

# Principles of cardiopulmonary bypass

David Machin BSc ACP  
Chris Allsager MB ChB FRCA

## Key points

Membrane oxygenators are commonly used for gas exchange during cardiopulmonary bypass (CPB).

Roller or centrifugal pumps are utilized in CPB.

Confirm adequate patient anticoagulation before initiation of CPB.

CPB is performed over a range of temperatures (37–15°C).

Cardiac surgery with CPB can promote a systemic inflammatory response syndrome.

The use of cardiopulmonary bypass (CPB) technology allows cardiac surgical procedures to be performed in a motionless, bloodless surgical field. It incorporates an extracorporeal circuit to provide physiological support. Typically, blood is gravity drained from the heart and lungs to a reservoir via venous cannulation and tubing, and returned oxygenated to the cannulated arterial system by utilizing a pump and artificial lung (oxygenator or gas-exchanger). The tubing and cannulae are manufactured of clear polyvinyl chloride, while the oxygenator casing and connectors consist of polycarbonate (Fig. 1).

## Gas exchange

Three basic types of blood oxygenators for CPB have been developed. Historically, oxygenators provided gas exchange by contact of a blood film to an oxygen rich atmosphere (e.g. disc oxygenators) or by bubbling oxygen through blood (e.g. bubble oxygenators). Modern day oxygenators provide gas exchange to blood through a membrane (e.g. sheet and hollow-fibre oxygenators). Sheet membrane oxygenators can either be configured as a flat plate microporous polypropylene membrane or spiral wound silicone membrane. Microporous membranes consist of 0.05–0.3 µm pores that initially create a direct blood gas interface until a thin protein film quickly forms, producing molecular membranes. Silicone membranes are considered ‘true membranes’ and prevent ‘plasma leakage’ into the gas phase, which is characteristic of microporous membranes after long periods of CPB. Plasma leakage is thought to occur when the micropores lose their hydrophobicity by the adsorption of protein, which leaks through the micropores and reduces gas exchange performance.<sup>1</sup> Hollow-fibre oxygenators allow high surface area-to-blood volume ratios and mainly consist of microporous polypropylene or polymethylpentene material.

The physical process of convection, diffusion and chemical reactions that occur

during gas exchange in the natural lung also apply to the artificial lung. However, gas exchange is less efficient. Diffusional distances are greater (approximately 200 µm in comparison with 10 µm in the human alveolus) and surface area for gas exchange is 1.7–3.5 m<sup>2</sup> compared with 70–100 m<sup>2</sup> in the human lung. Gas exchange obeys Fick’s law of diffusion:

$$V_{\text{gas}} \propto \frac{AD\delta P}{T}$$
$$D \propto \frac{\text{Sol}}{\sqrt{\text{MW}}}$$

where the amount of gas transferred ( $V_{\text{gas}}$ ) is proportional to the area ( $A$ ), a diffusion constant ( $D$ ) and the partial pressure difference ( $\delta P$ ) and is inversely proportional to the membrane thickness ( $T$ ).  $D$  is proportional to the specific gas solubility (Sol) and inversely proportional to the square root of its molecular weight (MW).

Applying Fick’s law to the artificial lung, a higher partial pressure difference of oxygen (maximum pressure gradient of 760 mm Hg minus oxygen tension in blood) and to some extent carbon dioxide (maximum gradient is equal to carbon dioxide tension in blood phase) is required to compensate for an increased diffusional distance and fixed, reduced surface area. Despite the pressure gradient for carbon dioxide (CO<sub>2</sub>) being considerably lower than oxygen (O<sub>2</sub>), the artificial lung material is more gas permeable to CO<sub>2</sub> than (O<sub>2</sub>); silicone membranes have a CO<sub>2</sub>:O<sub>2</sub> transmission ratio of about 5:1.<sup>2</sup>

