The concepts and principles that govern perfusion often go unchallenged; in this paper a number of concepts and principles that may potentially improve the practice of perfusion and cardiac surgery are discussed (1). Should the interpretation presented prove to be correct, following appropriate clinical evaluation, clinical practice may be altered.

The concepts include:

- Evaluating the target pressure on bypass,
- Cardiopulmonary bypass prime constitution,
- Gas exchange,
- Hemo-filtration on bypass,
- Flows during cardiopulmonary bypass (CPB),
- The timing of cross clamp removal,
- De-airing following X clamp removal,
- Set up of the heart lung machine

The concepts presented are not exhaustive, however they may provide an insight into a more “patient directed approach” to perfusion.

PRESSURE ON BYPASS

Little evidence exists as to the correct arterial pressure to run patients at during CPB (2,3). Given the majority of patients pre induction are well perfused, if the hematocrit and flow, which determine oxygen delivery, are adequate, then blood pressure and the effects of pulsatility are two remaining factors that are important to adequately perfuse the body. As cardiopulmonary bypass is often non pulsatile and the blood circulation in the body is pulsatile, then it may be reasonable to suggest that the non pulsatile equivalent pressure of the pre induction resting blood pressure should be your target on bypass. This can be calculated via calculating the root mean square, Figure 1 (4).

Patient directed bypass 1: Match the blood pressure on bypass to the patient’s preoperative blood pressure.

Cardiopulmonary Bypass Prime Constitution

Enormous variation exists as to the composition of the prime for CPB, with little evidence of clinical superiority between the commonest choices in clinical practice (5,6). An increasing number of patients are presenting for cardiac surgery with treated heart failure. Diuretic therapy and the underlying heart failure are associated with hyponatremia. Rapid correction of, and creation of hyponatremia, can, in susceptible patients, result in central pontine myelomatosi, a potentially irreversible brain injury (7–10). An acute large variation in patients’ serum sodium can occur in patients during the initiation of bypass if the CPB prime has a different sodium concentration to the patients’ serum sodium level. Figure 2 demonstrates “the theoretical” calculated change in serum sodium that could occur upon initiation of CPB using two alternate prime constituents.
The RMS for a collection of \( n \) values \( \{x_1, x_2, \ldots, x_n\} \) is
\[
x_{\text{RMS}} = \sqrt{\frac{1}{n} \sum_{i=1}^{n} x_i^2} = \sqrt{\frac{x_1^2 + x_2^2 + \ldots + x_n^2}{n}}
\]

The corresponding formula for a continuous function \( f(t) \) defined over the interval \( T_1 \leq t \leq T_2 \) is
\[
x_{\text{RMS}} = \frac{1}{T_2 - T_1} \int_{T_1}^{T_2} [f(t)]^2 \, dt
\]

The RMS of a periodic function is equal to the RMS of one period of the function.

The RMS value of a continuous function if signal can be approximated by taking the RMS value of a series of equally spaced samples.

**Figure 1.** Calculating root mean square: the non pulsatile equivalent of a pulsatile waveform.

**Patient directed bypass 2:** Match the prime on bypass to the patient.

**Gas Exchange**

Acid base management during CPB can be via the alpha stat, the pH stat, or a combination of each technique depending on temperature and the cooling/rewarming stage of the operation. A concern of utilizing the pH stat technique is that luxurious cerebral blood flow occurs (11), which can result in an excessive embolic load to the brain, due to the effects of a raised carbon dioxide (CO\(_2\)) level which is a potent cerebral vasodilator. In addition, a low CO\(_2\) level is associated with cerebral vasoconstriction, a fact utilized in the past in neurosurgery to reduce cerebral oedema. The range of normal CO\(_2\) levels in patients is quite wide, however the range in CO\(_2\) levels in a given patient is actually very narrow. Wide variations in blood CO\(_2\) levels occur during CPB during normal practice, (see Figure 3, data from over 2000 patients from Liverpool Heart and Chest Unit), and this may have a profound effect on cerebral blood flow. As hypercarbia causes excessive cerebral vasodilation and hypocarbia causes vasoconstriction, perhaps the CO\(_2\) levels should be maintained close to the patient pre operative level (12).

