Bloodless Medicine and Surgery

Aryeh Shander, M.D. **Englewood, New Jersey**

INTRODUCTION: A philosophy of blood management that incorporates bloodless medicine principles is appropriate for all patients. Although allogeneic transfusion is considered "safer than it has ever been", this level of safety has come at the price of increasing costs and decreasing supplies[1-4]. Liberal versus restrictive transfusion strategies have shown that more blood is not better[5]. No convincing Level One evidence exists that blood transfusion has a lifesaving role beyond its volume effect (i.e., no prospective, randomized, double-blinded trial has ever been conducted to result in FDA-licensed approval for blood transfusion). Cold storage of blood decreases its ability to release oxygen, questioning its efficacy during acute need for increased oxygen delivery.

A goal of every anesthesiologist should be the application of rational blood management techniques throughout the perioperative period. This course shall discuss current evidence supporting blood conservation as a central anesthetic strategy with blood transfusion being applied only as a last resort rather than a first principle. Moreover it will focus on strategies that exploit appropriate combination*s* of drugs, technological devices, and surgical/medical techniques,[6] along with an interdisciplinary team approach. An overview of the general principles of medical and surgical care to minimize or prevent allogeneic transfusion is presented in Table 1.

Table 1. Surgical and Anesthetic Principles of Bloodless Management

1. Preoperative Assessment/Planning: management of anemia, management of anticoagulation and congenital and drug-induced coagulopathies, prophylactic interventional radiology/embolization, prescribing/scheduling of cell salvage apparatus, restricted diagnostic phlebotomy.
2. Intraoperative Blood Conservation: meticulous surgical hemostasis, blood salvage, hemodilution, pharmaceutical enhancement of hemostasis, maintenance of normothermia, surgical positioning to minimize blood loss and hypertension.
3. Postoperative Blood Conservation: blood salvage, tolerance of anemia, optimum fluid and volume management, restricted diagnostic phlebotomy, adequate analgesia, maintenance of normothermia.
4. Maintain appropriate fluid resuscitation. Significant normovolemic anemia is well tolerated in hemodynamically stable patients.
5. In actively bleeding patients, the first management priority must be to stop the bleeding. Avoid attempts to normalize blood pressure until hemorrhage is controlled.
6. Prevent or treat coagulation disorders promptly.
7. Oral or parenteral iron may be used to improve iron stores. Recombinant (synthetic) human erythropoietin (rHuEPO) effectively increases red cell mass.
8. Hematology/oncology: aggressive rHuEPO and iron therapy for prophylaxis of anemia, individualized chemotherapy protocols to minimize hematologic toxicity, pharmacologic prophylaxis and treatment of bleeding, tolerance of anemia, and restricted diagnostic phlebotomy.

PREOPERATIVE MANAGEMENT

Thorough preoperative planning is essential to reducing or avoiding perioperative allogeneic transfusion. Preoperative assessment requires accurate history taking and physical examination. Attention should be paid to any personal or family history of bleeding disorders. In patients requesting transfusion-free care who require major cardiac and orthopedic surgical procedures, aggressive preoperative workups have yielded excellent results[7, 8]. Thoughtful presurgical assessments and careful planning can avoid unnecessary transfusions (Table 2).

Optimize Preoperative Hemoglobin Level

Patients with low hemoglobin levels prior to surgery are at higher risk of receiving allogeneic transfusion[9]. To minimize this risk, patients should have their red cell mass increased preoperatively. The use of recombinant human erythropoietin (EPO) and/or iron therapy has been effective for this purpose[10].

Preoperative Blood Conservation

A simple measure to conserve the patient's own blood consists of restricted diagnostic phlebotomy (reducing the number of tests and the volume of blood withdrawn)[11]. Another measure is careful management of anticoagulation, including discontinuation or substitution of agents that could adversely affect clotting in the perioperative period (e.g., ASA and medications containing aspirin, NSAIDs, anti-platelet agents and anticoagulants).