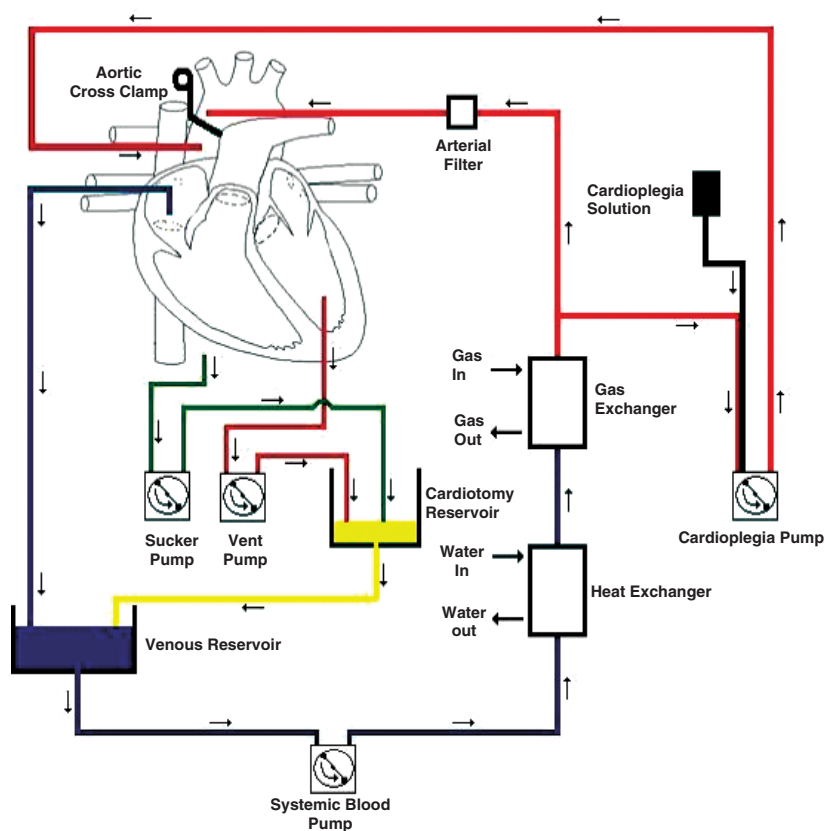
Oxygen transfer in modern blood oxygenators is described by the advancing front theory. Demonstrated by studies of oxygen transport through constantly moving blood films, the large binding capacity of haemoglobin for oxygen and rapid oxygen–haemoglobin kinetics are thought to create two distinct zones in the blood film. Oxygen diffuses through a fully oxygen saturated zone to an unsaturated front where the oxygen binds with unsaturated haemoglobin.<sup>3</sup>

## David Machin BSc ACP

Perfusionist  
Theatres  
Glenfield Hospital  
Groby Road  
Leicester  
LE3 9Q  
UK  
Tel: 0116 256 3604  
E-mail: machin\_david36@hotmail.com  
(for correspondence)

## Chris Allsager MB ChB FRCA

Consultant Anaesthetist  
Glenfield Hospital  
Leicester  
UK



**Fig. 1** Diagrammatic representation of a 'closed' extracorporeal circuit for cardiopulmonary bypass.

Carbon dioxide transfer in modern oxygenators is more difficult to predict, because of factors such as dissolved  $\text{CO}_2$ , plasma bicarbonate ions and varying partial pressure of  $\text{CO}_2$  in the gas phase. The latter can be decreased by increasing the ventilating gas flow rate (sweep gas) entering the oxygenator gas phase.

## Blood pumps

During CPB, constant blood flow is delivered to the patient by a mechanical pump. The characteristics of an ideal blood pump should consider properties that effect blood flow, as described by the Hagen–Poiseuille equation:

$$\text{Blood flow rate} = \frac{(\text{Pressure gradient}) \times (\text{Tube radius})^4 \times \pi}{(\text{Fluid viscosity}) \times (\text{Tube length}) \times 8}$$

Put simply,

$$\text{Blood flow rate} = \frac{\text{Pressure}}{\text{Resistance}}$$

Thus, the pump should be able to generate blood flow and pressure against a degree of resistance. It should be made of biocompatible materials, create no areas of blood stasis or turbulence and be able to adjust for different sizes of extracorporeal tubing. These mechanical pumps have low priming volumes, are easily controlled and produce a low index of

haemolysis (plasma haemoglobin per 100 ml of pumped blood). Roller pumps (RPs) and centrifugal pumps (CPs) are routinely used and can accurately deliver blood over wide range of flow rates against a variable resistance.

