the oxygen across the alveoli to capillary blood. The alveolar partial pressure of oxygen ($P_{A}O_{2}$) is dependent on the total alveolar pressure and the partial pressures of the other gases in the alveolus. The partial pressure is usually described as ‘tension’.

The alveolar gas equation explains the partial pressure of oxygen in the alveoli. It is:

$$P_{A}O_{2} = FIO_{2} (P_{B} – P_{H2O}) – PaCO_{2}/R ,$$

where $P_{A}O_{2}$ is partial pressure of oxygen in the lung alveoli, $FIO_{2}$ is the fraction of inspired oxygen concentration, $P_{B}$ is the barometric pressure, $P_{H2O}$ is the saturated water vapor pressure and $PaCO_{2}$ is the arterial carbon dioxide tension. $R$ is for respiratory quotient and has a value of 0.8.

Though the equation appears complex, it simply means that the oxygen tension in the alveoli is predominantly determined by the concentration of inspired oxygen, the barometric pressure and the carbon dioxide tension in the alveoli. Because carbon dioxide is very freely diffusible across the alveolar membrane, often arterial and alveolar carbon dioxide tension will be equal. That is why $PaCO_{2}$ which is easier to measure is used in the equation. Oxygen supplementation will increase alveolar oxygen content and hence the partial pressure. The oxygen tension in the alveoli will be low in higher altitudes like mountains and will be high in hyperbaric chambers. Conditions with increased carbon dioxide level in blood and hence in alveoli, as in hypoventilation, chronic obstructive airway diseases (COAD) etc. are associated with decreased oxygen tension in the alveoli.

As the oxygen reaches the alveoli from atmosphere, there is a drop in its tension. This is because of dilution of oxygen by water vapor from the airways and carbon dioxide that is let out from pulmonary capillaries. The alveolar oxygen diffuses through the alveolar membrane, interstitial tissues, and pulmonary capillary walls to enter the blood. Because of a phenomenon called physiological shunting, there is a further drop in arterial oxygen tension when compared to that in alveoli. As the arterial blood flows through different
tissues, oxygen is extracted to various extents depending on local requirements and there is progressive fall in the oxygen tension. This stepwise fall in the oxygen tension from the atmosphere as it reaches the peripheral tissue is described as ‘oxygen cascade’. In a healthy adult the arterial oxygen tension (PaO$_2$) is about 13 kPa. As it comes to the venous side (PvO$_2$) it falls to about 5.3 kPa.

**Driving carbon dioxide out**

CO$_2$ elimination is largely dependent on alveolar ventilation. 

Alveolar ventilation = Respiratory Rate x (Tidal Volume - Dead Space) 

Dead space is that portion of the tidal volume that does not take part in gas exchange. Therefore any changes in PaCO$_2$ are dependent on: respiratory rate, tidal volume and ventilation-perfusion (V/Q) matching. CO$_2$ crosses the alveolar membrane very readily and so diffusion abnormalities and shunting have little effect on CO$_2$ elimination. Terminologies such as dead space, shunting, diffusion abnormalities are discussed in detail later.

**Respiratory failure**

‘When you breathe you inspire; when you don’t you expire’

In general, patients require respiratory assistance due to airway problems, failure to ventilate or failure to oxygenate. Often all three problems exist simultaneously. The act of respiration grossly includes two components.

- a. Ventilation and b. Gas exchange

Ventilation is a mechanical process whereby the ambient gas is taken into the alveoli. Gas exchange takes place between alveoli and the capillary blood. Based on this, respiratory failure can be categorized into two groups depending on the cause, those due to ventilatory defects and those due to impaired gas exchange.

Conventionally respiratory failure is also classified as Type I and Type II based on the effects of the failure. Type I is just associated with hypoxaemia. The CO$_2$ level may be normal or even low. Type II is associated with hypoxaemia and hypercapnia.

- Hypoxaemia: PaO$_2$ less than or equal to about 8 kPa when breathing room air
- Hypercapnia: PaCO$_2$ more than or equal to about 6.5 kPa
Pathophysiological mechanisms of respiratory failure

Any pathophysiological mechanism (figure 9.1) that leads to the impaired gas exchange can result in respiratory failure. Impaired gas exchange may occur due to defect in diffusion or due to ventilation and perfusion mismatch.