**Patient directed bypass 3:** Match the CO\(_2\) on bypass to the patient.

**Hemo-Filtration on Bypass**

Patients with renal failure are frequently hemo-filtered on bypass to “remove fluid.” This may result in very large volume fluid exchanges and rapid serum urea falls. Rapid dialysis in the non cardiac surgery setting is known to be associated with cerebral oedema, and has been quantified via magnetic resonance imaging scanning to be up to 59 mL (13), Figure 4. Theoretical calculation, which concurs with magnetic resonance imaging studies before and after dialysis (14), reveals that this may occur during CPB, compounding the already deleterious effects of CPB on brain swelling that has previously been demonstrated (15).

**Patient directed bypass 4:** Don’t change patients’ osmotic status quickly.

**Flows during CPB in Dialysis Patients**

Flow during CPB can be calculated from either the body surface area or simply from the patients’ weight. These calculations rely on normal circulatory physiology. In renal failure, patients undergoing hemo-dialysis have a dialysis

**Figure 2.** The effect of CPB [Na\(^+\)] prime on serum sodium on initiation of bypass. High [Na\(^+\)] prime e.g., saline (154 mmol/L), low [Na\(^+\)] prime e.g., 5% dextrose in .45% saline, (77 mmol/L) or dextrose saline.

**Figure 3.** Frequency distribution of CO\(_2\) levels during CPB (data represents measurements from over 2000 patients).

**Figure 4.** The effect of changes in serum urea during CPB secondary to filtration on brain volume increase (13).
fistula, typically a radial artery to cephalic vein shunt. This results in a hyperdynamic circulation. Flow down the shunt varies between 51 and 2409 mL/min with an average blood flow volume of 521 mL/min (16). Native renal blood flow varies on a number of factors and ranges from near normal (25% of cardiac output) to less than 5% of cardiac output (17), so if assuming normal renal blood flow, flow during CPB may need to be increased by over 1 L/minute. Adequacy of perfusion is difficult to quantify, but changes in serum lactate may be helpful. It should not be forgotten that these patients frequently have a pre operative acidos, making base excess a poor marker, and correction of this acidos with bicarbonate may result in tissue hypoxia in the setting of adequate arterial saturations (18).

**Timing of Cross Clamp Removal**

Variation exists as to whether the aortic cross clamp is removed prior to the patient being rewarmed or after rewarmling has taken place. In addition, CPB flow is usually reduced during aortic cross clamp removal so that the blood pressure is reduced in the aorta and safe removal of the clamp can occur. Experience from off-pump surgery would indicate that as long as the pressure in the aorta is not excessive, this practice may not be necessary. Due to Henrys Law (see Appendix 1), less gaseous embolism should reach the brain if the clamp is removed with the patient still cold, and the flow up. This is due to the fact that gases are more soluble in blood at colder temperatures and higher pressures, so potentially reducing the gaseous embolic load to the brain.

**De-Airing**

De-airing of the heart is a requirement after all open chamber operations. It has two aims, firstly to remove particulate matter, and secondly to remove gaseous matter, i.e., air. From Henrys law, Appendix 1, carbon dioxide is 50 times more soluble in blood than nitrogen (air is 78% nitrogen, 21% oxygen). Flooding the operative field with carbon dioxide is predicted to reduce delivery of gaseous emboli (containing air) to the brain (carbon dioxide $k_H^i$ 29 vs. nitrogen $k_H^i$ 1639, Appendix 1, Table 1A). However, given the presented deleterious effects of increased PaCO$_2$, carbon dioxide flooding should be utilized with caution. Utilization at the end of the case prior to cardiac chamber closure to avoid systemic absorption and sucker entrainment may reduce hypercarbia and resulting increased cerebral blood flow and hence, potentially increased embolic load.

Patient directed bypass 5: Match the flow during CPB to the patients normal resting state.

The higher the solubility constant ($k_H^i$) the less soluble the gas. Figure 5 demonstrates that carbon dioxide is over 55 times more soluble than nitrogen. Oxygen is more soluble in blood than $k_H^i$, would predict secondary to hemoglobin, and carbon dioxide is more soluble than $k_H^i$ would predict secondary to carbonic anhydrase.

