

The systemic circulation

The systemic blood vessels are divided into arteries, arterioles, capillaries and veins. Arteries supply blood to the organs at high pressure, whereas arterioles are smaller vessels with muscular walls which allow direct control of flow through each capillary bed. Capillaries consist of a single layer of endothelial cells, and the thin walls allow exchange of nutrients between blood and tissue. Veins return blood from the capillary beds to the heart, and contain 70% of the circulating blood volume, in contrast to the 15% in the arterial system. Veins act a reservoir, and venous tone is important in maintaining the return of blood to the heart, for example in severe haemorrhage, when sympathetic stimulation causes venoconstriction. 🔴

Blood flow

The relationship between flow and driving pressure is given by the **Hagen-Poiseuille** formula. This states that flow rate in a tube is proportional to:

$$\frac{\text{Driving pressure} \times \text{Radius}^4}{\text{Length} \times \text{Viscosity}}$$

In blood vessels flow is pulsatile rather than continuous, and viscosity varies with flow rate, so the formula is not strictly applicable, but it illustrates an important point; small changes in radius result in large changes in flow rate. In both arterioles and capillaries changes in flow rate are brought about by changes in tone and therefore vessel radius.

Viscosity describes the tendency of a fluid to resist flow. At low flow rates the red blood cells stick together, increasing viscosity, and remain in the centre of the vessel. The blood closest to the vessel wall (which supplies side branches) therefore has a lower haematocrit. This process is known as **plasma skimming**. Viscosity is reduced in the presence of anaemia, and the resulting increased flow rate helps maintain oxygen delivery to the tissues. 🔴

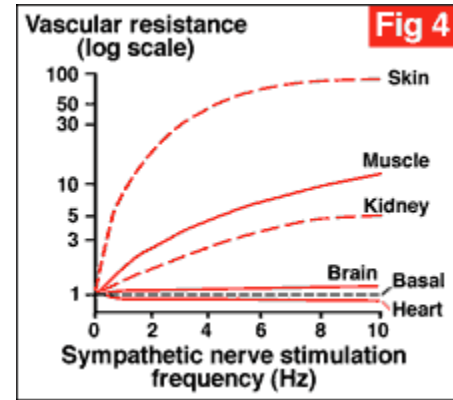
Control of the systemic circulation

Arteriolar tone determines blood flow to the capillary beds. A number of factors influence arteriolar tone, including autonomic control, circulating hormones, endothelium derived factors and the local concentration of metabolites.

Autonomic control is largely by the sympathetic nervous system, which supplies all vessels except capillaries. Sympathetic fibres arise from the thoracic and lumbar

segments of the spinal cord. These are under the control of the vasomotor centre in the medulla, which has distinct vasoconstrictor and vasodilator areas.

Although there is a baseline sympathetic discharge to maintain vascular tone, increased stimulation affects some organs more than others (Figure 4). This tends to redistribute blood from skin, muscle and gut to brain, heart and kidney. Increased sympathetic discharge is one of the responses to hypovolaemia, for example in severe blood loss, with the effect of protecting blood supply to the vital organs. The predominant sympathetic influence is vasoconstriction via alpha-adrenergic receptors. However, the sympathetic system also causes vasodilation via beta adrenergic and cholinergic receptor stimulation, but only in skeletal muscle.



This increased blood flow to muscle is an important part of the "fight or flight" reaction, when exercise is anticipated.

Circulating hormones such as adrenaline and angiotensin II are potent vasoconstrictors, but they probably have little effect on acute cardiovascular control. In contrast, endothelium derived factors play an important role in controlling local blood flow. These substances are either produced or modified in the vascular endothelium, and include prostacyclin and nitric oxide, both potent vasodilators. An accumulation of metabolites such as CO_2 , K^+ , H^+ , adenosine and lactate causes vasodilation. This response is probably an important mechanism of autoregulation, the process whereby blood flow through an organ is controlled locally, and remains constant over a wide range of perfusion pressure. Autoregulation is a particular feature of the cerebral and renal circulations. 🚩

Control of arterial pressure

Systemic arterial pressure is controlled closely in order to maintain tissue perfusion. The **mean arterial pressure (MAP)** takes account of pulsatile blood flow in the arteries, and is the best measure of perfusion pressure to an organ. MAP is defined:

$$\text{MAP} = \text{Diastolic arterial pressure} + (\text{pulse pressure} / 3)$$

where pulse pressure is the difference between systolic and diastolic arterial pressure.

