Blood conservation in practice: an overview

Allogeneic blood transfusions are associated with risks and unfavourable outcomes. Blood conservation provides an alternative, with potential to improve patient care with limited or no blood transfusion. Many approaches are available, but the most essential ones are simple and cost free.

The long and growing list of risks, complications, and unfavourable outcomes, as well as challenges posed by a shrinking supply, complicated logistics and staggering costs have long fuelled research on finding alternatives to allogeneic blood transfusion (Shander, 2004; Shander et al, 2007). What began years ago on a limited scale as a special service to populations who refused allogeneic transfusions (e.g. people of Jehovah's Witness faith) is now becoming a widely-available practice, which can benefit potentially all patients.

Blood conservation (also known as blood management) is defined as the appropriate use of blood components with a goal of minimizing their use (Goodnough and Shander, 2007). This is in contrast to 'bloodless' medicine and surgery, in which use of any allogeneic blood component is avoided. However, both practices share the same approaches for the most part, except for the needy patients with dangerously low blood oxygen-carrying capacity, who are still considered to be candidates for allogeneic blood transfusion. While continuing research on alternatives such as haemoglobin-based and other artificial oxygen carriers has the promise of freeing even these patients from the need to use allogeneic blood, currently these patients should be transfused to increase their haemoglobin level and maintain tissue oxygen delivery and consumption.

Transfusion practices in need of change

It is surprising to note the various myths and wrong perceptions that taint the use of blood (Clinical Excellence Commission, 2008). Many clinicians still hold the firm belief that transfusion is a fast and easy way of boosting their patients' health and accelerating recovery. The outdated and largely unsubstantiated 10/30 rule that calls for transfusion in surgical patients with haemoglobin below 10 g/dl or haematocrit below 30% still has many followers. Worse, some clinicians do not abide by any objective rules or guidelines in their transfusion practice at all, and handle each case on a subjective and haphazard basis. Use of blood in procedures such as cardiovascular operations is often considered to be inevitable (Fakhry and Fata, 2004).

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Contrary to the general belief that blood transfusion is a quick and efficient way of improving patients' condition by increasing haemoglobin level, several studies indicate otherwise. A review of 18 studies on critically ill patients shows that while transfusion was associated with increased haemoglobin in all studies, oxygen delivery was increased in 14 studies, and improvement in tissue oxygen consumption (the end goal of transfusion and the parameter that really matters) was observed in only five studies (Vincent et al, 2007). In other words, transfusion is not providing any benefits to many recipients, who are generally deemed to be in need of blood (critically ill patients). Moreover, a pivotal randomized trial has shown that a restrictive transfusion strategy is as effective as and possibly superior to a liberal transfusion strategy in many critically ill patients (Hébert et al, 1999).

While extra caution is warranted for older patients and those with cardiac disease, a restrictive transfusion strategy based on objective criteria is the first and perhaps most important step toward achieving blood conservation in various settings. It is estimated that just by applying a restrictive transfusion approach, one to two units of blood per surgical patient could be saved (Goodnough et al, 2003). The transfusion guidelines have traditionally been based on certain haemoglobin or haematocrit triggers (*Table 1*). Nonetheless, a single laboratory value cannot be an accurate indicator of actual oxygen consumption status of tissues, and physiological criteria should be used as the preferred transfusion triggers (*Table 2*) (Madjdpour et al, 2006).

Principles of blood management

While various blood conservation techniques and approaches are available and used when appropriate, a number of general principles apply to every case:

- A plan of care for avoiding and controlling blood loss should be formulated that is tailored to the clinical management of individual patients
- Blood conservation requires a multidisciplinary treatment approach using a combination of interventions

