Respiratory failure

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Abstract

Respiratory failure is a common complication of acute cardiorespiratory disease and exacerbations of chronic respiratory disease. It can be a feature of advanced chronic cardiac, respiratory and neurological diseases. Respiratory failure can manifest as hypoxaemia, hypercapnia or both. This article reviews the pathophysiology of these perturbations in respiratory homeostasis, the clinical features of acute and chronic respiratory failure and a brief discussion of the management.

Keywords Acidaemia; acidosis; dyspnoea; hypercapnia; hypoxaemia; non-invasive ventilation; oxygen therapy; respiratory failure

Key points

- All causes of hypoxaemia can be explained by five pathophysiological mechanisms: ventilation/perfusion mismatch (either impaired perfusion with preserved ventilation or, conversely, preserved perfusion with impaired ventilation), diffusion limitation, decreased inspired oxygen or alveolar hypoventilation
- Alveolar hypoventilation inevitably causes hypercapnia, because of either an insufficient neural respiratory drive (or its transmission) or a load that cannot be overcome by the capacity of the respiratory muscle pump
- Treatment must be directed at the underlying disorder and be supportive by preserving oxygenation and ventilation

Incidence

In the UK, approximately one-third of medical patients admitted to hospital have a respiratory problem, the most important of which is respiratory failure. In the USA, the number of hospital admissions for acute respiratory failure (ARF), and the associated costs, are increasing. The mortality associated with admission to hospital with ARF varies according to the cause, but overall US data suggest a 20% risk of death.[1] Pneumonia accounts for approximately 60% of all hypoxaemic ARF. By contrast, the most common cause of hypercapnic ARF is chronic obstructive pulmonary disease (COPD), with 44% of patients admitted with acute exacerbations showing a degree of hypercapnia.

Normal physiological functions of the respiratory system

The primary function of the respiratory system is gas exchange — the maintenance of oxygenation and the removal of carbon dioxide from the blood. The respiratory system consist of the substance of the lung — the parenchyma (including the alveoli) — the associated circulation (pulmonary vasculature) and the airways (trachea, bronchi, bronchioles). The lungs are only able to adequately perform their function with the assistance of the respiratory muscles, which themselves rely on intact neuronal connections to a functioning brain. Impaired function of any of these four major constituents can manifest as respiratory failure.

Measuring gas exchange

The most common method of measuring adequacy of gas exchange is by measuring arterial oxygen saturation using pulse oximetry. Arterial oxygen saturation (the percentage of haemoglobin that is oxygenated) provides information on the partial pressure of oxygen in the arterial system; the relationship between these variables is illustrated by the oxygen dissociation curve. The major limitation of using pulse oximetry in isolation is that it provides no direct information about carbon dioxide concentrations.

A more complete picture is obtained by sampling the arterial blood, usually from the radial artery, and analysing the partial pressure of oxygen (PaO_2), partial pressure of carbon dioxide ($PaCO_2$), pH and bicarbonate concentration — the 'blood gases'. Puncture of the radial artery to measure blood gases is painful so local anaesthetic should be used. An alternative is sampling blood from an arterialized ear lobe, but this has the limitation that PaO_2 is underestimated by 0.5—1.0 kPa and diverges from arterial values at higher concentrations of inspired oxygen. Patients who require repeat blood gases are often best cared for with an indwelling arterial cannula, but this is usually only available in critical care environments. Continuous estimation of arterial carbon dioxide can be achieved by using transcutaneous carbon dioxide monitoring in all patients, or end-tidal carbon dioxide in ventilated patients.

Categorizing respiratory failure

Hypoxaemia is commonly but arbitrarily defined as a PaO_2 less than 8 kPa (historically termed type 1 respiratory failure with a $PaCO_2$ <6 kPa), and associated hypercapnia is commonly defined as a $PaCO_2$ greater than 6 kPa (type 2 respiratory failure). Describing the underlying cause is, however, arguably more useful than dividing respiratory failure into types 1 and 2.

A diverse range of pathological conditions can cause acute and chronic respiratory failure but they all share common mechanisms.