Preoperative Autologous Donation (PAD)

In most jurisdictions physicians are obligated to inform their patients of PAD as part of blood management [12,13]. However, for every two units donated, on average only one unit gets transfused[14]. The patient may not avoid exposure to allogeneic blood since approximately 50% of patients who donate blood prior to surgery are anemic on the day of surgery[15]. PAD is also associated with higher rates of clerical errors than allogeneic blood and is not without infectious risks. Nonetheless, it is important to consider the patient's peace of mind and informed choice. However, enthusiasm for PAD has delayed scrutiny of more cost-effective autologous blood procurement strategies such as acute normovolemic hemodilution (ANH) and red blood cell recovery and reinfusion[16].

INTRAOPERATIVE MANAGEMENT

Surgical Approaches to Reducing Blood Loss

The sine qua non of reducing transfusion need in surgical patients is to prevent blood loss. Surgeons are trained in the art of gentle tissue handling, recognition and avoidance of potential bleeding sources and rapid control of unexpected hemorrhage. Traditionally, this has been accomplished with electrocautery, utilizing either monopolar or bipolar instruments.[17] Newer modifications to electrocautery include the use of an argon beam-enhanced device that produces a stream of argon gas around the cautery tip that can coagulate vessels up to 3 mm in diameter while minimizing tissue trauma.[18] Another technology combines fluid with radio frequency energy to produce a tissue effect with no charring, burning or perforation. It has been used to provide a nearly bloodless surgical field especially when performing solid organ resection[19].

Bleeding will occur despite these novel applications of technology[20]. It is at this point that the physician must rely upon the body's intrinsic ability to rapidly form clot through activation of a complex process requiring the interaction of both cellular and circulating blood elements. Research into the action of these components combined with recent advances in industry's ability to purify and concentrate these proteins has lead to the creation of tissue, or fibrin, sealants. These products are combinations of purified thrombin and fibrinogen from bovine or animal sources that reproduce the last states of the coagulation cascade: the conversion of fibrinogen into fibrin monomers and the cross-linking of these into an insoluble fibrin matrix.[21] These sealants typically are provided in two syringes, the first containing concentrated fibrinogen and aprotinin, the second containing thrombin and $CaCl_2$ in equal parts. A variety of mixing tips are available to permit pinpoint or spray application to a cut or bleeding surface. These products have been shown to reduce both blood loss and transfusion requirements in a wide variety of surgical procedures.

In massive trauma, and surgery for life-threatening injuries, an initial emergent procedure can be performed to rapidly control hemorrhage and contamination. This may include the introduction of temporary packs into the wound and rapid closure to allow for adequate resuscitation and stabilization to achieve a survivable physiology. Later, a planned re-operation can be performed more safely for definitive repair of injuries.

Performing complex elective procedures in stages can minimize blood loss in specific clinical situations. For operative procedures with a high-expected blood loss, staged surgery may be part of an overall blood conservation strategy.[22] Patient positioning to elevate the surgical site to reduce regional arterial pressure and facilitate venous drainage away from the surgical wound reduces blood loss.[23] Care must be applied not to introduce air into the venous circulation. Other measures include the use of tourniquets, infiltration of the surgical wound with local vasoconstrictors, direct control of bleeding, use of topical hemostats and hemostatic electrosurgical instruments. These valuable pharmacological and mechanical blood conservation procedures are useful adjuncts to rigorous hemostasis and good surgical technique and planning.[24]

Anesthetic Techniques

Controlled hypotension, maintenance of normothermia, blood cell salvage, hemodilution and tolerance of normovolemic anemia are all associated with reduced surgical blood loss. Data suggest that each can contribute to reduction of bleeding[25].

Blood Recovery and Reinfusion

Autologous blood cell salvage (intraoperative autotransfusion) involves recovery of the patient's shed blood from a surgical wound, washing or filtering, and reinfusion of the blood into the patient. Reinfusion can be performed continuously during surgery. Autotransfusion is an effective blood conservation option for surgical procedures characterized by massive blood loss or where religious objections exclude the use of allogeneic blood. Technological advances have increased system automation. Furthermore, newer devices can process very small blood volumes (30 mL or less), require low priming volumes, and offer higher processing speed and better end product quality.