MAP is the product of cardiac output (CO) and systemic vascular resistance (SVR):

$$\text{MAP} = \text{CO} \times \text{SVR}$$

If cardiac output falls, for example when venous return decreases in hypovolaemia, MAP will also fall unless there is a compensatory rise in SVR by vasoconstriction of the arterioles. This response is mediated by baroreceptors, which are specialised sensors of pressure located in the carotid sinus and aortic arch, and connected to the vasomotor centre. A fall in blood pressure causes reduced stimulation of the baroreceptors, and consequent reduced discharge from the baroreceptors to the vasomotor centre. This causes an increase in sympathetic discharge leading to vasoconstriction, increased heart rate and contractility, and secretion of adrenaline. Conversely, rises in blood pressure stimulate the baroreceptors, which leads to increased parasympathetic outflow to the heart via branches of the vagus nerve, causing slowing of the heart. There is also reduced sympathetic stimulation to the peripheral vessels causing vasodilation.

Baroreceptor responses provide immediate control of blood pressure; if hypotension is prolonged, other mechanisms start to operate, such as the release of angiotensin II and aldosterone from the kidneys and adrenal glands, which leads to salt and water being retained in the circulation.

Cardiovascular responses to anaesthesia

All anaesthetic agents have a direct depressant effect on the myocardium. Therefore they reduce myocardial contractility, and many also reduce sympathetic stimulation of the vascular system. The result is a decreased cardiac output accompanied by vasodilation, causing hypotension. This fall in blood pressure can compromise perfusion of vital organs, especially at induction of anaesthesia in the hypovolaemic patient. In **contrast**, agents such as **ketamine** and **ether** increase sympathetic activity, which opposes the direct depressant effect. Thus cardiac output and blood pressure are maintained despite the direct myocardial depressant action.

Volatile anaesthetic agents reduce discharge from the sinoatrial node. This can lead to **junctional** rhythms, when the atrioventricular node takes over as pacemaker, associated with an absent P wave on the ECG. Local anaesthetic agents depress conduction of the cardiac impulse. This effect can be therapeutic, for example in the treatment of ventricular arrhythmias with lignocaine. However, at higher concentrations local anaesthetics can cause cardiac arrest - it is vital to avoid accidental intravenous injection when using these agents.

Controlled ventilation in a paralysed patient has many effects. Firstly it increases intrathoracic pressure which reduces venous return and preload, causing a fall in cardiac output. Secondly, changes in the partial pressure of carbon dioxide (PaCO_2) resulting from changes in ventilation will also have cardiovascular effects. A low PaCO_2 , which commonly occurs during controlled ventilation, causes peripheral

vasoconstriction by a direct effect. This increases systemic vascular resistance, increases afterload and can result in a fall in cardiac output. It also causes cerebral vasoconstriction, reducing cerebral blood volume ([BACK](#) [Cerebral blood flow](#), *Update in Anaesthesia* 1998;8). A high PaCO₂ usually occurs in the anaesthetised patient during spontaneous breathing, and causes vasodilation and increased sympathetic activity, leading to increased cardiac output. However, the heart will be more likely to develop arrhythmias, particularly when using volatile agents.

Spinal and epidural anaesthesia blocks sympathetic nerves as well as sensory and motor fibres. This can lead to marked hypotension due to arteriolar and venous dilation because the sympathetic nerves to the lower extremities are blocked. Cardiac sympathetic nerve fibres, which arise from the high thoracic spinal cord, may also be blocked, allowing an unopposed vagal action on the heart. In this case there will not be an appropriate increase in cardiac output, and blood pressure will fall further with a bradycardia.

