Transfusion of red blood cells (RBCs) is one of the most common interventions carried out upon the cardiac surgery population in the postoperative period. Of late, this practice has received increasing attention in terms of the appropriateness of the decision to transfuse, the deleterious consequences of unnecessary transfusion, and the possibility for viable alternatives.\(^1\) We wish to highlight recent developments in these areas and suggest where the future may lie in terms of an evidence-based transfusion practice in cardiac surgery.

**Appropriate use of RBCs**

Since 1942, any decision to administer RBCs has largely been based upon a haemoglobin concentration [Hb] threshold with little consideration for any other patient variables.\(^2\) Largely prompted by the availability of high-quality data from the general intensive care unit population, this situation has gradually changed.\(^3\) When considering [Hb] alone, there is considerable debate as to an appropriate threshold for the transfusion of RBCs. Experimental haemodilution studies in healthy volunteers suggest that [Hb] levels as low as 5 g dl\(^{-1}\) may be adequately tolerated in healthy volunteers, albeit with the minor complication of a reversible cognitive deficit.\(^4\) Although limited in sample size, several studies have attempted to examine the impact of acute anaemia on the outcome after cardiac surgery. Although it is not possible to extrapolate what an appropriate [Hb] might be, the strong suggestion is that in the absence of hypovolaemia, current levels of RBC transfusion are excessive.\(^5\)\(^6\)

The premise behind any RBC transfusion is that it will improve the oxygen carrying capacity of the blood. Thus, investigators have attempted to identify several variables...
that may predict when systemic oxygen delivery (DO$_2$) is suboptimal in relation to tissue requirements and additional RBCs may be required. Although these ‘physiological triggers’ are only a suggestion, they provide an additional level of consideration to the transfusion decision-making process.$^1$ Considering such parameters in association with [Hb] is a logically appealing scenario. Unfortunately, however, this can only ever be applied to those patients in whom blood balance is stable. As cardiac surgery patients will lose red cell volume (RCV) to a varying degree, this must also be an important consideration. Our group has examined the relative contribution of haemodilution to postoperative anaemia and incorporated the findings into an RCV-based transfusion algorithm. Provisional findings with this model are favourable, although further investigation is required.$^7$

Any transfusion decision has to be based upon a risk–benefit analysis, that is, the benefits of an increase in oxygen carrying capacity, although itself an area of much debate, outweigh the risks of the RBCs themselves. Newer data are beginning to document that the risks are far greater than previously thought.$^8$

**Deleterious consequences of RBC transfusion**

The potential infectious risks of transfusion are well established. However, with modern screening techniques, these complications are of negligible significance to current practice. Less well recognized, and altogether more serious to the cardiac surgery population, is the impact of RBCs on lung function, circulatory status, and susceptibility to postoperative infection.$^9$ Although the aetiology of these adverse reactions is unclear, it almost certainly relates, at least in part, to alloimmune leucocyte material remaining after universal leuco-reduction.$^{10}$ At present, transfusion-related acute lung injury is a rarely diagnosed condition. It is reasonable to assume that as the clinical diagnostic criteria only describe the most severe forms, milder manifestations go unrecognized and may simply be dismissed as ‘pump lung’. This condition can be distinguished from transfusion-associated circulatory overload, in that the causality of the lung injury is non-hydrostatic.$^{11}$ The association between postoperative pneumonia and RBC transfusion is well established.$^{12}$ This susceptibility is often referred to as transfusion-related immunomodulation, that is, the host’s immune response is down-regulated in response to the aforementioned antigenic leucocyte material.$^{13}$

Good quality data have only recently emerged documenting the detrimental impact of RBC transfusion on outcome following cardiac surgery. In the first large prospective study of its kind,$^9$ RBC transfusion was identified as the strongest independent predictor of all-cause morbidity, and of more concern was the finding that the impact of each single unit was additive in its detrimental effects. As may be expected, this also has an adverse influence on survival outcomes. Several studies have identified a marked impact in the immediate postoperative phase while longer-term effects have been observed at 5 yr.$^{14}$ Given the undesirable results discussed above, it is no great surprise that a great deal of effort is going into the development of transfusion alternatives.

**Transfusion alternatives**

Broadly speaking, transfusion alternatives include pharmacological intervention, mechanical techniques (namely cell salvage), preoperative autologous donation, and the use of blood substitutes.

Pharmacological strategies for blood sparing are relatively well established and include interventions such as preoperative erythropoietin, improved strategies for cardiopulmonary bypass (CPB) anti-coagulation, and the use of anti-fibrinolics.$^{15}$ A recently and particularly exciting development is the use of drag-reducing polymers in animal models. The basic premise of these agents is that by a reduction in myocardial after-load, systemic oxygenation may be improved by an increase in cardiac output rather than an increase in arterial oxygen content.$^{16}$ This is an appealing prospect in cardiac surgery patients, as any reduction in after-load will also confer protective benefits on the heart.$^{17}$

Cell salvage has been proposed as an effective method of reducing allogenic RBC exposure. With this technique, shed RBCs are washed and returned to the patient, thus removing any pro-coagulant mediators. A recent Cochrane review has questioned the evidence base behind this method in terms of effectiveness, safety, and cost, as a result of the poor methodological quality of many studies.$^{18}$ In the authors’ experience, cell salvage is a valuable tool in reducing transfusion exposure, provided the perfusate remaining at the termination of CPB is processed.$^{19}$ An individual’s RBCs may also be returned to them after preoperative autologous donation (PAD). Although this is likely beneficial to the patient, PAD has never been widely adopted, again due to concerns over cost-effectiveness.$^{20}$

Artificial oxygen carriers are a relatively recent development, which aim to improve the oxygen carrying capacity of the blood, and thus DO$_2$, independent of RBCs. The primary benefit is the avoidance of transfusion risk. They can be divided broadly into modified [Hb] solutions and perfluorocarbon suspensions.$^{21}$ As the latter require a higher inspired oxygen concentration ($F_i(O_2)$) to improve tissue oxygenation, clinical investigation has been largely suspended. Modified [Hb] solutions continue to show promise, although their tendency to increase pulmonary artery pressure through nitric oxide scavenging may cause concern in cardiac surgery patients.$^{22}$

In conclusion, current evidence suggests that RBC transfusion in elective cardiac surgery patients is a potentially
counter-productive intervention that should only be performed where there is good evidence that systemic oxygenation is compromised, an individual is significantly bleeding, or both. The current development of synthetic oxygen carriers in tandem with compounds that increase tissue oxygenation via flow-mediated changes offers the possible prospect that the requirement for RBCs in this subgroup of patients will be all but removed.

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References
9 Blumberg N. Deleterious clinical effects of transfusion immunodulation: proven beyond a reasonable doubt. Transfusion 2005; 45 (2 Suppl): 33–95
10 Blajchman MA. The clinical benefits of the leukoreduction of blood products. J Trauma 2006; 60 (6 Suppl): S83–90
16 Cotoia A, Kameneva MV, Marascalco Pj, Fink MP, Delude RL. Drag-reducing hyaluronic acid increases survival in profoundly hemorrhaged rats. Shock 2008; June 27 (Epub ahead of print)