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Blood Conservation in Surgery: Current Concepts and Practice

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Blood conservation is based on the principle of avoiding allogeneic blood transfusion with the aim of improving outcome and protecting patients' rights. Surgical patients receive a significant proportion of the allogeneic blood transfused in the hospital. Blood conservation in surgery greatly reduces overall allogeneic blood use, thereby reducing costs, hazards, and adverse outcomes. Blood conservation techniques aim to lower the ''transfusion trigger,'' optimize the hematocrit, minimize blood loss, and optimize tissue oxygenation. Successful blood conservation involves a combination of techniques tailored to the individual patient. It requires planning and a multidisciplinary team approach but usually little technology. Bloodless medicine and surgery programs represent the gold standard in blood conservation. Blood conservation is evidence based, and it results in faster recovery, lower morbidity, lower mortality, shorter hospital stay, lower cost, and better patient (and physician) satisfaction while avoiding the hazards of allogeneic blood transfusion. Blood conservation is thus the current standard of care.

Key words: Blood conservation – Bloodless surgery – Acute normovolemic hemodilution – Iron therapy – Cell salvage – Transfusion-free surgery

Blood conservation is an emerging field of current medical practice based on the principle of avoiding allogeneic (homologous) blood transfusion by the use of various complementary strategies with the aim of improving outcome and protecting patients' rights.[1,2] Similar terms that were initially used synonymously but are gradually being redefined are *bloodless medicine and surgery* (or *transfusion-free medicine and surgery*), which emphasizes complete avoidance of allogeneic blood in patient care,[2] and *advanced transfusion practices*, in recognition of the fact that transfusion alternatives represent an advancement in the manner in which patients are treated.[3] These constitute a distinct and well-defined area in blood management. However, recently *blood management* itself has become almost synonymous with *transfusion-free medicine and surgery*, being currently defined as ''the philos-

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ophy to improve patient outcomes by integrating all available techniques to reduce or eliminate allogeneic blood transfusions.''[2]

A Brief History of Blood Transfusion

Karl Landsteiner's discovery of the ABO blood groups in 1900 began the modern era of transfusion medicine. In 1915 Richard Lewisohn introduced anticoagulation with sodium citrate. Blood transfusion was used for military casualties in World Wars I and II. Bernard Fantus established the first hospital-based blood bank in Chicago, Illinois around 1937 (2005, www.bloodbook.com). From then on blood transfusion became a universal practice in medicine, so that the popular dictum seemed to be ''When in doubt, transfuse!''

The Age of Blood Conservation

Blood conservation in modern surgery started as ''bloodless surgery,'' an attempt by some dedicated surgeons in the 1960s to accommodate patients who declined blood transfusion, notably Jehovah's Witnesses (Spence, 2000, www.nataonline.com).[4] Their religious belief is based on a distinctive interpretation of specific passages from the Bible, such as ''You are to abstain from…blood'' (Acts 15:29, New English Bible).[5,6] Denton Cooley, widely regarded as the founding father of modern bloodless surgery, performed the first bloodless open-heart surgery on a Jehovah's Witness on May 18, 1962 (Spence, 2000, www.nataonline.com).[4] In 1977, Ott and Cooley[9] published a pioneer report of 542 open-heart surgeries without allogeneic blood transfusion in patients ranging in age from 1 day to 89 years, demonstrating that the ''impossible'' was possible—and safer. Other surgeons joined, but their ingenious techniques did not gain wide acceptance then.[4]

The advent of HIV/AIDS in 1981 forced a reconsideration of blood transfusion practices and prompted a desire for bloodless surgery because of the epidemic proportions of HIV, and the fact that the surest (though not the most common) route of transmission is through blood transfusion. Many other old and new pathogens that are transmitted by blood (Table 1)[8] and many noninfectious hazards (Table 2)[9] received renewed attention and prominence. The cost of making blood ''safe'' rose astronomically while the supply of ''safe'' blood shrank. This added further impetus to the search for transfusion alternatives and the promotion of blood conservation techniques.[1,4]

Table 1 Infectious agents transmissible by blood transfusion[8]

