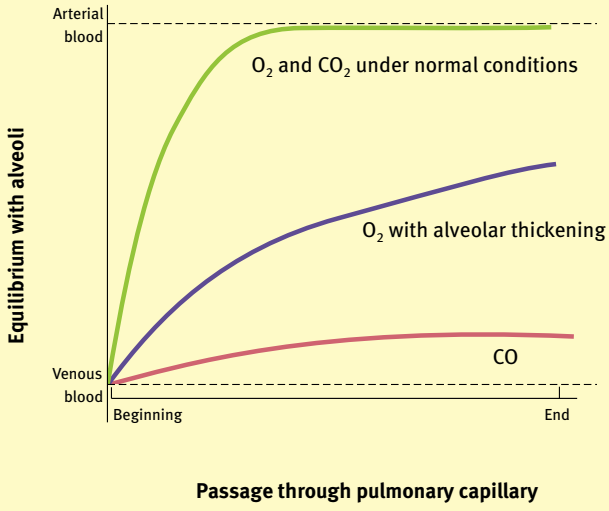
# Respiration: gas transfer

James Waterhouse
Iain Campbell

**Rates at which gases in the pulmonary blood equilibrate with alveolar air during passage through the capillaries**

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### Diffusion of gases across the alveoli

In the pulmonary circulation, gases move down the concentration gradient between the alveoli and the blood by diffusion. The rate of diffusion of a gas (D) between sites 1 and 2, is given by Fick's law of diffusion, which states that:

$$D = K \times (PP_1 - PP_2) \times \text{Area/Path length}$$

where: $PP_1$ is the partial pressure of the gas at site 1; $PP_2$ is the partial pressure of the gas at site 2; Area is the surface area across which diffusion can take place; Path length is the distance between sites 1 and 2; and K is a constant (the diffusion coefficient). K is directly proportional to the solubility of the gas, and inversely proportional to the square root of its molecular weight.

The thin alveolar walls and dense pulmonary capillary network ensure that the path length and area are conducive to diffusion. The continual replenishment of the air in the alveoli maintains the gradients of partial pressure of oxygen (down into the blood) and carbon dioxide (down out of the blood). In health, the processes of diffusion in the lung are so effective that equilibrium for oxygen has been achieved well within the time (less than 1 s) that the blood is in the pulmonary capillaries. This also applies to carbon dioxide, even though the partial pressure gradient (about 8 mm Hg) is small and it is a larger molecule, because it is very soluble.

The rates at which oxygen is removed from the alveoli, and carbon dioxide is delivered to them, are limited by pulmonary blood flow (Figure 1). For this reason, the excretion of carbon dioxide or the uptake of oxygen can be used to measure the cardiac output (or, more pedantically, the pulmonary blood flow). For the same reason, pulmonary diffusion capacity (a measure of the maximum rate at which a gas can diffuse across the lungs between the alveoli and the blood) cannot be measured using these gases.

***James Waterhouse*** *is Professor of Biological Rhythms at the Research Institute for Sport and Exercise Sciences, Liverpool John Moores University. He qualified as an animal physiologist at the University of Oxford and gained his DPhil there. His research interests are circadian rhythms in humans, with particular reference to jetlag and assessing the clock-driven component of a measured circadian rhythm.*

***Iain Campbell*** *is Consultant Anaesthetist at the University Hospitals of South Manchester NHS Trust and Visiting Professor of Human Physiology at Liverpool John Moores University. He qualified from Guy's Hospital Medical School, London, and trained in anaesthesia in Zimbabwe, Southend, Montreal and Leeds.*

By contrast, when carbon monoxide is breathed into the alveoli, the capacity of the blood for this gas is so great that the blood and alveoli have not equilibrated by the time the blood leaves the pulmonary capillaries (Figure 1). The uptake of this gas is not flow-limited, but diffusion-limited; its rate of uptake can therefore be used to assess pulmonary diffusion capacity, but not cardiac output.

### A perfusion gradient down the lungs

Just as there is a gradient of ventilation from the apical to the basal alveoli, there is also a gradient of their perfusion by pulmonary blood. This gradient is in the same direction as that of ventilation (more perfusion at the base than the apex), and it arises because of the effects of gravity on the pulmonary circuit.

The peak pressure of the pulmonary circuit is about 25 cm $H_2O$ during systole. Low capillary pressures reduce the loss of fluids into the surrounding tissue and alveoli, which is beneficial, because fluid accumulation would decrease diffusion by increasing the path length. The low pressures in the pulmonary circuit are achieved despite having to carry the whole of the cardiac output. This requires the resistance of the circuit to be low, which means that, compared with the systemic circuit, there is far less smooth muscle in the pulmonary arterioles. Because of this, the pulmonary arterioles do not damp the cardiac pulse and the vasculature is much more affected by transmural pressure changes caused by gravity and posture.

Any point, x, in a column of fluid has a pressure, $P_x$, that differs from the pressure, $P_f$, at some fixed point, f, by an amount given by the equation:

$$P_x = P_f \pm h.\rho.g$$

where: h is the vertical distance between the two points (it is + h.ρ.g if x is below f, and – h.ρ.g if x is above f); ρ is the density of the fluid; g is the acceleration due to gravity.