The RP comprises a length of PVC or silicone tubing situated against a curved metal backing plate (raceway) which is compressed by two rollers located on the ends of rotating arms at  $180^\circ$  to each other. The direction of compression of the tubing by the rotating arm containing the roller permits forward blood flow. Hence, this type of pump is described as a positive displacement device, allowing constant delivery of blood volume despite minor variations in the outlet afterload. Blood flow depends upon the pump tubing internal diameter (see Hagen–Poiseuille equation), rotation rate of the rollers and diameter of the pump head.

CPs consist of a vaned impeller or a nest of smooth plastic cones within a plastic casing. These impellers or cones are magnetically coupled (at the base) with an electric motor and, when rotated rapidly, generate a centrifugal force to the blood, which is received by the pump body. Centrifugal force is converted into kinetic energy, which gives flow, or potential energy, which gives pressure. An object that produces centrifugal force (CF) can be defined as

$$\text{CF} = \text{mass} \times \text{radius} \times \text{angular velocity}$$

In a clinical setting,

$$\text{CF} = \text{Mass of blood} \times \text{radius of pump head} \\ \times \text{speed of revolutions (RPM)}$$

Unlike RPs, CPs are totally non-occlusive and are afterload dependant. Any significant change in resistance/pressure at the outlet or inlet of the pump will alter blood flow rate. The non-occlusive feature of the CP prevents generation of excessive pressure in the extracorporeal circuit, thus preventing circuit rupture.

## Myocardial protection

To provide a dry, motionless, operative area, a cross-clamp is placed across the ascending aorta above the coronary ostia and proximal to the aortic cannula, thus isolating the coronary circulation and preventing blood entering the chambers of the heart. Therefore, techniques of myocardial protection are used to preserve myocardial function and prevent cell death. Cardioplegic techniques for myocardial protection involve the delivery of cardioplegic solution to the myocardium to provide diastolic electromechanical arrest. This is administered by an antegrade approach via the aortic root or direct coronary ostium access, or by a retrograde manner if severe coronary artery occlusions exist. The latter may not provide adequate right-heart protection; thus, the delivery of both antegrade and retrograde cardioplegia may ensure adequate distribution and subsequent improved myocardial protect. Intermittent cardioplegia delivery (i.e. every 15–30 min) allows a relatively bloodless surgical view during more challenging operative periods. Continuous administration would improve for myocardial protection but this is not always practical.

Potassium is the main agent used to induce cardiac arrest; in a concentration of approximately 20 mmol litre<sup>-1</sup> it causes a reduction in myocardial membrane potential. Fast inward sodium channels are inactivated preventing the upstroke of myocardial cell action potentials, causing the myocardium to become unexcitable in diastolic arrest.<sup>4</sup> Cardioplegia can be administered as a cold crystalloid cardioplegia, cold blood cardioplegia or warm blood cardioplegia. Blood cardioplegia is thought to offer the advantage of delivering oxygen at the cellular level via its haemoglobin content, but it may be less efficient during cold delivery because of the left shift of the oxygen-dissociation curve. Blood cardioplegia also provides other benefits including hydrogen ion buffering, free-radical scavenging, reduced myocardial oedema and improved micro-vascular flow.

Various ratios of blood to cardioplegic solution can be administered (e.g. 1 : 1, 2 : 1, 4 : 1) or even neat potassium (microplegia). The addition of glutamate and aspartate to cardioplegic solutions may promote oxidative metabolism in energy-depleted hearts. The use of esmolol and nicorandil as cardiac electromechanical arrest agents has also been considered as possible alternatives to potassium. The negative inotropic and chronotropic effects of esmolol result in a reduction in myocardial

oxygen consumption. The potassium channel opener, nicorandil, may offer advantages over potassium-based cardioplegia by providing cardiac arrest near its resting membrane potential, allowing balanced trans-membrane ion gradients and minimal energy requirements.<sup>5</sup>

Non-cardioplegic techniques include the use of moderate systemic hypothermia (i.e. core temperature of 30–32°C) with short periods of aortic cross-clamping and ventricular fibrillation (VF). A variation of this technique involves hypothermic systemic perfusion combined with prolonged VF, enabling continuous coronary perfusion. Unfortunately, this greatly increases myocardial oxygen consumption compared with the empty beating heart; it also reduces subendocardial perfusion.<sup>6</sup> Ischaemic preconditioning for myocardial protection is also practiced by introducing brief periods of myocardial ischaemia to tolerate a longer ischaemic challenge.

