The selection of priming fluids for cardiopulmonary bypass in the UK and Ireland

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The ideal prime for Cardiopulmonary Bypass (CPB) has never been fully established. The development of acid-base disorders during some routine cases and the possible contribution to this from priming fluids caused this hospital to question its protocol. As a result, we conducted a survey of UK perfusion units to analyse current practice. The response rate was 74%. It was found that no two units in the UK used the same prime. The most common reason for fluid choice was historical beliefs and there appeared to be little perceived association between prime and acidosis on bypass. The results revealed that there is no consensus in the UK of the preferential prime for CPB, suggesting the effect this aspect has is not fully understood.


Even after much research and discussion regarding primes for cardiopulmonary bypass (CPB), there has been, as yet, no agreement upon ‘the ideal prime’. The literature is extensive, comparing different types of colloids, colloid versus crystalloid, synthetic versus organic, and the inclusion of numerous additions in an attempt to make a grossly unphysiological state the least disruptive to the body as possible. The bypass circuit is to the blood a mass of foreign, nonendothelial, noncompatible surfaces and the CPB prime becomes a significant part of the patient’s own circulation, both of which will undoubtedly evoke a response. Inflammatory, immunological, haemostatic and haemolytic disturbances are often observed post-CPB, yet many of these have been accepted as an inevitable outcome, which the body can, in the main, tolerate. Most responses have been attributed to the circuit. However, may it be that the prime components play a role in this response? The very fact that the optimal prime has never been identified suggests that there is little appreciation as to the influence this area may be exerting on the already compromised system. It is difficult to ascertain the individual effects of a single factor when the patient is subject to surgical, anaesthetic and CPB stresses. However, optimization of one element can only help to minimize the combined insult to the body.

Recently, this unit questioned its prime components. Concern was raised at the low pH of the fluids used, often culminating in an acidic prime. The pH of commonly administered fluids can vary within quite large ranges (Table 1). The stress of surgery, anaesthesia and CPB are all known to generate a metabolic acidosis. However, this can only be exacerbated by the use of a prime with a low pH value. We were interested to ascertain if our prime could be contributing to an acidosis observed in a number of our routine cases. It became difficult, however, to critically evaluate a prime that has been used routinely for many years. In an attempt to assess our protocol, we decided to investigate current perfusion practice in the UK.

A literature search revealed that the only published priming survey was performed in 1994. Hett and Smith found wide variation in practice and concluded ‘no consensus exists as to the most suitable priming fluid for CPB’. The authors believed that most respondents thought the subject of prime unimportant. They were surprised to find the majority of units opted to use lactated Ringer’s (Hartmann’s) solution, particularly in a surgical population with high metabolic stress.

Table 1 The approximate pH values of various commonly used CPB priming fluids (from manufacturers’ data)

<table>
<thead>
<tr>
<th>Fluid</th>
<th>pH</th>
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<tbody>
<tr>
<td>Hartmann’s</td>
<td>≈6</td>
</tr>
<tr>
<td>Ringer’s/Saline</td>
<td>4.9</td>
</tr>
<tr>
<td>Plasmalyte</td>
<td>7.4</td>
</tr>
<tr>
<td>Gelofusine</td>
<td>7.4</td>
</tr>
<tr>
<td>Starch</td>
<td>4.7</td>
</tr>
<tr>
<td>Albumin</td>
<td>≈6</td>
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large numbers of insulin- and non-insulin-dependent diabetics and their associated impaired lactate metabolism. In comparison, a survey performed in 1996 by Myers\textsuperscript{3} of Canadian and US centres found wide variation in practice across the Atlantic. Forty-four per cent of units surveyed were using albumin as a component of their prime compared with no units in the UK in 1994\textsuperscript{2}. Myers states that, in the US, consensus believes ‘the most desirable crystalloid solutions for CPB are those that...possess a balanced pH (7.4)’. He claims that most North American centres are using either Normosol R (Abbott Lab, Berks, UK) or Plasmalyte A (Baxter Healthcare, Norfolk, UK), both pH 7.4, and those using nonbuffered solutions usually add sodium bicarbonate to neutralize the acid. Leutschaft\textsuperscript{4} investigated acidity and various solutions and the results indicated that the pH of fluids was one of the most important factors in determining the extent of haemolysis after infusion.

Liskaser et al.\textsuperscript{5} investigated the role of pump prime in CPB-associated acidosis. The authors hypothesized that prime fluids are primarily responsible for its development. They compared Ringer’s solution with Plasmalyte (an unbalanced and a balanced solution) and concluded that CPB-induced acidosis varies in extent and duration according to the pump prime. Acidosis that developed on bypass was resolved by the end of the case when a pH-balanced solution was used, but prevailed postsurgery when the prime was a nonbuffered solution.