For patients with coronary artery disease, it is important to use an anaesthetic technique which does not cause further myocardial ischaemia. The important principle is to ensure that **myocardial oxygen supply** is greater than **myocardial oxygen demand**. The balance between these two variables is influenced by the following factors:

Myocardial oxygen supply	Myocardial oxygen demand
Heart rate Diastolic time	Heart rate
Coronary perfusion pressure Aortic diastolic blood pressure Ventricular end-diastolic blood pressure	Ventricular wall tension Preload Afterload
Arterial oxygen content Arterial oxygen partial pressure Haemoglobin concentration	Contractility
Coronary artery diameter	



The Physiology of Oxygen Delivery

Introduction

In order to survive humans have to be able to extract oxygen from the atmosphere and transport it to their cells where it is utilised for essential metabolic processes. Some cells can produce energy without oxygen (anaerobic metabolism) for a short time, although it is inefficient. Other organs (e.g. brain) are made up of cells that can only make the energy necessary for survival in the presence of a continual supply of oxygen (aerobic metabolism). Tissues differ in their ability to withstand anoxia (lack of oxygen). The brain and the heart are the most sensitive. Initially a lack of oxygen affects organ function but with time irreversible damage is done (within minutes in the case of the brain) and revival is impossible. ▲

OXYGEN TRANSPORT FROM AIR TO TISSUES

Oxygen is transported from the air that we breathe to each cell in the body. In general, gases move from an area of high concentration (pressure) to areas of low concentration (pressure). If there are a mixture of gases in a container, the pressure of each gas (partial pressure) is equal to the pressure that each gas would produce if it occupied the container alone. ▲

Atmosphere to alveolus

The air (atmosphere) around us has a total pressure of 760 mmHg (1 atmosphere of pressure = 760mmHg = 101kPa = 15lbs/sq. in). Air is made up of 21% oxygen, 78% nitrogen and small quantities of CO₂, argon and helium. The pressure exerted by the main two gases individually, when added together, equals the total surrounding pressure or atmospheric pressure. The pressure of oxygen (PO₂) of dry air at sea level is therefore 159 mmHg ($21/100 \times 760 = 159$). However by the time the inspired air reaches the trachea it has been warmed and humidified by the upper respiratory tract. The humidity is formed by water vapour which as a gas exerts a pressure. At 37°C the water vapour pressure in the trachea is 47 mmHg. Taking the water vapour pressure into account, the PO₂ in the trachea when breathing air is $(760-47) \times 21/100 = 150$ mmHg. By the time the oxygen has reached the alveoli the PO₂ has fallen to about 100 mmHg. This is because the PO₂ of the gas in the alveoli (PAO₂) is a balance between two processes: the removal of oxygen by the pulmonary capillaries and its continual supply by alveolar ventilation (breathing). ▲

Alveolus to blood

Blood returning to the heart from the tissues has a low PO₂ (40 mmHg) and travels to the lungs via the pulmonary arteries. The pulmonary arteries form pulmonary capillaries, which surround alveoli. Oxygen diffuses (moves through the membrane separating the air and the blood) from the high pressure in the alveoli (100 mmHg) to

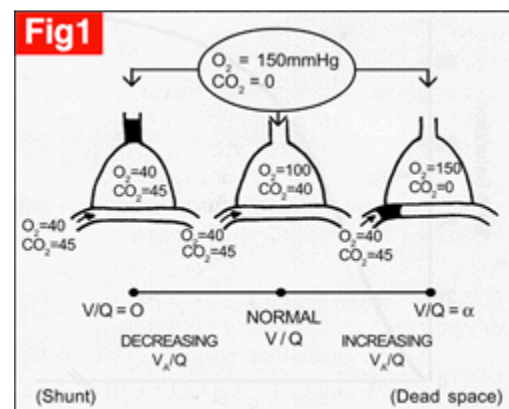
the area of lower pressure of the blood in the pulmonary capillaries (40 mmHg). After oxygenation blood moves into the pulmonary veins which return to the left side of the heart to be pumped to the systemic tissues. In a 'perfect lung' the PO_2 of pulmonary venous blood would be equal to the PO_2 in the alveolus. Three factors may cause the PO_2 in the pulmonary veins to be less than the PAO_2 : ventilation/perfusion mismatch, shunt and slow diffusion. ▲

Ventilation/perfusion mismatch

In a 'perfect lung' all alveoli would receive an equal share of alveolar ventilation and the pulmonary capillaries that surround different alveoli would receive an equal share of cardiac output ie. ventilation and perfusion would be perfectly matched.