Table 1. Examples of haemoglobin-based transfusion guidelines

Setting	Criteria		Reference
General	Transfusion is rarely indicated if Hb >10 g/dl		American Society of Anesthesiologists (1996)
	Transfusion decision should be made based on the patient's risk for complications of inadequate oxygenation if 10 ≥Hb ≥6 g/dl		
	Transfusion is almost always indicated if Hb <6 g/dl		
General	Transfusion unlikely to be of benefit in patients not at risk of coronary artery disease if Hb >8 g/dl		Canadian Medical Association (Innes, 1998)
	The presence of coronary artery disease can be an important factor in determining a patient's tolerance to low Hb		
Perioperative	Transfusion is rarely required if Hb ≥10 g/dl		National Institutes of Health (1988)
	Transfusion is frequently required if Hb <7 g/dl		
Cardiac surgery	Transfusion is unlikely to improve oxygen transport if Hb >10 g/dl and is not recommended		The Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists (Ferraris et al, 2007)
	Transfusion is reasonable and can be life saving with Hb <6 g/dl		
	Transfusion is reasonable in most postoperative patients with Hb <7 g/dl		
	During cardiopulmonary bypass with moderate hypothermia and Hb ≤6 g/dl, transfusion is reasonable		
	In patients at risk of decreased cerebral oxygen delivery (history of cerebrovascular accident, diabetes mellitus, cerebrovascular disease, carotid stenosis) transfusion with higher Hb may be justified		
	If Hb >6 g/dl while on cardiopulmonary bypass, transfusion should be carried out based on the patient's clinical situation		
Critically ill	Administer 1 unit of red blood cell and re-evaluate in:	Patients with no acute bleeding if Hb <7 g/dl	Hébert et al (2007)
		Patients with septic shock (>6 h) if Hb <7 g/dl	
		Patients with septic shock (<6 h) if 8 <Hb <10 g/dl	
		Patients with chronic cardiac disease if Hb <7 g/dl	
		Patients with acute cardiac disease if 8 <Hb <10 g/dl	

From Consensus Conference (1988). Hb= haemoglobin

- The lead clinician should assume a proactive role in management of the patient, and anticipate and be prepared to address potential complications
- Anaemia should be screened for, properly investigated and treated, preferably before surgery
- A restrictive transfusion strategy guided by objective criteria should be pursued
- A watch and wait approach should generally be avoided in a bleeding patient, especially if blood transfusion is not available or not an option
- Routine practice should be modified, exercising clinical judgment when appropriate
- A specialist experienced in blood conservation should be consulted at an early stage if there is physiological deterioration or if complications arise
- Blood drawing for laboratory tests should be minimized, or replaced with non-invasive methods (e.g. pulse oximetry)
- The perioperative use of anticoagulants and antiplatelet agents should be adjusted and minimized

Table 2. Suggested physiological criteria for red blood cell transfusion in surgery and critical care. These criteria are applicable only if normovolaemia is maintained and anaemia is the only probable cause

Relative hypotension (mean arterial pressure <70–80% of baseline or 60 mmHg)
Relative tachycardia (heart rate >120–130% of baseline or 110–130 beats/min)
New ST segment depression >0.1 mV
New ST segment elevation >0.2 mV
New wall motion abnormality in transoesophageal or transthoracic echocardiography
Mixed venous oxygen partial pressure (PvO_2) <32 mmHg
Oxygen extraction rate >40%
Mixed venous oxygen saturation (SvO_2) <60%
Decrease in oxygen consumption (VO_2) >10%

From Madjdpur et al (2006)

- Emergencies require a pre-established management plan for rapid control of bleeding and transfer to an appropriate centre if necessary (Goodnough et al, 2003).

As evident, blood conservation approaches are not limited to specific time periods in patient management. Rather, every step in patient care can be adjusted and optimized to reduce blood loss and improve haemoglobin level and ultimately minimize transfusion requirement. For example, anaemia screening in patients scheduled for elective surgery is recommended as early as 4 weeks before the surgery to allow sufficient time to investigate and manage anaemia (Goodnough et al, 2005). An overview of multimodality blood conservation approaches in patients undergoing cardiac surgery at Englewood Hospital and Medical Center is presented in *Figure 1* (Shander and Goodnough, 2006). Most of these approaches can be applied to other surgeries (Ferraris et al, 2007). In general, the primary emphasis during the preoperative and postoperative periods should be given to managing anaemia and increasing red blood cell mass, while the mainstay of intraoperative blood management is reducing blood loss.