This can be used to calculate the extra changes in blood pressure in blood vessels that arise because the site under consideration is above or below the heart. If the pressure is measured in cm $H_2O$, then, since the density of blood is about that of water, the pressure changes can be calculated simply. For example, when an individual is standing up, the blood pressure in the retinal artery is about 25 cm $H_2O$ lower than when lying down. This is because the eyes are about 25 cm above the heart when standing, but about level with the heart when lying down. Similarly, the pressure inside the arterioles and veins in the feet when standing is raised by about 100 cm $H_2O$, because these vessels are 100 cm below the heart. Note that all vessels in a circulation are affected equally, so the force driving blood through the capillaries is not changed. However, whereas the raised pressure in the veins of the feet causes them to become distended, and causes the opening of more blood vessels (recruitment), this does not occur with the arterioles. This is because the veins contain little smooth muscle, and so cannot resist the distending force, whereas the arterioles contain much smooth muscle, which contracts automatically when distended by the increased pressure inside the vessel.

The pulmonary circuit behaves more like systemic veins because it contains less smooth muscle. The distension caused reduces the resistance to blood flow provided by the arterioles. Thus, even though the arteriovenous pressure difference is unchanged, the resistance of the system is decreased. As a result, the pulmonary blood flow increases from the apical to the basal alveoli in an upright individual. Recruitment of blood vessels adds to this effect.

In practice, the position is more complicated for two reasons. The first concerns the pressures in the surrounding tissues (including the alveoli). The lungs in an upright individual can be divided into three zones, each covering about one-third of the lung. In the basal zone, both arterial and venous blood pressures are greater than those in the surrounding tissue throughout the respiratory cycle, and so the above description (of the effects of hydrostatic forces on the amount of distension of the arterioles) applies directly. Blood flows are highest in this zone of the lung. In the middle zone, even though the arterial pressure is always greater than the pressure in the surrounding tissues, the venous pressures are lower. In these circumstances, blood flow is determined by vessel resistance and the difference between arterial and tissue pressure. Blood flows here are lower than in the basal zone. In the apical zone, there is no blood flow during diastole, the fall in pressure due to the height of the apex of the lung being greater than the blood pressure at this time. During systole, however, the blood pressure is raised sufficiently for the system to act like the middle zone. Blood flows are lowest in this zone. Nevertheless, in spite of these differences between the three zones, the pressure relationships change in such a way that there is also, within each of them, an increase in blood flow from the top to the bottom of the zone.

The second complication arises because as the lungs are expanded, so too are all the blood vessels and bronchioles. This reduces the resistance of both sets of vessels, but it is most evident at the base of the lung, owing to the proximity of the diaphragm and its role in promoting inspiration.

In summary, in the upright individual there is a gradient of blood flow past the alveoli from the apex (where it is lowest) to the base of the lung (where it is highest).

### Ventilation–perfusion balance

Blood flow past the alveoli (perfusion) and airflow into them (ventilation) increase from the apex to the base of the lungs, and both are caused in part by gravity. (For this reason, the gradients are in the reverse direction if the subject is inverted, and disappear in a zero-gravity environment.) However, the causes of these two gradients are not identical, and their sizes are unequal. The gradient of perfusion is greater than that of ventilation. Accordingly, there is a gradient in the ventilation–perfusion ratio, which decreases from the apex to the base of the lung. The alveoli at the apex are over-ventilated for the (very small) amount of perfusion that they receive, while those at the base of the lung are under-ventilated, the larger amount of ventilation being less than the much increased perfusion.

Such ventilation–perfusion imbalances threaten to decrease the efficiency with which gas exchange takes place in the lung. Further, there is wasted work because the respiratory muscles over-ventilate the apical alveoli, and the heart over-perfuses the basal alveoli. In practice, these inefficiencies are minimized by local reflexes that act to balance perfusion and ventilation.

At the lung apex, the over-ventilation results in a fall of carbon dioxide levels in the bronchiolar tree. This causes bronchoconstriction, tending to direct airflow away from the over-ventilated/under-perfused regions at the lung apex. At the base of the lung, the excessive perfusion results in an increased uptake of oxygen from the alveoli and a tendency for hypoxaemia (a low tension of oxygen in the blood) to develop. However, the pulmonary arterioles show a remarkable property that is the opposite of that shown by systemic arterioles. In systemic arterioles, hypoxaemia leads to vasodilatation, therefore an exercising tissue gets more blood, and a balance exists between the metabolic need and local perfusion of the tissue. In pulmonary arterioles, hypoxaemia has the opposite effect, causing vasoconstriction. This property, though not fully understood, is vital when the relationship between alveolar ventilation and perfusion is considered, because it means that blood tends to be directed away from the over-perfused/under-ventilated regions at the base of the lung. The stimulus to hypoxic vasoconstriction comes mainly from the low partial pressure of oxygen in the alveolus and also in the mixed venous blood (pulmonary artery). In the presence of chronic hypoxia (high altitude and some forms of lung disease) pulmonary artery pressure rises due to pulmonary vasoconstriction.

## Transport of gases by the blood

### Oxygen

Oxygen is carried in the erythrocytes, bound reversibly to haemoglobin. Haemoglobin is a complex molecule consisting of four subunits, each containing a molecule of ferrous iron, a tetrapyrrole ring and a protein chain. The reaction involves four molecules of oxygen and one of haemoglobin; it is one of oxygenation, reduced haemoglobin being converted to oxyhaemoglobin.

At the lungs, where the partial pressure of oxygen is high, the reaction can be represented as:

$$Hb_4 + 4O_2 \longrightarrow Hb_4O_8 + \text{heat} + H^+$$

At the tissues, where the partial pressure of oxygen is low, the opposite reaction takes place. In health, the haemoglobin is

 