**CPB Machine Set-up**

Henry’s law (see Appendix 1) also predicts that the higher the pressure, and the lower the temperature, the more soluble a gas is in a given solute. The typical layout of a bypass machine is shown in Figure 6. As the blood travels from the main pump to the capillaries, the pressure drops from 300 mmHg to 24 mmHg—capillary pressure. This means that any gases will be 10 times less soluble and have the potential to come out of solution and obstruct the vasculature. Oxygen and carbon dioxide are probably of no consequence, as they will either be dissolved or utilized, however nitrogen may be very harmful. Whilst the consequences of full blown decompression sickness (divers’ disease, the bends, or caisson disease) are unlikely, as the arterial pressure drop is too low, micro emboli in critical parts of the brain may have subtle neuropsychological effects.

Rewarming is currently thought to be the dangerous part of the hypothermic process in cardiac surgery (19). When cooling, blood is cooler than tissue, however when the blood warms in the capillaries there is a chance of gases, especially nitrogen coming out of solution, causing tissue damage. When rewarming gases become less soluble in blood, Table 1B meaning there is a chance of gases, especially nitrogen coming out of solution, causing tissue damage again. The rate of warming/cooling may be important with regard to “bubble” dispersion. The rate of patient temperature change is more affected by patient heat capacity, which is roughly proportional to body weight, than temperature gradients used clinically in the heat exchanger of the CPB circuit.

The lower the pressure blood is under when it is passes through the oxygenator, potentially the less nitrogen that
will be dissolved in the blood. The less nitrogen dissolved, the less there will be to come out of solution due to pressure drop and temperature increases that occur between the pump head and the capillary bed. The implication for bypass machine layout is that potentially a second line pump operating at the minimum pressure to get blood through the membrane oxygenator and heat exchanger may be advantageous (Figure 7). This would result in gases being under the minimum pressure to allow gas exchange to occur, but result in little excessive soluble gas load in the blood that could undissolve when the conditions of temperature and pressure are favorable, via Henrys Law.

CONCLUSION

In this paper a number of concepts relating to current bypass have been highlighted. Some of these innovations may result in improved CPB in clinical practice in the future. Using basic concepts from engineering, in combination with our understanding of CPB, we may be able to tailor a more patient directed bypass that may have the potential to improve CPB.

REFERENCES


APPENDIX 1: HENRY'S LAW

Gases become more soluble in colder solutions—warming causes bubbles as the gas comes out of solution. The extent of a gas dissolving in solution depends on Henry’s law. Henry’s Law states that “At a constant temperature, the amount of a given gas dissolved in a given type and volume of liquid is directly proportional to the partial pressure of that gas in equilibrium with that liquid.”

\[ p = k_h c \]

\( p \) is the partial pressure of the solute, \( c \) is the concentration of the solute and 
\( k_h \) is a constant known as the Henry’s law constant, but depends on the solute, the solvent, and the temperature.

### Table 1A. Lists of some values for constant \( k_h \) in the equation above.

<table>
<thead>
<tr>
<th>Gas</th>
<th>O₂</th>
<th>CO₂</th>
<th>N₂</th>
<th>H₂</th>
<th>He</th>
<th>Ne</th>
<th>Ar</th>
<th>CO</th>
</tr>
</thead>
<tbody>
<tr>
<td>( k_h )</td>
<td>769</td>
<td>29</td>
<td>1639</td>
<td>1282</td>
<td>2703</td>
<td>2222</td>
<td>714</td>
<td>1053</td>
</tr>
</tbody>
</table>

\( k_h \) can be calculated for different temperatures by utilizing the Van’t Hoff equation.
\[ \text{Van’t Hoff equation} \quad k_h(T) = k_h(T^0) \exp[-C(1/T - 1/T^0)] \]

\( k_h \) for a given temperature is the Henry’s Law constant, \( T \) is the thermodynamic temperature, \( T^0 \) refers to the standard temperature (298 K).

### Table 1B. Values for constant \( C \) in the Van’t Hoff equation.

<table>
<thead>
<tr>
<th>Gas</th>
<th>O₂</th>
<th>CO₂</th>
<th>N₂</th>
<th>H₂</th>
<th>He</th>
<th>Ne</th>
<th>Ar</th>
<th>CO</th>
</tr>
</thead>
<tbody>
<tr>
<td>( C/K )</td>
<td>1700</td>
<td>2400</td>
<td>1300</td>
<td>500</td>
<td>230</td>
<td>490</td>
<td>1300</td>
<td>1300</td>
</tr>
</tbody>
</table>