Preoperative management

Achieving the full potentials of blood management strategies requires planning and preparation in advance. The first step in preoperative blood management involves taking a detailed and comprehensive medical history and physical examination with emphasis on family and past history of bleeding disorders as well as medications that affect coagulation (Goodnough and Shander, 2007). This allows identification of high-risk patients who are more likely to need transfusion. Accordingly, a more aggressive blood conservation strategy can be planned for these patients (Ferraris et al, 2007).

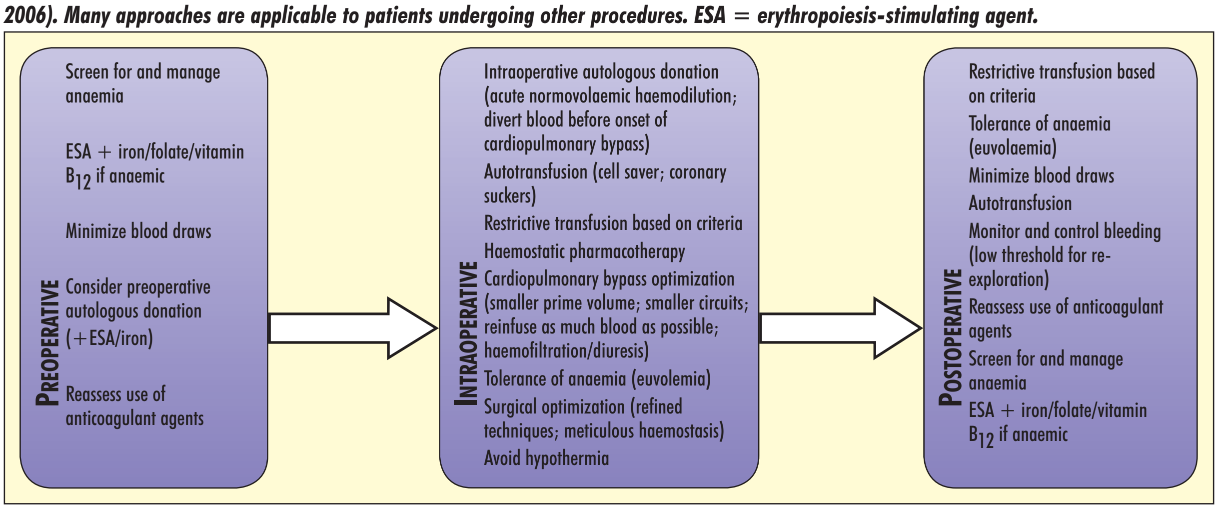
Screening for anaemia should be done as early as possible. An algorithm for investigating anaemia in elective surgical patients has been developed. Anaemia is a major risk factor for perioperative transfusion, as well as an independent risk factor of morbidity and mortality (Shander and Goodnough, 2006). Correction of low haemoglobin and increasing the red cell mass with pharmacotherapy before the surgery is an effective measure to avoid transfusion. Every effort to prevent further blood loss (e.g. minimizing blood draws, use of paediatric-sized blood tubes, readjusting and/or discontinuing anticoagulative use) should be made.

Erythropoiesis-stimulating agents

Erythropoiesis-stimulating agents have gained considerable attention as a fast and efficient way of increasing haemoglobin level. As recombinant variants of naturally occurring erythropoietin, these agents promote survival and expansion of red cell precursors. To keep up with the increased demand of accelerated haematopoiesis, supplemental iron, folic acid and vitamin B_{12} should be provided, otherwise bodily iron reserves can be quickly depleted (in spite of initial apparent normal iron levels), resulting in a condition known as physiological iron deficiency. Continuous administration of erythropoiesis-stimulating agents can produce the equivalent of one blood unit in 1 week and up to five blood units in 4 weeks (Shander and Goodnough, 2006). The time required to achieve the increase in red blood cell mass to avoid transfusion underscores the importance of planning in advance of elective procedures as a central pillar of blood management. On average, proper use of erythropoiesis-stimulating agents can prevent transfusion of two units of blood per surgical patient (Goodnough et al, 2003).

