Introduction

Technologies and techniques that reduce the need for allogeneic blood transfusion during surgery through the conservation of a patient's own blood, (sometimes referred to as "bloodless surgery"), are currently of interest in many countries.\(^1\) The topic has received particular attention since the problems of "tainted" blood infected with HIV and hepatitis, in the 1980s. More recently, concern regarding the possibility of transmitting Creutzfeld-Jacob disease through blood transfusions has led to a renewed interest in blood conservation initiatives, and has resulted in further restrictions on the donor blood supply.

A Canadian study\(^2\) has found that there is substantial variation in the use of blood conservation techniques in Canadian hospitals. The authors conclude that this could be interpreted in two ways: either the technologies available are underused, or the low level of use of these technologies reflects the "limited quality evidence for the efficacy of blood-sparing technologies."

Some of the available blood conservation technologies are:\(^2,3\)

(a) drugs:
- erythropoeitin (EPO)
- desmopressin (DDAVP)
- aprotinin
- tranexamic acid
- aminocaproic acid (fibrin sealants)

(b) procedures:
- cell salvage (auto-transfusion)
- preoperative autologous donation (PAD)
- acute normovolemic hemodilution

Research Questions

Blood conservation initiatives may offer an alternative to the risks and costs associated with allogeneic blood transfusion; however, these alternatives are also associated with risks and costs. Moreover, the options to reduce or avoid blood transfusion vary depending on the medical condition of the patient and the type of surgery. There is uncertainty surrounding the optimal thresholds for transfusion, and this area lacks quality evidence.\(^4\)

Emerging technologies, such as the many artificial oxygen carriers currently under development, may soon provide further options.
Assessment Process

Literature searches were conducted of the Cochrane Library, the CRD Databases (DARE, NHS EED and HTA), and of health technology assessment agencies and related web sites. A preliminary search of PubMed, using text words such as "blood conservation" and "bloodless surgery", and MeSH terms such as hemodilution, erythropoetin, aprotinin and blood transfusion, and restricted to "systematic reviews", identified over a hundred studies. This preliminary search did not include all of the appropriate terms for these technologies; undoubtedly further relevant information will be retrieved if a more comprehensive search strategy is undertaken.

Summary of Findings

There has been some work in this area by HTA agencies, such as the 1993 consensus conference organized by the Agence Nationale d'Accreditation d'Évaluation en Santé in France and its 1997 synthesis on the use of blood products for transfusion. The University Health System Consortium (UHC) in the US has also produced assessments in this area, with a 1995 report on aprotinin and a 1997 guideline on red blood cell transfusion.

A major study in this area, the International Study of Perioperative Transfusion (ISPOT), is a study of "evidence, attitudes and practices relating to the use of alternatives to perioperative allogeneic blood transfusion". This study involves ten countries and is coordinated through Ottawa researchers (http://www.lri.ca/programs/ceu/ispot/default.htm). ISPOT has produced a number of the systematic reviews and other assessments in this field, several of which are cited here. Furthermore, a Canadian Expert Working Group reviewed the published evidence and issued their Guidelines for red blood cell and plasma transfusion for adults and children, in 1997. The Ministry of Health in Ontario has also established the Ontario Blood Conservation Program to "provide a basis for evidence-based practice for the treatment of anemia in the perioperative setting, employing alternative therapies and techniques to avoid allogeneic blood transfusion…"
The table below lists a selection of the studies published since 1998, as well as those currently underway.