Pathophysiology of hypoxaemia

Five pathophysiological mechanisms can cause hypoxaemia (Table 1 and Figure 1):

- Diffusion limitation is best exemplified by idiopathic pulmonary fibrosis. The oxygen concentration in the alveoli is unchanged (PAO_2), but the gas transfer capability of the alveolar membrane is impaired, leading to arterial

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Pathophysiological mechanisms causing hypoxaemia

Mechanism	Alveolar partial pressure of oxygen (PAO_2)	Alveolar–arterial oxygen difference ('A–a gap')	PaO_2 response to increased inspired oxygen (FiO_2)
Diffusion limitation	Normal	Increased	Improves
Hypoventilation	Reduced	Normal	Improves
Decreased inspired oxygen	Reduced	Normal	Improves
Low ratio of ventilation to perfusion (V/Q mismatch)	Reduced locally	Increased	Improves
Shunt	Reduced locally	Increased	Minimal

Table 1

hypoxaemia (low PaO_2) and a resultant increase in the alveolar–arterial oxygen difference.

- Any cause of significant hypoventilation (a classic example being acute opiate toxicity) leads to hypercapnia because of the inverse relationship between alveolar ventilation and arterial CO_2 ($PaCO_2$). Increases in $PaCO_2$ result in matched increases in alveolar CO_2 ($PACO_2$). In the absence of an increased fraction of inspired oxygen (FiO_2), an increased $PACO_2$, via the law of partial pressures, causes a decrease in the PAO_2. This is an often underappreciated cause of hypoxaemia in hypoventilation and can be completely masked by the use of an increased FiO_2.
- An area of lung can receive little ventilation in proportion to the extent to which it is being perfused. A common example is lobar pneumonia, with one lobe receiving (almost) normal perfusion but decreased ventilation because the air spaces are congested with inflammatory exudate. The ventilation/perfusion (V/Q) mismatch is partially offset by the protective mechanism of hypoxic pulmonary vasoconstriction. A less common example is heterogeneous emphysema and the demonstration of diminished ventilation in the upper lobes (relative to the lower lobes) with the use of nuclear medicine imaging (V/Q scans). This technique is practically useful in planning best-therapy options for patients with advanced COPD who are being considered for lung volume reduction surgery.
- The opposite type of V/Q mismatch is normal ventilation and decreased perfusion, which can be termed a right-to-left shunt. This is best exemplified by a very significant pulmonary embolism — the lungs are adequately ventilated in the face of compromised perfusion.

Pathophysiology of hypercapnia

By contrast there is only one clinically practical cause of hypercapnia — alveolar hypoventilation, which results from failure of the respiratory muscle pump. It is useful to consider the components of the pump. First is the neural respiratory drive. This refers to the central neurological impetus to breathe, which is paired with the normal function of the spinal cord, peripheral nerves and neuromuscular transmission. Second is the capacity of the muscular pump, and finally is the load. Alveolar hypoventilation results from an impairment of normal physiological function of the neural respiratory drive or muscular pump, or an increase in load that cannot be overcome (Figure 2).

Respiratory muscle capacity can be impaired by a range of diverse processes, including muscular dystrophy, inflammatory

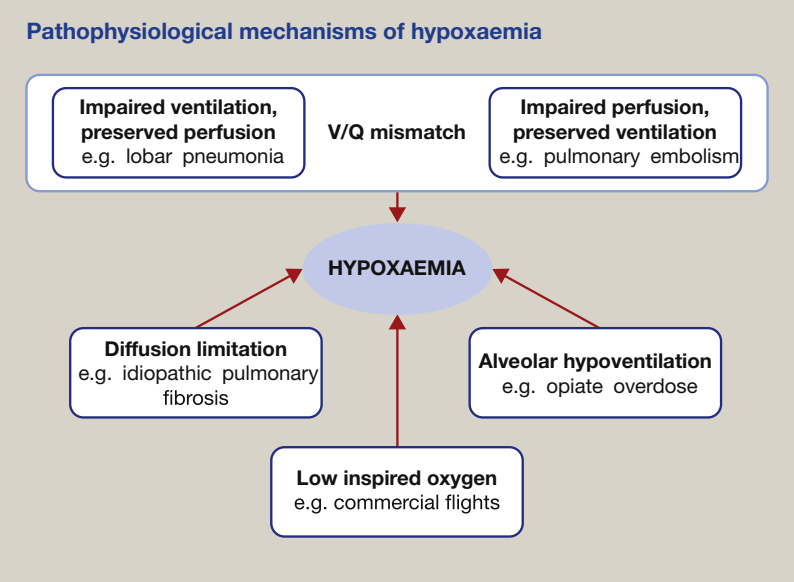

Figure 1