Viruses
Hepatitis viruses
Hepatitis A virus
Hepatitis B virus
Hepatitis C virus
Hepatitis D virus (requires co-infection with Hepatitis B virus)
Hepatitis E virus
Retroviruses
Human immunodeficiency virus 1 and 2 (and other sub-types)
Human T-cell leukemia virus I and II
Herpes viruses
Human cytomegalovirus
Epstein-Barr virus
Human herpes virus 8
Parvoviruses
Parvovirus B19
Miscellaneous viruses
GBV-C (previously referred to as hepatitis G virus)
Transfusion transmitted virus (TTV)
West Nile virus
Bacteria
Endogenous
Treponema pallidum (syphilis)
Borrelia burgdorferi (Lyme disease)
Brucella melitensis (brucellosis)
Yersinia enterocolitica
Salmonella spp
Exogenous (environmental species and skin commensals)
Staphylococcal spp
Pseudomonas
Serratia spp
Rickettsiae
Rickettsia rickettsii (Rocky Mountain spotted fever)
Coxiella burnettii (Q fever)
Protozoa
Plasmodium spp (malaria)
Trypanosoma cruzi (Chagas disease)
Toxoplasma gondii (toxoplasmosis)
Babesia microti/divergens (babesiosis)
Leishmania spp (leishmaniasis)
Prions
Variant Creutzfeldt–Jakob disease

Recently, however, the focus has shifted from the hazards of allogeneic blood to its efficacy—or lack thereof. The Canadian Critical Care Trials Group study on transfusion requirements in critical care by Hérbert and co-workers[10] in 1999 was a landmark prospective randomized study of 838 intensive care unit patients comparing a liberal transfusion policy versus a restricted one. The study revealed better results with the restricted transfusion group: lower intensive care unit mortality, lower hospital mortal-

Table 2 Noninfectious serious hazards of transfusion[9]

Immune-mediated
Hemolytic transfusion reactions
Febrile nonhemolytic transfusion reactions
Allergic/urticarial/anaphylactic transfusion reactions
Transfusion-related acute lung injury
Posttransfusion purpura
Transfusion-associated graft versus host disease
Microchimerism
Transfusion-related immunomodulation
Alloimmunization
Nonimmune-mediated
Septic transfusion reactions
Nonimmune hemolysis
Mistransfusion
Transfusion-associated circulatory overload
Metabolic derangements
Coagulopathic complications from massive transfusion
Complications from red cell storage lesions
Overtransfusion/undertransfusion
Iron overload

ity, lower 30-day mortality, and a trend toward decreased organ failure. Several other studies[11–16] have confirmed adverse outcomes unrelated to infectious hazards in transfused patients. Allogeneic blood has been found to increase hemorrhage, impair perfusion of microcirculation, impair oxygen release from hemoglobin, and *worsen* rather than improve tissue oxygenation.[17–21] Some of these effects are thought to be due to storage lesions. On the other hand, it has not been possible to demonstrate the benefits of red blood cell (RBC) transfusion.[11,21–23]

Thus, while blood conservation started as an advocacy and then became widespread because of the infectious hazards and high cost/scarcity of allogeneic blood, evidence-based medicine has recently emerged as the driving force behind current practice in blood conservation, with improvement of outcome as the major aim.

Techniques in Blood Conservation

Blood conservation techniques may be grouped under 4 basic categories, or ''pillars'': (1) lowering the transfusion trigger, (2) optimizing the hematocrit, (3) minimizing blood loss, and (4) optimizing tissue oxygenation. The first 3 are widely recognized,[22] while the last can be deduced as a separate and indispensable element[4] and should therefore be added for completeness in this author's view. Virtually all techniques of blood conservation are meant to buttress one or another of these pillars, and when used in combination they effectively reduce or eliminate the use of allogeneic blood and improve clinical outcome (Table 3).

Table 3 Approximate contributions of selected modalities to blood conservation in the surgical patient (adapted from Goodnough et al[1]*)*

Modality	No. units of blood conserved
Preoperative	
Tolerance of anemia (lowering the transfusion trigger)	1–2
Increasing preoperative red blood cell mass	2
Intraoperative	
Meticulous hemostasis and operative technique	1 or more
Acute normovolemic hemodilution	1–2
Blood salvage	1 or more
Postoperative	
Restricted phlebotomy	1
Blood salvage	1

Surgical patients receive approximately 40% of the transfused allogeneic blood in the United Kingdom (2008, http://www.aagbi.org/) and comparably high figures may be expected everywhere else. Therefore blood conservation in surgery significantly reduces the overall allogeneic blood use in any health care setting, thereby reducing costs, hazards, and adverse outcomes from blood transfusion.