![Diagram of respiratory failure mechanisms]

**Figure 9.1 mechanisms producing respiratory failure**

Ventilation defects

Hypoventilation is marked by a rise in PaCO$_2$ and a fall in PaO$_2$. The causes of hypoventilation can be enumerated in a systematic way starting from the central control in brain above to the respiratory apparatus below (figure 9.2).

- **Brainstem**
  - brainstem injury e.g. to trauma, haemorrhage, hypoxia, infection
  - metabolic encephalopathy
  - depressant drugs
- **Spinal cord**
- trauma, tumour, transverse myelitis
  - Nerve root injury
  - Nerve
    - trauma
    - neuropathy e.g. Guillain Barre
    - motor neuron disease
  - Neuromuscular junction
    - myasthenia gravis
    - Eaton-Lambert syndrome
    - neuromuscular blockers
  - Respiratory muscles
    - fatigue
    - disuse atrophy
    - myopathy
    - malnutrition
  - Respiratory system
- airway obstruction (upper or lower)

- decreased lung, pleural or chest wall compliance, e.g. pneumothorax and pleural effusion.

**Figure 9.2 Causes of hypoventilation**

**Impaired Gas Exchange**

Gas exchange failure (often leading to hypoxemia) most often occurs at a microscopic level at pulmonary capillary-alveolar interface. Classically injuries are divided up into

1. Diffusion defects and

2. Ventilation perfusion (V/Q) mismatch. V/Q mismatch can either be dead space or shunt or a mixture of both to varying extent.

- Dead space ventilation is at one extreme (alveoli are perfused but not ventilated)
• Shunt is at the other (alveoli are ventilated but not perfused).

Often, in acute lung injury, a variety of abnormalities are present in the same lung.

**Diffusion defects**

This is caused by conditions such as thickening of the alveoli as in pulmonary fibrosis or increased extracellular fluid as in pulmonary edema. This results in impaired gas exchange. As the passage of oxygen from alveolus to capillaries is more difficult, hypoxemia ensues. CO₂ is more freely diffusible than O₂. Therefore hypercapnia occurs only in advanced stages.

**Ventilation/Perfusion Mismatch**

**Dead Space Ventilation:** Alveoli that are ventilated but not perfused resulting in wasted ventilation. An extreme example of this is a pulmonary embolus. More frequent clinical situations are hemorrhage or hypotension where perfusion pressure to apical lung units may fall, leading to alveolar dead space.

**Shunt:** Alveoli are perfused but not ventilated; well oxygenated blood becomes mixed with deoxygenated blood. This occurs in airway collapse, pneumonia, pulmonary contusion, ARDS/ALI (acute respiratory distress syndrome / acute lung injury). The intracardiac causes for shunting include right to left shunt e.g. Fallot's tetralogy, Eisenmenger's syndrome. This form of respiratory failure is relatively resistant to oxygen therapy.

**Clinical signs**

The features of respiratory failure are those due to increased work of breathing, due to hypoxia and hypercarbia and due to end-organ hypoxia. Clinically patients can be cyanotic due to accumulation of deoxygenated haemoglobin (> 5 gm/dl).

*Signs of respiratory compensation*

• tachypnoea is an early and sensitive indicator

• use of accessory muscles

• nasal flaring
- intercostal, suprasternal or supraclavicular recession

*Effects of hypoxia and hypercarbia on autonomic nervous system*

There is an initial stimulation of sympathetic nervous system causing tachycardia, hypertension and sweating. Later, bradycardia and hypotension ensues.

*End-organ hypoxia*

Virtually all tissues in the body are dependent on oxygen. Depending on the severity and duration of hypoxia the findings may include altered mental status, loss of consciousness, convulsions, cardiovascular depression, cardiac arrest, multi organ failure.

**Monitoring and Investigations**

**Pulse oximetry**

The principle behind pulse oximetry is described in chapter 4. The relationship between saturation and PO$_2$ is described by the oxygen dissociation curve (ODC). Pulse oximeter is a very useful non invasive mean to monitor oxygenation status of haemoglobin. Saturation (SpO$_2$) of about 90% is described as a critical threshold. This corresponds to a PaO$_2$ of 8 kPa. As demonstrated by the oxygen dissociation curve (figure 9.3), below this level of even a small fall in PaO$_2$ produces a sharp fall in SpO$_2$.

