Mechanisms of hypoxaemia and the interpretation of arterial blood gases

Rhodri Jones
Robin Berry

Abstract

Whilst there are many causes for hypoxia, an appreciation of the underlying physiology will assist in the correct diagnosis and management of this condition. This article describes the normal delivery of oxygen to the tissues, conceptual mechanisms of hypoxia and the clinical relevance of these pathological processes. Interpreting arterial blood gases (ABGs) is an essential part of managing sick patients and a logical method of reading ABGs is presented, alongside examples of deranged ABGs and the conditions causing these changes.

Keywords Blood gas; hypoxia; oxygen cascade; shunt

Introduction

The terms hypoxia and hypoxaemia are frequently used interchangeably (Table 1), but there are important differences between the classes of hypoxia. Many tissues can metabolize anaerobically for short periods, but this is physiologically inefficient and some organs, (such as the brain) are highly dependent on aerobic metabolism to avoid ischaemic injury.

Traditionally, hypoxia is classified according to the underlying mechanism:

1. Hypoxic hypoxia – reduced delivery of oxygen from the alveoli to the arterial blood.
2. Anaemic hypoxia – reduced oxygen carrying ability of the blood.
3. Stagnant hypoxia – reduced blood supply to tissues.
4. Cytotoxic hypoxia – inability of tissues to metabolize delivered oxygen.

This list is a simple aide memoire, but in reality the situation is more complex. Some classifications do not include anaemic hypoxia, since the partial pressure of oxygen is not reduced and others list shunt as a separate cause, rather than a mechanism of hypoxic hypoxia. Clinicians must appreciate that multiple processes are often involved in hypoxia. A pulmonary embolism may cause both anaemic hypoxia from the disruption of pulmonary blood flow and stagnant hypoxia from reduced organ perfusion secondary to poor cardiac output.

Hypoxaemia, is frequently defined as a $PaO_2 < 12.0$ kPa, but physiologically this is dependent on the subject tested. A healthy young adult breathing room air would be considered hypoxaemic with a $PaO_2 < 12$ kPa, whilst under the same conditions an elderly person may have a PaO_2 of < 10 kPa without ill effect. Therefore, ABGs should be interpreted in context and with the mechanism for hypoxia identified since *simply* applying oxygen may not reverse the state.

Terminology

Hypoxia: reduced oxygen availability for tissue respiration	Acidosis/alkalosis: the underlying cause of acidaemia or alkaemia
Hypoxaemia: reduced oxygen in the blood	Acidaemia/alkalaemia: a state of acidic or alkaline blood
Oxygen tension: the pressure exerted by oxygen	Oxygen content: the amount of oxygen contained in the blood, both bound to haemoglobin and dissolved in the blood
P_AO_2: the partial pressure of oxygen in the alveoli	PaO_2: the partial pressure of oxygen in the arterial blood

Note: 1 kPa = 7.6 mmHg.

Table 1

The oxygen cascade

The oxygen cascade is the reduction in the partial pressure of oxygen from the atmosphere to that at the mitochondria and is illustrated in Figure 1.

Any process reducing oxygen concentration at one stage of the cascade will be perpetuated throughout the cascade, determining the final concentration available to the mitochondria. Understanding this process allows the clinician to direct therapy where required.

Hypoxic hypoxia

Reduced delivery of oxygen to alveolar blood because of:

- low inspired oxygen concentration

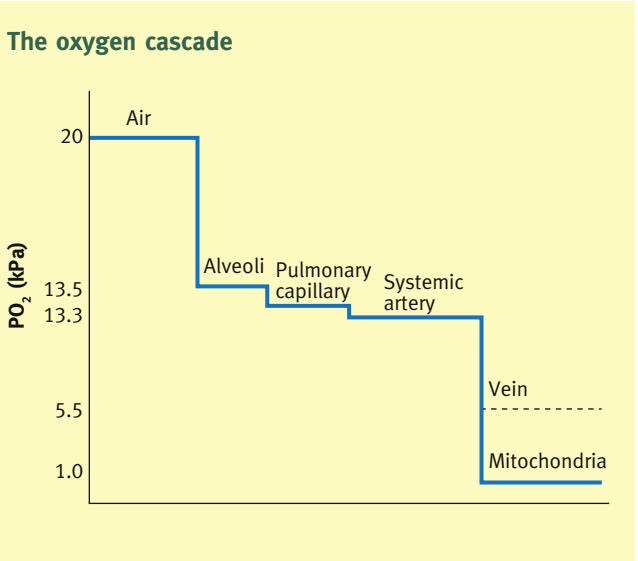

Figure 1

Rhodri Jones *MD BSc MRCS is a Trust Grade Physician in Intensive Care at Derriford Hospital Plymouth, UK. Conflicts of interest: none declared.*

Robin Berry *PhD FRCA DICM FFICM is a Consultant in Anaesthesia and Intensive Care at Derriford Hospital, Plymouth, UK. Conflicts of interest: none declared.*

- reduced alveolar ventilation
- impaired gas exchange.

Low inspired oxygen concentration: the pressure exerted by a mixture of gases is derived from the sum of the pressures exerted by the component gases (Dalton's Law). Dry air contains approximately: 78% nitrogen, 21% oxygen, 0.03% carbon dioxide, 0.97% other gases.