Diseased lungs may have marked mismatch between ventilation and perfusion. Some alveoli are relatively overventilated while others are relatively overperfused (the most extreme form of this is shunt where blood flows past alveoli with no gas exchange taking place (figure 1). Well ventilated alveoli (high PO_2 in capillary blood) cannot make up for the oxygen not transferred in the underventilated alveoli with a low PO_2 in the capillary blood. This is because there is a maximum amount of oxygen which can combine with haemoglobin (see haemoglobin-oxygen dissociation curve figure 2a). The pulmonary venous blood (mixture of pulmonary capillary blood from all alveoli) will therefore have a lower PO_2 than the PO_2 in the alveoli (PAO_2). Even normal lungs have some degree of ventilation/perfusion mismatch; the upper zones are relatively overventilated while the lower zones are relatively overperfused and underventilated.

Shunt occurs when deoxygenated venous blood from the body passes unventilated alveoli to enter the pulmonary veins and the systemic arterial system with an unchanged PO_2 (40 mmHg). (Figure 1.) Atelectasis (collapsed alveoli), consolidation of the lung, pulmonary oedema or small airway closure (see later) will cause shunt. ▲



Diffusion

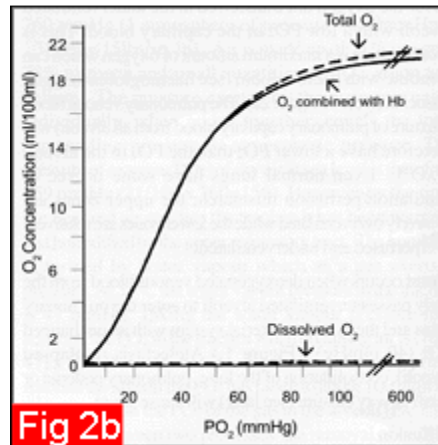
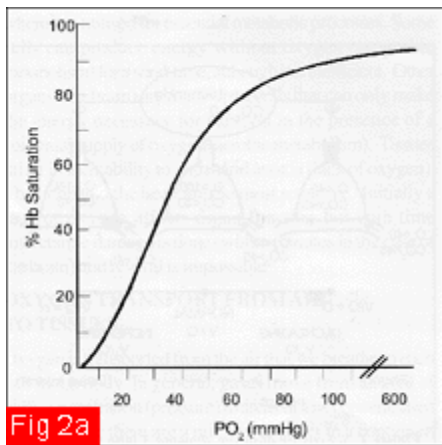
Oxygen diffuses from the alveolus to the capillary until the PO_2 in the capillary is equal to that in the alveolus. This process is normally complete by the time the blood has passed about one third of the way along the pulmonary capillary.

In the normal lung, the diffusion of oxygen into the blood is very rapid and is complete, even if the cardiac output is increased (exercise) and the blood spends less time in contact with the alveolus. This may not happen when the alveolar capillary network is abnormal (pulmonary disease). However, the ability of the lung to compensate is great and problems caused by poor gas diffusion are a rare cause for hypoxia, except with diseases such as alveolar fibrosis.

In order to decrease the detrimental effect that shunt and ventilation/perfusion mismatch have on oxygenation, the blood vessels in the lung are adapted to vasoconstrict and therefore reduce blood flow to areas which are underventilated. This is termed hypoxic pulmonary vasoconstriction and reduces the effect of shunt. ▲

Oxygen carriage by the blood

Oxygen is carried in the blood in two forms. Most is carried combined with haemoglobin (figure 2b) but there is a very small amount dissolved in the plasma. Each gram of haemoglobin can carry 1.31 ml of oxygen when it is fully saturated. Therefore every litre of blood with a Hb concentration of 15g/dl can carry about 200 mls of oxygen when fully saturated (occupied) with oxygen ($PO_2 > 100$ mmHg). At this PO_2 only 3 ml of oxygen will dissolve in every litre of plasma.

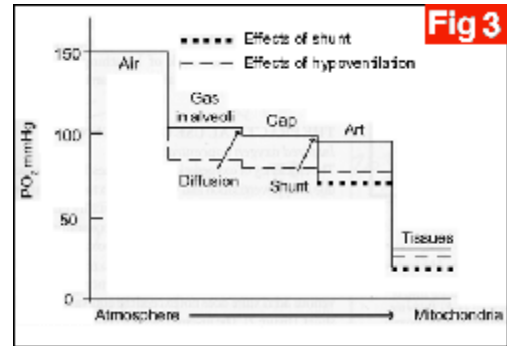


If the PO_2 of oxygen in arterial blood (PAO_2) is increased significantly (by breathing 100% oxygen) then a small amount of extra oxygen will dissolve in the plasma (at a rate of 0.003 ml O_2 /100ml of blood /mmHg PO_2) but there will normally be no significant increase in the amount carried by haemoglobin, which is already >95% saturated with oxygen. When considering the adequacy of oxygen delivery to the

tissues, three factors need to be taken into account, haemoglobin concentration, cardiac output and oxygenation. ▲