Cell recovery devices have been used extensively in surgery and have found their place in cardiac, orthopedic, vascular and trauma procedures. Evidence suggests that blood recovery is cost effective when there is a high-expected surgical blood loss or when hospital stay can be reduced.[26,27] Additionally, there is mounting evidence supporting the use of leukocyte depleting filters (LDFs) with cell salvage devices in cancer and obstetric patients undergoing surgery with large blood loss.[28-30] Historically, cell salvage use had been excluded in obstetrics and oncologic surgery because of concerns that amniotic fluid or cancer cells would be introduced into the patient's circulation. New data has challenged this thinking. In addition, irradiation of blood recovered during oncologic surgery is another option enhancing the safe management of these patients without allogeneic transfusion.[31] Table 2 provides estimates of the blood sparing potential of blood conservation techniques available for bloodless management.

Acute Normovolemic Hemodilution (ANH)

Acute normovolemic hemodilution (ANH) is a low-cost and effective blood conservation technique that can significantly reduce loss of red cell mass in surgical cases with a high-expected blood loss.[32] Figure 1 offers a model of ANH. During ANH, several units of blood are collected from a patient immediately before or after the induction of anesthesia and replaced with either a crystalloid or colloid solution or both. Although bleeding during surgery remains essentially unchanged, blood lost during the surgical procedure contains fewer red cells and clotting factors because the patient's blood has been diluted. At the conclusion of surgery or when clinically indicated, collected blood may be returned to the patient. ANH offers several practical advantages over PAD. Minimal preoperative preparation and negligible patient inconvenience makes it suitable for both urgent and elective procedures. Moreover, ANH units are collected and stored at room temperature at the patient's bedside, thus reducing the administrative costs associated with collection, cold storage and testing of PAD units as well as the risk of human error[16].

Precautions should be taken with anesthetized patients undergoing ANH due to concerns regarding dilutional coagulopathy and recurarization from neuromuscular blocking agents in re-infused blood at the end of surgery[33-35]. These concerns are rarely if ever of clinical significance. There has been concern that perioperative anemia is a cause of blindness. To date no data have linked ANH with perioperative blindness. Animal data show an increase in perfusion and oxygenation of the optic nerve during ANH[36].

In summary, data on these issues are clear: ANH does not pose a risk to patients when managed with clinical vigilance.

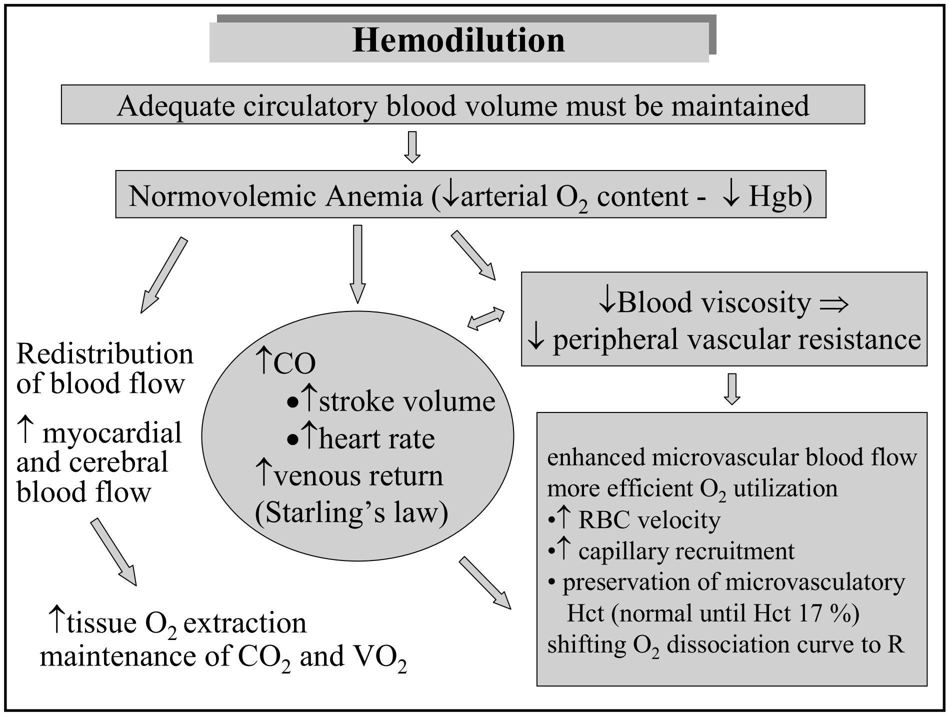

Figure 1: A conceptual model of acute normovolemic hemodilution.