Erythropoiesis-stimulating agents are not without risks and they have been linked to increased thromboembolic events and hypertension. Special attention should be given to cancer patients as erythropoiesis-stimulating agents are growth factors and can potentially promote the growth of tumour cells via a number of mechanisms (Sinclair et al, 2007). It has been suggested recently that

Figure 1. Blood management in practice: a multimodality approach to reduce transfusion need in cardiac surgeries (Shander and Goodnough, 2006). Many approaches are applicable to patients undergoing other procedures. ESA = erythropoiesis-stimulating agent.



use of these agents is associated with increased risk of venous thromboembolic events and higher mortality rates in cancer patients (Bennett et al, 2008), although high quality evidence from randomized controlled trials is missing and more investigation is needed. The safety profile of erythropoiesis-stimulating agents is under continuous evaluation and clinicians should consult the regulatory agencies, as the published data can become quickly outdated. The US Food and Drug Administration (2008) recently issued a warning indicating the increased mortality, serious cardiovascular and thromboembolic events and increased risk of tumour progression or recurrence for these agents, and recommended individualized dosing to achieve and maintain haemoglobin levels within the range of 10–12 g/dl, as well as deep vein thrombosis prophylaxis.

Preoperative autologous donation

Concerns over blood units contaminated with human immunodeficiency virus (HIV) and hepatitis C virus stirred interest in autologous blood donation some 30 years ago. Preoperative autologous donation involves collection of a few units of a patient's blood during the weeks preceding elective surgery, these are stored and reinfused perioperatively if the patient requires transfusion. Use of preoperative autologous donation can prevent transfusion of one to two units of blood per surgical patient (Goodnough et al, 2003). However, the popularity of preoperative autologous donation is declining because of the inconvenience to patients and several other limitations of this procedure. In particular, the donated autologous blood units share some of the prominent risks of allogeneic blood (transfusion errors, storage lesion), the efficacy and cost-effectiveness is not established, and the required aggressive phlebotomy may make the patient anaemic by the day of surgery and increase the ultimate risk of transfusion, if haematopoiesis is not augmented by erythropoiesis-stimulating agents and iron administration (Shander and Goodnough, 2006).

Intraoperative management

As discussed earlier, the focus of intraoperative blood management is to reduce blood loss. This goal can be achieved through improved surgical techniques and surgical planning and/or rehearsal, retrieval and reinfusion of patient's shed blood, use of devices and agents that improve haemostasis and avoidance of coagulopathy.

Surgical planning and, especially in case of complex procedures, surgical rehearsals can increase the speed and efficiency of performing procedures and reduce duration or surgery and surgical blood loss. Tourniquets can be used to locally limit the blood flow to the site of surgery. Patients can be positioned properly to elevate the surgical site and reduce arterial pressure and facilitate venous drainage away from the surgical wound. Controlled systemic hypotension during anaesthesia can also reduce bleeding from the surgical site. In addition, platelet function is adversely affected by hypothermia and its avoidance can reduce surgical bleeding (Shander and Goodnough, 2006; Goodnough and Shander, 2007).

Various types of electrocautery and argon beam coagulation, local vasoconstriction with adrenaline and topical haemostatic agents are other methods for minimizing bleeding at the site of incision. Topical haemostatic agents come in various types and forms and can be applied as fluids, gels or coupled with various matrices. Some common components of these agents include thrombin (from human, bovine or recombinant sources), fibrinogen, collagen, and cellulose preparations. Products containing human- or animal-derived components pose the potential risk of transmitting infective agents, and use of recombinant technology to produce these components in vitro is likely to become the prevailing trend in the near future (Voils, 2007).