## Temperature management during CPB

CPB is performed under systemic hypothermia (typically a nasopharyngeal temperature of 25–32°C) or normothermic conditions. More challenging operations may require deep hypothermia (15–22°C) to allow periods of low blood flow or deep hypothermic circulatory arrest. Systemic hypothermia has remained a cornerstone of cardiac surgical practice, with a great deal of evidence demonstrating that it decreases myocardial oxygen consumption. This ensures protection and increased tolerance for ischaemia of vital organs and allows periods of low blood flow during CPB. At a biochemical level, temperature changes the reaction rates and metabolic processes by a factor known as the Q<sub>10</sub> effect, which defines the amount of increase or decrease in these processes relative to a 10°C difference. Total body oxygen consumption is said to have a Q<sub>10</sub> factor of approximately 2.6 in adults and 3.65 in infants.<sup>7</sup> However, because of many of the detrimental processes associated with hypothermia (e.g. impaired myocardial cell membrane function, possible excessive postoperative bleeding), normothermic CPB is practiced by some surgeons to provide a more physiological state. It is also hypothesized that electromechanical work is the main determinant of myocardial oxygen requirement rather than cooling of the heart.<sup>5</sup> Hence, a chemically induced mechanical arrested heart, without added hypothermia, is expected to reduce myocardial metabolic requirements to such a degree that it can be matched by regular doses of blood cardioplegia.

## Acid–base management

Management of the acid–base status throughout the hypothermic CPB period remains controversial. Arterial blood gas parameters are either corrected for temperature and pH is kept constant (i.e. pH-stat) or blood gas levels are uncorrected (measured at 37°C) and alkalosis is permitted during cooling

(i.e. alpha-stat). pH-stat blood gas management increases CO<sub>2</sub> content during cooling and, as cerebral blood flow is dependent on P<sub>CO<sub>2</sub></sub>, cerebral blood vessels dilate. Autoregulation, which normally keeps cerebral blood flow constant at arterial pressures of 50–150 mm Hg, is lost during pH-stat and cerebral blood flow becomes pressure-dependent. Alpha-stat blood gas management seems more appropriate as it maintains autoregulation, offers better control of cerebral blood flow and demand, and limits cerebral microemboli load. However, the pressure-dependent characteristics of pH-stat may improve cooling and oxygen delivery to the brain.<sup>8</sup>

## Filtration

Recycling of suctioned blood from the surgical field is accomplished by a cardiotomy reservoir incorporating a screen and depth filter to reduce fat emboli, fibrin and surgical contamination. Screen filters comprise a woven mesh material such as polypropylene, with a defined pore size to determine its filtration ability. Depth filters incorporate packing materials such as Dacron wool or polyurethane foam that have no definite pore size; thus, filtration depends on the thickness, tightness and tortuous nature of the packing. Generation of gaseous (e.g. drug injection and venous air) and particulate (e.g. circuit material debris) emboli exiting the oxygenator is associated with vital organ injury, for example cognitive dysfunction. An arterial screen filter is often used to limit sources of embolic load to the patient. Air emboli retention within the wetted filter is accomplished by surface-active forces, which maintains fluid in the pores and prevents displacement of fluid by gas through the pores. However, excessive pressure across the filter medium can allow the passage of air through the pores; this is termed the ‘bubble point pressure’. Bacterial filtration of the gas flow line to the oxygenator and the use of pre-bypass filters to reduce extracorporeal circuit debris are often practiced. There is a current trend to utilize leucocyte depleting filters, as activated leucocytes are considered to have a pivotal role in the inflammatory response to CPB and post-ischaemic injury. The application of this technique during all or part of CPB (i.e. before aortic cross-clamp removal, during blood cardioplegia delivery or both) has demonstrated some clinical benefits.<sup>9</sup>

Haemofilters (haemoconcentrators or ultrafilters) are utilized in CPB circuitry to remove excess fluid and electrolytes, attenuate inflammatory mediators and raise haematocrit. These devices mainly consist of a hollow-fibre semipermeable membrane to allow the passage of water and electrolytes from the blood to a filtrate compartment. Conventional ultrafiltration (haemoconcentration) and zero balance ultrafiltration (filtrate replaced with equal crystalloid volume) can be performed during CPB; modified ultrafiltration can be initiated at the termination of CPB.