![Oxygen dissociation curve](image)

**Figure 9.3 Oxygen dissociation curve**

**Arterial Blood Gas Analysis**

Warwick Medical School- Handbook of Anaesthesia 2006
Blood gas analysis gives rapid assessment of PaO$_2$, PaCO$_2$, pH, bicarbonate levels and other values like hemoglobin saturation etc. It is useful in identifying the severity of respiratory impairment and subsequently to monitor the response to treatment.

Other investigations like electrocardiogram, electrolytes, complete blood picture, urine toxicology screen, x-ray, CT-scan of chest, pulmonary function tests such as peak expiratory flow rate, spirometry, flow-volume loop, carbon monoxide gas exchange are performed depending on the clinical presentation and the urgency of the situation.

Management of Respiratory failure

Prompt recognition of signs of acute respiratory failure, early involvement of critical care team & initiation of treatment is important in the management of respiratory failure. An attempt should be made to find out and treat the underlying cause. Principles of management include optimising gas exchange and tissue oxygenation. Gas exchange can be optimised by increasing the inspired oxygen concentration and providing ventilatory support. Tissue oxygenation can be optimised by increasing tissue blood flow by means of adequate cardiac output and an adequate haemoglobin concentration.

- The initial management of any type of respiratory failure is – ABC: airway, breathing circulation (for more details refer to chapter 11).
- Hydration with intravenous fluids is required to optimise cardiac output.
- Chest physiotherapy: Percussion and vibration along with breathing exercises and adequate coughing helps to clear the secretions.
- Inotropic support may be required to optimise tissue blood flow.
- Bronchospasm should be treated using salbutmol or intravenous aminophylline.
- Antibiotics may be necessary to treat existing respiratory infection. Appropriate antibiotic should be chosen as per the local guidelines and culture results.
- Ventilatory support: Non invasive positive pressure ventilation or continuous positive pressure ventilation improves the oxygenation. Tracheal intubation and invasive ventilation may be required to treat hypercapnia associated ventilatory failure.

Oxygen therapy
In acutely ill patients oxygen delivery relies on maintaining a patent airway. Give oxygen empirically in all sick patients or when there is respiratory distress or hypotension. Arterial blood gases should be analysed as soon as possible to assess the degree of hypoxaemia, hypercapnia, and acid-base state. Even in patients with history of COAD, the conventional myth that oxygen administration can eliminate the ‘hypoxic drive’ and depress respiration is over emphasized. Till the vitals parameters are stabilized and clinical condition improves, give oxygen!

Increasing the fraction of inspired oxygen (FIO\textsubscript{2}) increases oxygen transport by ensuring that haemoglobin is fully saturated and by raising the quantity of oxygen dissolved in the plasma. However, the solubility of oxygen in blood is low. Even when the inspired oxygen concentration is 100%, dissolved oxygen provides only one third of resting tissue oxygen requirements. Therefore, oxygen treatment must be aimed at correcting the underlying cause for arterial hypoxaemia and tissue hypoxia such as heart failure, anaemia, carbon monoxide poisoning etc.

In the acute situation the concentration of oxygen administered may be critical. Inadequate oxygen accounts for more deaths and permanent disability than can be justified by the relatively small risks associated with high dose oxygen. In many acute conditions (for example, asthma, pulmonary embolus), inspired oxygen concentrations of 60-100% for short periods may preserve life until more specific treatment can be instituted. Thereafter oxygen should be given at a dose that will correct hypoxaemia (to maintain the between PaO\textsubscript{2} to 8.0-10.6 kPa). When necessary, oxygen must be given continuously. When oxygen is used for long period it should be humidified by passing through a humidifier or a simple water bottle (Figure 9.5). Humidified oxygen helps to clear the secretions and minimises the respiratory loss of heat and moisture.

High concentration of oxygen is given to patients with chronic obstructive pulmonary disease who have type II respiratory failure can reduce the hypoxic drive to breathe and increase ventilation-perfusion mismatching. This causes carbon dioxide retention and a respiratory acidosis that may be lethal. In these patients, if rest of the haemodynamic parameters are stable, initial treatment with low oxygen concentrations (24-28%) should be progressively increased on the basis of repeated blood gas analysis with the aim of correcting hypoxaemia to a PaO\textsubscript{2} > 6.65 kPa without decreasing arterial pH below 7.26. Non-invasive positive pressure ventilation and respiratory stimulants may help achieve adequate oxygenation and prevent carbon dioxide retention by raising minute ventilation in patients with type II respiratory failure. It is more effective and safer than respiratory stimulation and should be used when available. Type II respiratory failure occurs in 10-15% of patients with chronic obstructive pulmonary disease. When in doubt, give oxygen!