Pharmacological interventions

Some systemic haemostatic agents have recently been the subject of much discussion and heated debate. Antifibrinolytics include aprotinin (from bovine source) and synthetic lysine analogues (ε-aminocaproic acid and tranexamic acid). These agents achieve haemostasis by inhibiting plasminogen and plasminogen-mediated fibrinolysis, thus maintaining the fibrin clots formed at sites of bleeding. They are effective in reducing transfusion requirements during surgery, with aprotinin being more effective than tranexamic acid and tranexamic acid being more effective than ε-aminocaproic acid (Goodnough and Shander, 2007). However, reviews suggest that, while cheaper, lysine analogues (especially tranexamic acid) are probably as effective as aprotinin (Henry et al, 2007).

More importantly, while lysine analogues have generally enjoyed an acceptable safety profile, aprotinin has been linked to increased mortality and renal dysfunction in retrospective studies (Shaw et al, 2008), and the safety concerns have been recently confirmed in a randomized controlled trial on patients undergoing high-risk cardiac surgery, resulting in early termination of the trial because of increased mortality rates in patients receiving aprotinin (Fergusson et al, 2008). Aprotinin was voluntarily withdrawn from the market by the manufacturer and it is currently only available as an investigational drug.

Another debated haemostatic agent is recombinant activated factor VII (rFVIIa). Approved indication of rFVIIa is limited to treatment of bleeding episodes in haemophilia A or B patients with inhibitors against factors VIII or IX. However, it has shown some efficacy in controlling intractable and massive bleeding in general patients (von Heymann et al, 2008). rFVIIa has been suggested as a potential haemostatic agent for use during surgery, and reviews indicate some effect in reducing transfusions in surgical patients with an acceptable safety profile (Hsia et al, 2008; Ranucci et al, 2008). However, more studies are needed before rFVIIa can be considered as a haemostatic agent for routine use in blood management. Similarly, desmopressin (a vasopressin analogue) has shown some effect in reducing blood loss, but its routine prophylactic use as part of a blood conservation strategy is not recommended except in patients with platelet dysfunction known to respond to desmopressin (Ferraris et al, 2007).

Intraoperative autologous donation

Most of the approaches described above aim to reduce bleeding at the site of surgery. However, a number of intraoperative blood conservation approaches are available to mitigate the effects of surgical bleeding on transfusion requirement by diluting or retrieving the shed blood. In acute normovolaemic haemodilution, a pre-calculated amount of the patient's blood is removed and replaced with colloids and/or crystalloids at induction of anaesthesia to achieve haemodilution, while keeping the patient normovolaemic. Therefore, what the patient bleeds during the surgery is essentially diluted blood. The patient's removed blood is kept in the operating room and it is reinfused back to the patient at wound closure or any time during the surgery that the blood is needed. Compared with preoperative autologous donation, acute normovolaemic haemodilution offers several advantages. It can be done conveniently in elective as well as emergent procedures and since the blood is stored by the patient's side and used within hours, there is little, if any, risk of clerical errors and adverse effects of blood storage (Shander and Perelman, 2006). This technique is most effective in procedures with anticipated significant blood loss, where it can prevent transfusion of one to two units of allogeneic blood (Weiskopf, 2001; Goodnough et al, 2003).

Autologous blood cell salvage is another effective blood conservation approach, in which the patient's shed blood is retrieved from the surgical site with sponges, washed and/or filtered and reinfused back to the patient. Overall, cell salvage is estimated to reduce the rate of exposure to allogeneic blood transfusion by 39%, without having any adverse impact on outcome (Carless et al, 2006). However, concerns over the risk of reinfusing unwanted cells or material (e.g. bacteria, tumour cells, amniotic fluid, urine) have hampered the use of these techniques in some settings. Use of leukoreduction filters appears to be an effective measure to reduce the risk, and cell salvage has been used successfully in various surgical settings and populations (Goodnough and Shander, 2007).

Case Report

A 62-year-old man was referred for elective abdominal aortic aneurysm repair surgery. His past medical history was remarkable for hypertension and peripheral vascular disease. Cardiac evaluation confirmed an ejection fraction that was within the normal range despite the presence of some diastolic dysfunction. The patient's height and weight were 170 cm and 97 kg respectively. A preoperative blood count showed a haemoglobin level of 10.9 g/dl. In anticipation of the large blood loss, erythropoiesis-stimulating agents, iron and multivitamin injections were administered. A workup for blood-loss anaemia was negative.