POSTOPERATIVE PERIOD

Methods relevant to the immediate postoperative period include close surveillance for bleeding, adequate oxygenation, restricted phlebotomy for diagnostic tests, postoperative cell salvage, pharmacologic enhancement of hemostasis, avoidance of hypertension, tolerance of normovolemic anemia and meticulous management of anticoagulants and antiplatelet agents.

Tolerance of Anemia

Although hemoglobin level as a transfusion trigger has been drifting downward over the years, reproducible criteria for RBC transfusions are lacking. Historically, an arbitrary hemoglobin level of 10 g/dl has been used as a trigger to transfuse. This practice continues despite recent studies indicating that patients are able to tolerate lower hemoglobin levels than previously believed. A randomized, controlled trial involving 838 normovolemic critically ill patients demonstrated that a restrictive red cell transfusion strategy (hemoglobin level between 7 and 9 g/dl) was as safe as a liberal transfusion strategy (hemoglobin level between 10 and 12 g/dl) in critically ill patients,[5] with the possible but not conclusive exception of patients with ischemic cardiovascular disease.[37]

Table 2. Approximate Contributions of Blood Conservation in the Surgical Patient		
Preoperative Options	**Blood Units**	**Reference**
Tolerance of anemia (reduce transfusion trigger)	1 - 2 units	38
Increase preoperative RBC mass	2 units	40,43
Preoperative autologous donation	1 - 2 units	40
Intraoperative Options		
Meticulous hemostasis and operative technique	1 or more units	24
Acute normovolemic hemodilution	1-2 units	16,32
Blood salvage	1 or more units	26
Postoperative Options		
Restricted phlebotomy	1 unit	11
Blood salvage	1 unit	13

CLINICAL STRATEGIES

Although the alternatives discussed above can be used individually with success, they are most effective when employed together in a blood management strategy that is individualized to a specific patient. For example, a patient scheduled for an elective joint replacement surgery that typically leads to a two-unit red cell transfusion should be assessed several weeks before surgery to look for anemia or iron deficiency. If present, these can be corrected with the use of iron and erythropoietin therapy to increase hematocrit, thereby improving the patient's tolerance to anticipated blood loss. The use of ANH can reduce the number of shed red cells per unit volume, thus decreasing red blood cell volume lost. Shed blood can be collected and reinfused within the first 6 hours after surgery. If the post-operative hemoglobin remains above 8 gm/dL in patients without known cardiovascular risk factors[38], transfusion to a higher level is not indicated.[5,37]

The value of combining alternatives has been proven in a series of 100 consecutive patients who underwent coronary artery bypass grafting without the use of blood. Mortality in this group was 4%, which is comparable to large series of similar patients who received blood[8]. The key to success in this series was the use of multiple alternatives – iron, erythropoietin, cell salvage, ANH, careful surgical technique, lowered transfusion trigger – and commitment of all the treating personnel. Restoration of red cell mass by erythropoietin has been carefully described over the past ten years[39-45]. The early response especially when combined with intravenous iron can aid perisurgical anemia and may avoid allogeneic blood transfusions[46-52].

CONCLUSION

In conclusion, there are a number of safe and cost-effective therapeutic options for the potential management of all patients without allogeneic blood transfusion. Anesthesiologists should consider blood management using these options for all patients[53]. This philosophy will provide patients with safe and effective therapy, will minimize the risks of allogeneic blood and will help preserve our decreasing blood resources. Future developments to expect in the field are summarized below:

- There is a need to develop educational curricula focused on clinical aspects of transfusion practice and the use of transfusion alternatives, i.e. why the dictum "transfuse last" is a "best practice".
- Red-cell and platelet "substitutes," now in various stages of clinical trials, hold out new therapeutic options.

- Wider use of hematopoietic agents, including new products now in clinical trials (e.g., new forms of recombinant erythropoietin, recombinant thrombopoietin), may reduce dependence on allogeneic blood.

Anesthesiologists can be leaders in peri-operative medicine by using "best practices" to provide blood conservation to all critical care patients to significantly and economically improve outcomes.

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