**Oxygen therapy devices**

They are classified as fixed and variable performance devices. Normally when we breathe, we create a pressure difference between the atmosphere and alveoli. This pressure difference facilitates gas flow. The degree of flow during inspiration is
quantified as ‘inspiratory flow rate’. When a given oxygen therapy device can meet the flow requirements of the patient, then even when the inspiratory effort of the patient changes still the inspired oxygen concentration remains reasonably stable. These are ‘fixed performance devices’. On the other hand, if the given device cannot meet the peak inspiratory flow rate requirements of the patient and hence there is resultant admixture of atmospheric air diluting the inspired gas, the inspired oxygen concentration varies breath to breath based on patients’ inspiratory effort. These are ‘variable performance devices’.

**Fixed performance devices:** As described above, these devices are patient independent as the patient receives a constant predetermined FIO\textsubscript{2} regardless of changes in respiratory parameters. e.g.: face mask with reservoir bag, HAFOE (high air flow oxygen enrichment device)

Facemask with reservoir bag delivers a FIO\textsubscript{2} of 0.85 at flow rates of 10-15 L/min. Unlike a simple face mask which can only provide a set oxygen flow rate, the one with the reservoir bag has an additional reserve for oxygen. For example, if a patient creates an inspiratory flow rate of 30 L/min, 15 L/min is taken from the flowmeter and the rest from the reservoir bag. Hence, when using these masks with reservoir bag, care should be taken to ensure that the bag is well inflated and not obstructed.

HAFOE e.g.: Ventimask. They are ‘air entrainment masks’ that function based on Venturi principle. There are slits in the venture mask adaptors size of which become smaller or larger depending on whether a high or low FIO\textsubscript{2} is required. These slits are designed to entrain air from the environment. Therefore, the set oxygen flow and the entrained air together meet the inspiratory flow requirement of the patient. The rate of delivery of oxygen is calibrated for the size of the Venturi and amount of mixing therein. For example, a 60% oxygen Venturi requires 15 L/min fresh gas flow.

**FIO\textsubscript{2}**

<table>
<thead>
<tr>
<th>Colour coding</th>
<th>Oxygen Flow L/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blue</td>
<td>0.24</td>
</tr>
<tr>
<td>White</td>
<td>0.28</td>
</tr>
<tr>
<td>Brown</td>
<td>0.31</td>
</tr>
<tr>
<td>Yellow</td>
<td>0.35</td>
</tr>
</tbody>
</table>

Warwick Medical School- Handbook of Anaesthesia 2006 10
Variable performance devices: The performance varies with patients’ respiratory efforts. Variable performance devices use the dead-space of the nasopharynx or face masks as a reservoir of oxygen. They cannot deliver high inspired concentrations of oxygen. Variable performance devices fit into two categories, nasal cannula and facemasks.

Nasal cannulae: It uses the dead space of the nasopharynx as a reservoir for oxygen. When the patient inspires, entrained air mixes with the reservoir air and the inspired gas is enriched. Obviously, the FIO\(_2\) depends on the magnitude of flow of oxygen, the patient’s minute ventilation and peak flow. For most patients, each addition 1 litre per minute of O\(_2\) flow with nasal cannula represents an increase in the FIO\(_2\) by 4%. So 1 litre is 24%, 2 liters is 28% and so on. At 6 liters (44%), it is not possible to raise the FIO\(_2\) further, due to turbulence, in the tubing and in the airway.

There are few problems with nasal cannulae: if they are not properly positioned at the nares, they are useless. Secondly, the effectiveness may be disrupted by the pattern of breathing: there appears to be little difference whether the patient is a mouth or a nose breather, but it is preferable if the patient exhales through his/her mouth rather than nose, so the reservoir is maintained. Nasal cannulae are suitable for long term oxygen therapy as it is better tolerated.
Figure 9.4 Oxygen delivery devices.

**Hudson face mask** typically delivers FIO$_2$ of 0.35 at 4 L/min of oxygen flow rate and with a normal respiratory pattern. Ambient air is entrained through the holes on both sides of the mask. Holes also allow exhaled gases to be vented out. Inspired oxygen concentration depends on the oxygen flow rate, pattern and rate of ventilation, maximum inspiratory flow rate and how well the mask fits the patients’ face.