Lowering the transfusion trigger

Lowering the ''transfusion trigger'' means accepting lower hemoglobin/hematocrit levels for treatment without blood transfusion. The ''10/30'' (hemoglobin/hematocrit) transfusion trigger employed for decades to dictate blood transfusion practices was based on a study in dogs by Adams and Lundy in 1942 and has been demonstrated to be invalid in humans. Lowering the transfusion trigger from 10 g/dL to 7 g/dL in critically ill patients in intensive care reduced red cell unit transfusions by 54% and improved clinical outcomes.[4,10]

The Association of Anaesthetists of Great Britain and Ireland affirms that ''a haemoglobin concentration of 8–10 $g.dL^{-1}$ is a safe level even for those patients with significant cardiorespiratory disease'' (2008, http://www.aagbi.org/). The current guidelines of the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists[24] suggests a transfusion trigger of hemoglobin less than 7 g/dL. However, patients have survived with hemoglobin below 3 g/dL, and so currently there is no universal trans-

fusion trigger (Spence, 2004, www.orthosupersite.com).

Optimizing the hematocrit

Optimizing the hematocrit increases the tolerable blood loss or the margin of safety in the event of blood loss. Iron therapy is at the center of current efforts in this regard, with or without erythropoiesis-stimulating agents (ESAs), even in the absence of absolute iron deficiency[4,25]:

a. Oral iron therapy is the modality of choice for eligible patients. Ferrous sulfate, gluconate, or fumarate may be used to administer ideally 200–220 mg of elemental iron per day. Adjuncts to be given daily include vitamin C, 500 mg; vitamin B_{12}, 150 μg; folic acid, 5 mg; multivitamins; and nutritional support.[2,25] The author avoids folic acid in malignant disease.[26]
b. Parenteral iron therapy corrects anemia more rapidly and may be used alone or in conjunction with ESAs. Iron dextran is the classical preparation, but less allergenic preparations are favored when available, such as iron sucrose (preferred) and iron gluconate.[25] Dose in mg can be weight × [normal *Hb* − actual *Hb*] × 0.24 + 500 (where *Hb* = hemoglobin concentration in g/L),[25] or [normal *Hb* − actual *Hb*] × 200 + 500 (where *Hb* is in g/dL).[2]

   Iron dextran is diluted in normal saline at a ratio of 5 mL (250 mg):100 mL saline and administered intravenously initially at 20 drops/min for 5 minutes, then 60 drops/min if no side effects occur. The total dose may be given at once to a maximum of 20 mg/kg body weight over 4–6 hours or in divided doses on alternate days (preferably).[2,25] The author found that administering 100 mg hydrocortisone intravenous (*i.v.*) 15 minutes before iron dextran and diluting 5 mL (250mg) of iron dextran in 250–500 mL of normal saline successfully averts allergic reactions, even in a patient who previously reacted when those measures were not taken.[26]
c. Erythropoietin alfa, which has been in use for blood conservation in oncology since 1989, was approved for perisurgical use in the United States in 1996. Beta preparations are also available. In general surgery 100–150 U/kg subcutaneous (*s.c.*) for 6 doses (*e.g.*, twice weekly for 3 weeks) is recommended.[2] In oncology 150 U/kg *s.c.* 3 times weekly or 40,000 U *s.c.* weekly is the recommended starting dose.[27] Darbopoietin alfa is a long-acting ESA that can be administered *s.c.* weekly (2.25 μg/kg) or every 3 weeks (500 μg). Intravenous iron is recommended in conjunction with ESAs as it potentiates the response and averts functional iron deficiency.[2,28]

   ESAs stimulate RBC production by up to 4 times the basal marrow rate. Reticulocyte count increases by day 3, and hemoglobin typically increases at 1 g/dL every 4–7 days.[28] Use of ESAs is not recommended when the hemoglobin is above 12 g/dL in oncology.[27]

Optimizing the hemoglobin with the appropriate medication is indicated in virtually all surgical patients, in elective and emergency cases, and for treatment and prophylaxis of anemia.[2] Interventions in this regard do not start working slowly after 21 days, as some may imagine; they start working immediately and build up over time.[25,28] Provided the main pathology is properly treated, the patient's improvement with bloodless care is sometimes dramatic, compared with patients who are transfused.