Oxygen cascade

Oxygen moves down the pressure or concentration gradient from a relatively high level in air, to the levels in the respiratory tract and then alveolar gas, the arterial blood, capillaries and finally the cell. The PO_2 reaches the lowest level (4-20 mmHg) in the mitochondria (structures in cells responsible for energy production). This decrease in PO_2 from air to the mitochondrion is known as the oxygen cascade and the size of any one step in the cascade may be increased under pathological circumstances and may result in hypoxia (figure 3). ▲



Oxygen delivery

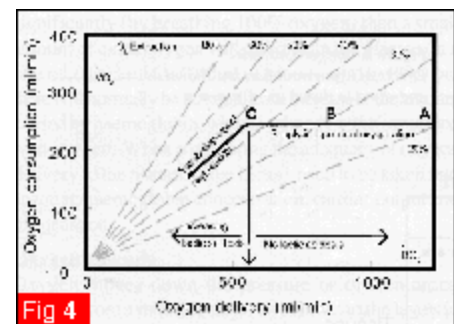
The quantity of oxygen made available to the body in one minute is known as the oxygen delivery and is equal to the cardiac output x the arterial oxygen content (see previously) ie. $5000\text{ml blood/min} \times 200\text{ mlO}_2/1000\text{ ml blood} = 1000\text{ml O}_2/\text{min}$.


Oxygen delivery ($\text{mls O}_2/\text{min}$) = Cardiac output (litres/min) x Hb concentration (g/litre) x 1.31 ($\text{mls O}_2/\text{g Hb}$) x % saturation ▲

Oxygen consumption

Approximately 250 ml of oxygen are used every minute by a conscious resting person (oxygen consumption) and therefore about 25% of the arterial oxygen is used every minute. The haemoglobin in mixed venous blood is about 70% saturated (95% less 25%).

In general there is more oxygen delivered to the cells of the body than they actually use. When oxygen consumption is high (eg. during exercise) the increased oxygen requirement is usually provided by an increased cardiac output - see formula above for how this works. However, a low cardiac output, a low haemoglobin concentration (anaemia) or a low haemoglobin O_2 saturation will result in an inadequate delivery of oxygen, unless a compensatory change occurs in one of the other factors. Alternatively, if oxygen delivery



falls relative to oxygen consumption the tissues extract more oxygen from the haemoglobin (the saturation of mixed venous blood falls below 70%)(a-b in figure 4). A reduction below point 'c' in figure 4 cannot be compensated for by an increased oxygen extraction and results in anaerobic metabolism and lactic acidosis. 

OXYGEN STORES


In spite of the great importance of oxygen, the stores of oxygen in the body are small and would be unable to sustain life for more than a few minutes. If breathing ceases, oxygen stores are limited to the oxygen in the lung and in the blood. The amount of oxygen in the blood depends on the blood volume and haemoglobin concentration. The amount of oxygen in the lung is dependent on the lung volume at functional residual capacity (FRC) and the alveolar concentration of oxygen. The FRC is the volume of air (about 3 litres in an adult) that is present in the lungs at the end of a normal expiration ie when the elastic recoil of the lung is balanced by the relaxed chest wall and diaphragm. While breathing air the total stores (oxygen in blood and lung) are small and because the major component of this store is the oxygen bound to haemoglobin (see Table 1) only a small part of these stores can be released without an unacceptable reduction in PaO₂ (when haemoglobin is 50% saturated with oxygen the PaO₂ will have fallen to 26 mmHg). Breathing 100% oxygen causes a large increase in the total stores as the FRC fills with oxygen. The major component of the store is now in the lung and 80% of this oxygen can be used without any reduction in haemoglobin saturation (PAO₂ still about 100mmHg). This is the reason why pre-oxygenation is so effective. (see later) 

Table 1. Principle stores of oxygen in the body		
	While breathing <i>AIR</i>	While breathing <i>100% O₂</i>
In the lungs (FRC)	450ml	3000ml
In the blood	850ml	950ml
Dissolved or bound in tissues(FRC)	250ml	300ml
Total	1550ml	4250ml