<table>
<thead>
<tr>
<th>Type of Report</th>
<th>Title</th>
<th>Reference</th>
<th>Main Findings</th>
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<tbody>
<tr>
<td>Systematic review</td>
<td>Pre-operative autologous donation for minimising perioperative allogeneic blood transfusion [Cochrane review]</td>
<td>Henry DA, Carless PA, Moxey AJ, O’Connell D, Forgie MA, Wells PS, et al. Cochrane Database Syst Rev 2002;(2):CD003602.</td>
<td><em>“Although the trials of [pre-operative autologous donation] PAD showed a reduction in the need for allogeneic blood, the methodological quality of the trials was poor and the overall transfusion rates (allogeneic and/or autologous) in these trials were high, and were increased by recruitment into the PAD arms of the trials. This raises questions about the true benefit of PAD. In the absence of large, high-quality trials using clinical endpoints, it is not possible to say whether the benefits of PAD outweigh the harms.”</em></td>
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<tr>
<td>Systematic review</td>
<td>Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion [Cochrane review]</td>
<td>Hill SR, Carless PA, Henry DA, Carson JL, Herbert PC, McClelland DBL, et al. Cochrane Database Syst Rev 2002;(2):CD002042.</td>
<td><em>“The limited published evidence supports the use of restrictive transfusion triggers in patients who are free of serious cardiac disease. However, most of the data on clinical outcomes were generated by a single trial. The effects of conservative transfusion triggers on functional status, morbidity and mortality, particularly in patients with cardiac disease, need to be tested in further large clinical trials. In countries with inadequate screening of donor blood the data may constitute a stronger basis for avoiding transfusion with allogeneic red cells.”</em></td>
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<td><strong>Emerging health technology bulletin</strong></td>
<td><strong>Artificial oxygen carriers</strong></td>
<td><strong>Birmingham (UK): National Horizon Scanning Centre; 2002. [New and emerging technology briefing]. Available: <a href="http://www.publichealth.bham.ac.uk/horizon/PDF_files/ArtificialOxygenCarriers.PDF">http://www.publichealth.bham.ac.uk/horizon/PDF_files/ArtificialOxygenCarriers.PDF</a></strong></td>
<td>- “Blood substitutes could significantly reduce the need for donor transfusions if proven to be efficacious, although the diffusion of the products will depend on the clinical acceptance. The cost of the blood substitutes may partially replace expenditure on allogenic and autologous blood storage and transfusion in some situations, but not totally replace it. As the relative cost of the blood substitutes is currently unknown, it is difficult to predict the overall cost impact…”</td>
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<td><strong>Emerging technology bulletin</strong></td>
<td><strong>Oxygen carriers (“blood substitutes”)</strong></td>
<td><strong>Topfer LA, Hailey D. Ottawa: Canadian Coordinating Office for Health Technology Assessment; 2001. [Issues in emerging health technologies; issue 21]. Available: <a href="http://www.ccohta.ca">http://www.ccohta.ca</a></strong></td>
<td>- “…the current generation of “blood substitutes” are intended for use only in certain applications as oxygen carriers. They will not replace the need for whole blood. At least initially, they will probably be used in conjunction with other blood conservation methods, in particular, preoperative hemodilution. The cost-effectiveness and safety of these products must still be determined.”</td>
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<td><strong>HTA</strong></td>
<td><strong>Preoperative autologous blood donation (PABD)</strong></td>
<td><strong>St. Paul (MN): Minnesota Health Technology Advisory Committee; 2000. Available: <a href="http://www.health.state.mn.us/htac/pabd.htm">http://www.health.state.mn.us/htac/pabd.htm</a></strong></td>
<td>- “Studies suggest that while PABD decreases, it does not totally eliminate, the need for allogeneic transfusion for elective surgery. However, it does greatly increase the likelihood of any transfusion and is not entirely without medical risks.”</td>
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<td><strong>Systematic review</strong></td>
<td><strong>A meta-analysis of the effectiveness of cell salvage to minimize perioperative allogeneic blood transfusion in cardiac and orthopedic surgery</strong></td>
<td><strong>Huet C, Salmi LR, Fergusson D, Koopman van Gemert AW, Rubens F, Laupacis A. Anesth Analg 1999;89(4):861-9. A Cochrane Collaboration review based on this study is currently in progress (see Laupacis et al., cited below.)</strong></td>
<td>- “We conclude that cell salvage in orthopedic surgery decreases the proportion of patients requiring allogeneic blood transfusion perioperatively, but postoperative cell salvage is only marginally effective in cardiac surgery.”</td>
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<td>Systematic review</td>
<td>The efficacy of technologies to minimise perioperative allogeneic transfusion</td>
<td>Laupacis A, Fergusson D. In: Smitt Sibinga C Th, Das PC, Fratantoni JC, editors. <em>Alternative approaches to human blood resources in clinical practice</em>. Dordrecht, The Netherlands: Kluwer Academic Publishers; 1998. p. 17-36.</td>
<td>“The use of aprotinin significantly decreased the proportion of patients receiving at least one unit of allogeneic blood… Patients receiving aprotinin were significantly less likely to require re-operation because of bleeding after surgery than controls.”</td>
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<tr>
<td>Systematic review</td>
<td>Desmopressin for minimising perioperative allogeneic blood transfusion [Cochrane review]</td>
<td>Henry DA, Moxey AJ, Carless PA, O’Connel D, McClelland B, Henderson KM, et al. <em>Cochrane Database Syst Rev</em> 2001;(2):CD001884 A substantive amendment to this systematic review was last made in 1998.</td>
<td>“There is no convincing evidence that desmopressin minimises perioperative allogeneic RBC transfusion in patients who do not have congenital bleeding disorders. These data suggest that there is no benefit of using DDAVP as a means of minimising perioperative allogeneic RBC transfusion…”</td>
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**Conclusion**

A synthesis of available high quality evidence on various blood conservation options may be of value. However, there are three systematic reviews in progress. Contact should first be made with researchers involved in the relevant Cochrane Collaboration reviews, the ISPOT investigators, and other significant Canadian initiatives such as the Blood Conservation program in Ontario, to ensure this is not a duplication of their current research efforts. This would determine how appropriate it is for CCOHTA to enter this arena, as others who are very knowledgeable in this area may currently be providing this information.

**References**