The patient's subsequent preoperative haemoglobin was 11.7 g/dl. At surgery, general endotracheal anaesthesia was initiated and a right internal jugular vein 16-gauge introducer line, a radial arterial line and two intravenous lines were established. Pre-incision thromboelastography was normal. Before incision, three units of acute normovolaemic haemodilution blood (whole blood) were removed and plasma sequestration was performed. To maintain haemodynamics, 1300 ml of colloid as 6% hydroxyl starch was infused. Post-acute normovolaemic haemodilution haemoglobin was 8.9 g/dl. Following aortic cross clamping, haemoglobin dropped to 6.4 g/dl, but the patient's remained haemodynamically stable. Half a unit of the acute normovolaemic haemodilution red blood cell was given to increase the haemoglobin level to 8 g/dl, and the haemoglobin was maintained around 8 g/dl by reinfusing cell salvage blood. After aorta unclamping, thromboelastography showed moderate platelet abnormality. Acute normovolaemic haemodilution platelet-rich plasma and platelet-poor plasma was returned along with the remaining red blood cells and cell salvage blood. The patient had an estimated blood loss of 2.4 litres, and maintained good urinary output throughout the procedure.

Postoperative haemoglobin was 8.7 g/dl. The patient remained with stable vital signs and good urinary output. He was extubated on the same day. Blood draws were kept at a minimum and erythropoiesis-stimulating agents and iron were reinstated.

Postoperative management

Patients should be closely monitored for bleeding and every effort (including returning to the operating room for re-exploration) should be made to promptly arrest the bleeding. Temperature and blood pressure should be maintained within the normal range, and hypoxia and hypovolaemia should be avoided. Autologous blood cell salvage can continue postoperatively and recovered blood can be reinfused back to the patient. Other methods to improve haemostasis described before can be used as well. A restrictive transfusion strategy based on objective criteria (*Tables 1* and *2*) should be followed. While diagnostic phlebotomies should be limited as in the preoperative period, anaemia should be tested for and treated if present, using iron, folate, vitamin B_{12}, and possibly erythropoiesis-stimulating agents if required (Shander and Goodnough, 2006; Goodnough and Shander 2007).

Conclusions

Blood transfusion is one of the oldest methods used in treatment of patients. However, its deep roots in medicine and aliases such as 'gift of life' have precluded many from questioning its efficacy. Evidence supporting the benefits of transfusion in most of clinical settings is lacking. On the other hand, a host of evidence points to its risks and deleterious effects.

Most patients can be managed equally well, if not better, with limited or no allogeneic blood transfusion, and blood conservation (or management) seeks to achieve this goal. The case report presented here serves as an example to show the feasibility of performing complex procedures generally known to be associated with significant blood loss, without the need to transfuse allogeneic blood. Approaches focus on detecting and treating anaemia, increasing red blood cell mass and reducing blood loss. Many options are available and many more (artificial blood substitutes for example) are at various stages of research and development. Blood conservation is a rapidly evolving field, with many options under continuous research and scrutiny. However, it is never enough to emphasize that beyond fancy devices and drugs, blood conservation can be easily achieved through a change in attitude towards transfusion and adopting objective criteria to identify patients who are likely to benefit from transfusion from the majority who are receiving unnecessary and potentially harmful transfusions every day in hospitals and medical centres around the world. **BJHM**

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KEY POINTS

- With doubtful benefits and proven risks of allogeneic blood transfusions, only a small percentage of patients currently transfused are likely to actually benefit from it.
- Blood conservation (management) is defined as the appropriate use of blood components with the goal of minimizing their use.
- Blood management is a multimodality approach, requiring planning and multidisciplinary team work.
- Screening for and management of anaemia is essential.
- A restrictive transfusion strategy based on evidence-based criteria/guidelines should be applied.
- Blood loss should be minimized, and every drop of blood (literally) should be saved.
- A myriad of blood conservation techniques, devices and agents are available, and while some have been proven safe and effective, more research is needed to delineate the safety and efficacy of others.