In an attempt to evaluate current thought and practice, we devised our own survey. This sought to determine the current trends in priming and, more importantly, to assess reasoning behind choice. The emphasis was on the crystalloid component. The survey asked:

1. What was the unit’s current priming protocol?
2. Does the unit believe this to be their optimal prime? If not, why not, and what would be?
3. What influences the unit’s choice of priming fluid?
4. Do they experience acid base disturbances during routine CPB (as defined by a base deficit greater than 3 units (base excess ≤3))?
5. Does the unit measure lactate levels; if so, what concentrations are routinely observed?

The survey was posted to 45 perfusion units throughout the UK and Ireland. Completion was optional (33 replies) and could be performed anonymously (38%). The total response rate was 73%. This resulted in the accumulation of 31 adult and 11 paediatric primes. Due to the additional complexities of looking at paediatric primes, only those used for adult systems were examined for this part of the evaluation.

The results of the predominant crystalloid fluid used is shown in Figure 1.

As illustrated, the most common component was Hartmann’s solution, used routinely for four-fifths of all adult bypasses. This compares with the results found in 1994\textsuperscript{2} (Table 2). Hartmann’s is an isotonic solution containing lactate to act as a buffering agent. It does not contain bicarbonate ions. The lactate combines with hydrogen ions in solution to form lactic acid. This is metabolised within the hepatic circulation, over time, to generate bicarbonate,\textsuperscript{6} the buffer. However, prior to this, the acid can influence blood pH. The time for conversion to bicarbonate to occur is reported to be between 1 and 2 h.\textsuperscript{6} Studies have shown that the peak production of bicarbonate in haemorrhaged swine was not until 120 min post-lactated Ringer’s infusion,\textsuperscript{7} and 180 min in normovolemic dogs.\textsuperscript{8} Dilution with an unbalanced solution may compromise the acid–base status of the blood from the initiation of CPB. The rationale for using a solution, when the surgical stress is prevalent, whose metabolism is often longer than the actual bypass period, would, therefore, seem questionable. The other utilized crystalloids were Ringer’s solution, saline and Plasmalyte. Ringer’s solution and saline are also isotonic solutions with low pH values, whereas the Plasmalyte range consist of balanced, buffered fluids, but are inevitably more expensive.

Our study revealed that all units except one used a crystalloid component and this made up the predominant portion in 90% of primes. The most common combination was crystalloid and colloid (58% of units). The average crystalloid:colloid ratio was 3:2. Mannitol was the most common additive, included in 81% of adult primes. Bicarbonate was administered to the prime in 19% of cases; of these, two-thirds used Hartmann’s. Bicarbonate is used to balance this and other, unbuffered solutions. The average amount of

![Figure 1](chart-illustrating-primary-fluid-component-of-cardiopulmonary-bypass-primes-in-the-UK-n=33)
bicarbonate administered was 45 mmol; this results in, and balances with, a patient plasma concentration of approx. 25 mmol/l (mean prime volume 1800 ml). One of the most striking observations revealed by the survey was that, of the 31 adult surveys collected, no two units used the same prime!

The predominantly administered colloid was gelatin, e.g., Gelofusine (Braun, Sheffield, UK) or Haemaccel (Beacon Pharma, Kent, UK). Forty-five percent of units used these in their prime and for fluid replacement on bypass. This compares with 12% routinely using a medium or low molecular weight starch solution, e.g., hetastarch. Colloid oncotic pressure (COP) falls greatly as a consequence of the large dilutional effect at the initiation of bypass. Beshere et al. reported that COP as low as 12.5 mmHg (normal range supine 19–23 mmHg) can be tolerated without evidence of complications. However, crystalloid CPB can result in levels lower than this. Colloids, both synthetic and organic, are given to reduce this effect. There is, however, contradicting evidence as to the necessity for colloid on bypass, and reports exist as to its effect upon haemostasis postsurgery. In comparison, crystalloids are more easily eliminated through the renal system and urine output is significantly enhanced with their use. Haematocrits were found to be higher using crystalloids when compared to colloids, but this may have been caused by extravascular fluid movement as a consequence of the low COP. Colloids are administered to increase the COP, prevent ‘third spacing’, reduce oedema, and lessen the fluid requirements on bypass.

Commonly used starches have a moderately higher molecular weight in comparison to gelatins (approx. 200000 versus 40000) and, therefore, take longer to be degraded and removed from the circulation. As a consequence, the body takes longer to restore haemostasis, which has been associated with decreased diuresis, low Hb and coagulopathies. The starch molecules are believed to become embedded in the clot, building the fibrin structure compromising its strength. Decreases in fibrinogen, ATIII and factor VIII, resulting in altered aPTT, PT and TT, have all been described. The half-life of gelatin is approximately half that of starch and is not associated to the same extent with the described disturbances. The method of gelatin elimination is both renal and faecal; therefore, unlike starches, they are not contraindicated in renal failure. The pH of gelatins is adjusted to maintain the fluids within the physiological range, making them more suitable for fluid replacement on bypass. However, they do not contain bicarbonate and, therefore, will not buffer or maintain the blood’s bicarbonate concentration on bypass. Concerns have also been raised regarding the bovine nature of the gelatin molecules and, in particular, the potential to transmit new v-CJD. Recently, however, Peano et al. provided evidence that the manufacturing process significantly reduces the possible infection risk. The ability to cause a serious anaphylaxis is also known and well documented, yet manufacturers claim that this has been significantly reduced by recent refinement in the manufacturing processes.