![Hudson face mask](image)

Figure 9.5 Method of delivering humidified oxygen via face mask.

**Use of CPAP and BiPAP in Acute Respiratory Failure**

There is now Level I evidence that CPAP (Continuous Positive Airway Pressure) and BiPAP (Bilevel Positive Airway Pressure) are effective in preventing tracheal intubation and decreasing mortality in patients with acute respiratory failure in properly selected patients.
CPAP delivers a continuous positive airway pressure, most frequently at about 10 cmH\textsubscript{2}O. This is delivered throughout the respiratory cycle and has been described as being similar to breathing with your head stuck out of a moving car. There are multiple reasons why this might improve breathing.

1. Counteracts intrinsic PEEP (see below)

2. Decreases preload and afterload in Congestive cardiac failure (CCF)

3. Improves lung compliance in CCF

4. Decreases the work of breathing

Intrinsic PEEP (positive end expiratory pressure) is the concept that in patients with severe COPD, the lung does not fully empty due to the obstruction in the airway resulting in a positive pressure in the airways at end expiration. Therefore to breathe in, the COPD patient must first overcome this positive airway pressure before he can generate a negative pressure to inhale more air. This is called intrinsic PEEP and in patients with respiratory failure due to COPD it is often about 5 cmH\textsubscript{2}O, but it can be higher. When CPAP is begun, the usual starting level is 10, though one can start at 5 and work up. Oxygen can be delivered at flow rates high enough to maintain O\textsubscript{2} saturation above 90%.

BiPAP delivers CPAP but also senses when an inspiratory effort is being made and delivers a higher pressure during inspiration. When flow stops, the pressure returns to the
CPAP level. This positive pressure wave during inspirations unloads the diaphragm decreasing the work of breathing. This form of ventilation has been used for years in patients with chronic respiratory failure due to neuromuscular problems or chest wall abnormalities. In patients with respiratory failure, a common technique is to begin with the expiratory level at 5 cmH\textsubscript{2}O and the inspiratory level at 15 cmH\textsubscript{2}O. The levels are adjusted based on patient comfort tidal volume achieved and blood gases.

The use of BiPAP machines is often called non-invasive face mask ventilation. This is because the trachea is not intubated so there is lesser trauma to the airway and more importantly there is a lower incidence of nosocomial infections. If the patient has a decreased level of consciousness, copious secretions, can not protect his airway or is unstable hemodynamically, then intubation is warranted.

In conclusion, for those patients who present to the emergency department with acute respiratory failure but with normal levels of consciousness, no major secretion problems and who are hemodynamically stable, a trial of BiPAP or CPAP should be attempted prior to considering intubation and a mechanical ventilator.

### Indication for tracheal intubation

The main indication for intubation is airway protection / control of airway: *‘When in doubt intubate! When in doubt do not extubate!’* Such circumstances may be:

1. Loss of gag/cough reflex e.g. head injury with GCS <8 (to prevent aspiration).
2. Airway obstruction: acute laryngeal edema – e.g. inhalation burn, Ludwig’s angina, epiglottitis.
3. Anticipated loss of control of the airway: anticipated laryngeal edema– e.g. neck trauma, acute stridor etc.

Patients are usually intubated for controlled mechanical ventilation as an endotracheal tube or tracheostomy will provide a good seal for controlled ventilation: inspired volumes and pressures are consistent; compared with non invasive methods. Finally, the presence of an artificial airway facilitates removal of obstructive material from the airway (airway toileting – suctioning of secretions).

Indications for mechanical ventilation can be either ventilation failure or oxygenation failure as discussed under the topic of causes for respiratory failure. At times, even when ventilatory efforts are good and gas exchange is intact, still there can be impaired oxygen extraction at tissue level such as in low cardiac output states, sepsis, cyanide toxicity etc. warranting assisted ventilation. The modes of ventilation and description about the various ventilatory parameters are beyond the scope of this section. Readers interested in ventilator management are advised to refer to books on critical care and visit intensive care unit to see ventilated patients for more knowledge.

### For further reading

Warwick Medical School- Handbook of Anaesthesia 2006

Bateman NT, Leach RM. Acute oxygen therapy. BMJ 1998; 317: 798-801