## Conduct of CPB

Components selected for the extracorporeal circuit are determined to minimize haemodilution, while being able to achieve

blood flow requirements without excessive resistance or pressure generation. The CPB circuit is typically primed with a crystalloid solution with electrolyte composition and osmolarity similar to plasma and a colloid solution to provide a degree of plasma colloidal oncotic pressure, which is reduced as a repercussion of haemodilution in CPB. Other prime additives may include mannitol (diuresis, oedema reduction, possibly free-radical scavenging); sodium bicarbonate (buffers the prime); heparin; and blood, if required. CPB blood flow, estimated haematocrit on CPB and the amount of blood required in the prime are calculated:

$$\text{CPB blood flow rate} = \frac{\text{Body surface area (BSA)} \times \text{Cardiac index (CI)}}{(\text{litre min}^{-1}) \quad (\text{m}^2) \quad (\text{litre m}^{-2} \text{min}^{-1})}$$

where BSA is calculated by DuBois formula/DuBois BSA nomogram; CI is 2.4–2.8 (dependant upon age) at 37°C, 2.1 at 32°C, 1.8 at 28°C, 1.2 at 25°C, 0.6 at 15°C.

$$\text{Estimated haematocrit on CPB} = \frac{\text{PBV} \times \text{Hct}}{\text{TCV}},$$

where PBV is the patient blood volume; Hct is the patient haematocrit; TCV is the total circulatory volume, that is PBV + circuit prime volume + estimated cardioplegic solution volume.

$$\text{Blood required in prime} = \frac{(\text{Target Hct} \times \text{TCV}) - (\text{Hct} \times \text{PBV})}{\text{Hct of RBCs}},$$

where Target Hct is the required haematocrit on initiation of CPB (typically above 20% in adults and 28% in children); TCV is the total circulatory volume; PBV is patient blood volume; Hct is patient haematocrit; Hct of RBCs is haematocrit of donor blood.

Before initiation of CPB, the patient is adequately anticoagulated with heparin (300–400 iu kg<sup>-1</sup>) to achieve an activated clotting time (ACT) generally above 480 s (celite ACT above 750 s when aprotinin is used) to maximize inhibition of thrombin generation. The placement of arterial and venous cannulae to perform CPB is generally via a median sternotomy, to the ascending aorta and right atrium or directly/indirectly to the superior and inferior venae cavae. Alternative cannulation sites include the femoral vessels, axillary artery, left ventricular apex (e.g. redo procedures and aortic aneurysm), and both ascending and descending aorta (e.g. interrupted arch). Venous cannula size is important, as blood flow is determined by the Hagen–Poiseuille equation. To achieve sufficient venous drainage for effective CPB, the cannula radius is the predominant factor (a small change in dimension can have a drastic effect on venous drainage); fluid viscosity and tubing length remain relatively fixed. Arterial cannulae sizing is less significant as the blood can be pumped at relatively high pressures oxygen (generally 160–180 mm Hg). However, maintenance of blood flow at higher pressures with smaller diameter arterial cannulae may result in turbulent flow, as predicted by the Reynolds number, which is determined by the density, velocity and viscosity of blood for a given temperature. Correct positioning of the arterial cannula is verified by arterial line pressure measurement within the



extracorporeal circuit. After cannulae insertion, CPB is commenced by releasing the venous line clamp and increasing the blood pump until calculated blood flow is achieved. Maintenance of adequate venous drainage into the reservoir is essential to provide CPB support and prevent patient air embolism. The application of pulsatile blood flow during CPB may increase or preserve arterial blood flow to organs such as the kidney, liver, gut and brain, and reduce systemic vascular resistance. However, the generation of an arterial waveform to provide substantial 'physiological' blood flow is a significant a technical challenge.