These concentrations are usually maintained throughout the atmosphere. Thus, the relative concentration of oxygen is constant but the pressure exerted by oxygen is a function of the total pressure exerted by all the gases present (atmospheric pressure). At sea level this is typically 101.3 kPa (Table 2). The partial pressure of oxygen (PO_2) is therefore calculated as: $PO_2 = 0.21 \times 101.3 = 21.3$ kPa at sea level.

Pressure falls inversely with altitude (being 50% of sea level at 5500 m and 25% at 10,300 m) and consequently the oxygen content of air will also fall e.g. at 5500 m: $PO_2 = 0.21 \times 50 = 10.5$ kPa.

Such changes are largely irrelevant in the UK, but are important for travellers with chronic lung disease who might wish to visit destinations such as Mexico City (altitude 2240 m, atmospheric pressure 76.4 kPa) or those who might wish to fly, since commercial airliners are pressurized to between 1800 and 2500 m.

The effect of water vapour and carbon dioxide

The respiratory mucosa adds water vapour to inspired air, which is fully saturated by the time it reaches the alveoli.

When water molecules are added to a given volume of air, the dry air molecules must decrease by the same number to keep the pressure and temperature constant (Avogadro's Law). The partial pressure of water vapour in alveoli is determined by body temperature (6.3 kPa at 37 C) and does not change with altitude. Therefore water vapour represents an increasing proportion of the inspired gas mixture as atmospheric pressure falls (Table 2).

Additionally, in health, alveolar PCO_2 is in equilibrium with pulmonary capillary PCO_2^- around 5.3 kPa.

Thus, the alveolar gas equation can be constructed to calculate the alveolar PO_2:

$$P_AO_2 = (\text{Barometric pressure} - \text{Water vapour pressure}) \times FiO_2 - PaCO_2 \,/\, \text{Respiratory quotient}$$

$$P_AO_2 = (101.3 - 6.3) \times 0.21 - 5.3/0.8 = 13.3 \text{ kPa at sea level}$$

$$P_AO_2 = (76.4 - 6.3) \times 0.21 - 5.3/0.8 = 8.1 \text{ kPa in Mexico City}$$

The effects of altitude, water and CO_2 on oxygenation

Location (altitude, metres)	Atmospheric pressure (kPa)	Atmospheric partial pressure of oxygen (kPa)	Alveolar partial pressure of oxygen (kPa)
Sea level (0)	101.3	21	13.3
Mexico City (2240)	76.4	10.5	8.1
Everest Summit (8848)	33	7	3.7

Table 2

PaO_2 cannot be higher than P_AO_2 and therefore even healthy individuals can be hypoxaemic when taking a commercial flight or standing at the summit of Mount Everest ($P_AO_2 = (33-6.3) \times 0.21 - 1.5/0.8 = 3.7$ kPa). At this height, extreme hyperventilation (to a PCO_2 of 1.5 kPa) would be necessary to compensate for the very low P_AO_2 and supplemental oxygen is required by all but the most highly adapted climbers.

P_ACO_2 is an important determinant of P_AO_2, since for practical purposes $PaCO_2 = P_ACO_2$. As $PaCO_2$ rises, P_AO_2 must fall and the addition of other gases (e.g. cigarette smoke, volatile anaesthetics) to the inspired mixture exacerbates this problem unless the FiO_2 is increased.

Reduced alveolar ventilation: common causes of reduced ventilation include pain, neuro-muscular disorders and opiate toxicity. Alveolar ventilation is the volume of gas entering the alveoli per minute (4–4.5 l/min) and is derived thus:

$$(\text{Tidal volume} - \text{dead space}) \times \text{respiratory rate}.$$

Dead space is the volume of inspired air that takes no part in gas exchange. It is composed of:

- Anatomical dead space; that part of the respiratory tree not lined with respiratory epithelium, in the mouth, nose, pharynx and large airways.
- Alveolar dead space; that part of the ventilated lung which could be involved in gas exchange but has inadequate perfusion (Figure 2b).

Physiological dead space is the sum of these two values and is normally around 150 ml in an adult. If tidal volume (normally around 500 ml) falls, patients maintain their alveolar ventilation by increasing their respiratory rate, making tachypnoea, a sensitive (but non-specific) physiological marker for acute illness.

In health 1–5% of total energy expenditure is used for breathing, but in acute illness this may increase to 40% or more and this increased work of breathing causes fatigue. An initial increase in alveolar ventilation from rapid breathing may allow respiratory compensation and hypocapnia, but eventually, as the patient becomes fatigued, alveolar ventilation reduces resulting in both hypercapnia and hypoxia.

Impaired gas exchange:

The alveolar-capillary unit

Alveolar oxygen must diffuse across the alveolar and pulmonary capillary membranes into the pulmonary capillary blood and this process is dependent on a number of factors:

- the concentration gradient across the membrane (Fick's Law)
- the rate of effusion of a gas is inversely proportional to the square root of its density (Graham's Law)
- area of membrane available for transfer
- the pressure gradient across the membrane
- alveolar ventilation
- cardiac output
- solubility of oxygen in blood.

Alveolar-capillary units can be considered to exist in a number of states (Figure 2) and single units may change state during the respiratory cycle or with changing posture.