Only two units (6%) surveyed revealed that they routinely added human albumin solution (HAS). Another three suggested they would prefer to use this constituent, but are prevented by an undisclosed factor, e.g., cost, possibility of disease transmission, and others. This is interesting when, as previously stated, almost half of North American units routinely include albumin as a prime constituent. HAS is very acidic and can affect the pH of the prime considerably. Although HAS affects the oncotic pressure when used for CPB, recently there has been much interest in its ability to coat the internal surfaces of the bypass circuit. The positively charged nature of the albumin molecules bind to the negatively charged internal surfaces, creating a deposition layer. This increases biocompatibility, reducing activation and lowering fibrinogen and platelet adsorption. HAS is also reported to reduce the occurrence of trans-oxygenator pressure excursions, a well-documented phenomenon that occasionally results in oxygenator failure and change-out.

One quarter of units believe their current priming protocol to be suboptimal. The reasons for this were varied and are shown in Table 3, but were all aimed at optimizing patient response. Influences in choice of fluid mainly centred on cost, ease of use and maintenance of colloid oncotic pressure. Twenty-six percent of respondents stated their current protocol

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Our survey</th>
<th>Hett and Smith (1994)</th>
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<tbody>
<tr>
<td>Hartmann’s</td>
<td>(80%)</td>
<td>(71%)</td>
</tr>
<tr>
<td>Ringer’s</td>
<td>(10%)</td>
<td>(13%)</td>
</tr>
<tr>
<td>Plasmalyte</td>
<td>(7%)</td>
<td>(7%)</td>
</tr>
<tr>
<td>Colloid</td>
<td>(3%)</td>
<td>0</td>
</tr>
<tr>
<td>Saline</td>
<td>0</td>
<td>(9%)</td>
</tr>
</tbody>
</table>

Table 3 Most common survey responses when asked why people believe current protocol to be suboptimal

<table>
<thead>
<tr>
<th>Reasons given why respondents believe prime suboptimal</th>
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<tbody>
<tr>
<td>Prefer to use surface modified circuit/add albumin</td>
</tr>
<tr>
<td>Prefer to reduce volume</td>
</tr>
<tr>
<td>Not patient specific</td>
</tr>
<tr>
<td>Prefer higher colloid component</td>
</tr>
</tbody>
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was based primarily upon historical use, suggesting that there is little scientific reasoning behind fluid choices. One unit used Ringer’s solution as opposed to Hartmann’s to eliminate the lactate component, and one used Plasmalyte B (Baxter Healthcare, Norfolk, UK) as they preferred a pH-balanced solution.

The survey asked if the respondent felt that their unit routinely saw a base deficit of greater than 3 units (base excess ≤ 3) during routine CPB. Thirteen percent stated that this did occur. However, some disagreement did arise in individual appreciation of the frequency of routine acidosis, and this may have influenced the results. Only one unit added bicarbonate to their prime and still claimed to experience a significant fall in pH.

Metabolic acidosis can occur due to a range of influences, e.g., flow, temperature, patient physiology, and so forth. However, going onto bypass and diluting the patient with a solution not balanced with blood bicarbonate levels (the primary blood buffer), as the majority of priming fluids are not, may result in the development of a deficient system. In the normal state, acid–base balance is maintained within very narrow limits to ensure that the functional capacity of the internal environment is preserved. The body does have a tremendous buffering capacity and, in the majority of stable cases, this will be tolerated and corrected. However, in an already compromised patient (as many requiring surgery are), the insult from CPB may produce an unphysiological alteration that the body cannot cope with; this is when a state of acidosis may develop. It is preferable to prevent an acidosis from developing rather than treating it once it has occurred.

The survey also enquired whether units routinely measured blood lactate levels; 30% did and, of these, one-third routinely experienced concentrations outside of the normal range. Again, blood lactate is affected by several influences. However, all of these units used lactated Ringer’s solution as their primary prime component. Lactate accumulation is not preferable due to its effect on acid–base.

The results from the survey have led us to conclude that there is little consensus as to prime components in the UK and, in particular, which is preferable and why. This is affirmed by our finding that no two perfusion centres in the UK use the same prime. There appears to have been little evolution in practice over time and, therefore, in the main, no significant changes or advances have occurred. CPB affects and disrupts so many systems within the body that it is impossible to conclude that the acidosis observed on bypass is due primarily to priming fluids. However, it seems logical to balance the prime with the blood wherever possible to minimize any disturbance. Metabolic acidosis has been accepted as a consequence of CPB and perhaps this could be better controlled with more consideration to prime and other fluids administered perioperatively. The utilization of pH-balanced fluids may assist in this aim. This has led us to consider further research and evaluation of our own prime solution.

References

14 London MJ, Franks M, Verrier ED, Merrick SH, Levin J,