Adequacy of blood flow and oxygen requirements requires frequent, if not continuous (i.e. in-line monitoring) arterial and venous blood gas monitoring, in addition to haematological and biochemical analysis. Effective blood flow during CPB can be monitored by whole body oxygen consumption ( $VO_2$ ), according to the Fick principle:

$$VO_2 = (CaO_2 - CvO_2) \times CO$$

where  $VO_2$  = oxygen consumption,  $(CaO_2 - CvO_2)$  = arterio-venous oxygen content difference and  $CO$  = cardiac output.

Thus, with the additional knowledge of the level of oxygen extraction (arteriovenous oxygen content difference) and haemodilution (total haemoglobin) during CPB, the patient's requirements can be accommodated. To enable  $VO_2$  to be a reliable indicator of blood flow adequacy, the age, size and temperature of the patient need to be considered.  $VO_2$  to body weight ratio in the infant is about twice that of the adult (approximately 8:4 ml kg<sup>-1</sup> min<sup>-1</sup>). The use of in-line mixed venous oxygen saturation monitoring during CPB allows quick assessment of sufficient oxygen delivery, but should be interpreted with caution. Certain patient conditions, such as anatomical or physiological shunts, and abnormal haemoglobin types, may under or overestimate oxygen delivery and uptake. Other parameters assessed during CPB include oxygenation, arterial perfusion pressure, venous pressure, temperature, ECG, urine output and periodic assessment of the anticoagulant status (ACT > 480 s to prevent extracorporeal circuit thrombosis).

During CPB with the aorta cross-clamped and the heart in an arrested state, gradual distension and potentially irreversible damage to the heart can occur. This is because of bronchial and coronary vessels (e.g. myocardial sinusoids, arterio-sinusoidal, arterio-luminal vessels) draining into the heart, which can contribute to 1–2% of the cardiac output.<sup>10</sup> These circulations, including the presence of non-coronary circulations (e.g. connections between mediastinal and coronary vessels), can result in a blood-flooded operative field and cause cardioplegic 'wash-out' with subsequent recurrent cardiac electrical activity. The improper placement or inappropriate fixation of the venous cannula also has a significant influence on these problems. The use of a vent cannula placed in the left ventricle, left atrium, pulmonary artery or aortic root can prevent over-distension of the heart and its consequences. Likewise, reducing perfusion

**Table 1** Suggested target blood chemistry values for termination of CPB

pH	7.35–7.45
$PaO_2$	20–30 kPa
$PaCO_2$	4.6–5.5 kPa
$SvO_2$	>65%
Base excess (arterial)	&minus;2 to +2
$Na^+$ (plasma)	135–144 mmol litre <sup>-1</sup>
$Cl^-$ (plasma)	95–105 mmol litre <sup>-1</sup>
$Ca^{++}$ (plasma)	2.1–2.6 mmol litre <sup>-1</sup> (adjusted for albumin)
$Mg^+$ (plasma)	0.7–1.0 mmol litre <sup>-1</sup>
$K^+$ (plasma)	3.3–5.3 mmol litre <sup>-1</sup>
Glucose	3.3–6.0 mmol litre <sup>-1</sup>
Haematocrit	>25% (adults); >28% (children)

pressure and blood flow during hypothermia can facilitate in reducing this problem.

Weaning from CPB is considered when surgical intervention has been completed. The patient should be fully warm with physiological biochemical and haematological values (Table 1) and an appropriate ECG. After confirmation of mechanical ventilatory support, the venous line is clamped and volume is infused from the CPB circuit until a desired filling pressure is obtained. Patient heparinization can be reversed with protamine sulphate after stabilization and discontinuation of the extracorporeal circuit.

## Reducing consequences of CPB

CPB and cardiac surgery induce a systemic inflammatory response and cause disturbances of the inflammatory and fibrinolytic system. Pharmacological agents are used to reduce these consequences. Such agents include aprotinin; anti-fibrinolytics; corticosteroids; and novel approaches with angiotensin-converting enzyme inhibitors, exogenous antioxidants, monoclonal antibodies and phosphodiesterase inhibitors. Surface coated and miniaturized extracorporeal circuits are being continually developed to potentially improve biocompatibility.<sup>11</sup> Isolation of cardiotomy suctioned blood and utilization of cell salvage devices to reduce activated blood components and particulate emboli are of recent interest.

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**Please see multiple choice questions 6–8.**