Minimizing blood loss

Efforts towards minimizing blood loss in the surgical patient start from the first contact and span through the entire perioperative period.

a. Good history, physical examination, and laboratory investigations are essential even in emergencies, taking note of the following among others:
   i. History of bleeding disorders
   ii. Anticoagulant therapy
   iii. Site of external hemorrhage (to be promptly arrested)
   iv. Estimate of blood loss
   v. Full blood count
   vi. Clotting profile (if indicated)

b. Pharmacological agents that can reduce hemorrhage include the following[2]:
   i. Vitamin K, 10 mg (2.5–50 mg) per os (*p.o.*), intramuscular (*i.m.*), *s.c.*, *i.v.*
   ii. Tranexamic acid, between 1.5 g 3 times per day and 1 g 6 times per day for 5–7 days, first *i.v.* then *p.o.* (for prophylaxis, 1 g *p.o.* preoperative).
   iii. Aprotinin, 500,000 KIU *i.v.*, then 150,000 KIU/h in infusion (low-dose regimen for non-cardiac surgery); or 2,000,000 KIU *i.v.*, then 2,000,000 KIU in cardiopulmonary bypass (CPB) prime, then 500,000 KIU in infusion for duration of surgery (Hammersmith high-dose regimen for cardiac surgery).

iv. Epsilon aminocaproic acid, 0.1 g/kg *i.v.* over 30–60 minutes, then 8–24 g/d or 1 g every 4 hours. When bleeding stops, 1 g every 6 hours. The same dosage can be given *p.o.*
v. Desmopressin (1-deamino-8-D-arginine vasopressin or DDAVP), 0.3 μg/kg *i.v.* or *s.c.*, 2 times perioperative, second dose 6–8 hours after the first; or 2 intranasal ''standard puffs'' totaling 300 μg for home use (*e.g.*, menorrhagia), repeated as necessary after 8–12 hours.
vi. Recombinant factor VIIa, 90 μg/kg *i.v.*; repeat dose every 2–3 hours or as needed.
vii. Somatostatin
viii. Vasopressin

c. Noninvasive monitoring such as pulse oximetry, whenever possible, minimizes blood loss.

d. Restriction of diagnostic phlebotomies reduces blood wastage. Microsampling is a recent technique that drastically reduces the volume of blood needed for tests, with obvious benefit in blood conservation.

e. Intraoperative strategies that could be employed to reduce blood loss include the following:
i. Normothermia averts coagulopathy due to hypothermia[1,2,29] and may be achieved by (1) maintaining room temperature above 27°C, (2) using thermal suits or blankets, and (3) warming intravenous infusions.
ii. Acute normovolemic hemodilution involves withdrawal of some of the patient's blood in theatre prior to incision and replacement with colloids and/or crystalloids, so that intraoperatively the patient loses dilute blood with less effect on the total red cell mass. The withdrawn blood is kept within view in theater and is reinfused at the end of surgery.

Up to 4 units may be withdrawn safely using the formula V = [Baseline HCT − Target HCT] / Average $HCT \times EBV$, where V = volume, HCT = hematocrit, and EBV = estimated blood volume (Loubser, 2009, http://wiki.noblood.org/Acute_Normovolemic_Hemodilution).
iii. Regional anesthesia results in less intraoperative blood loss than general anesthesia through mechanisms not yet fully elucidated.[2]
iv. Positioning of patients to minimize blood loss is guided by two principles[2]: (1) elevate the operation site above the right atrium (*e.g.*, Trendelenburg for prostatectomy, reverse Trendelenburg for thyroidectomy), and (2) avoid compression of venous drainage (*e.g.*, tilting patient in supine position slightly to the left to avoid compression of inferior vena cava in abdominal surgery).
v. Meticulous hemostasis and good operative technique can save up to 1 or more units of blood.[1] Use of diathermy and topical adhesives like fibrin glue and Surgicel (Johnson & Johnson, Somerville, New Jersey) limits blood loss, as does judicious use of tourniquet. Argon beam coagulator and Cavitron Ultrasonic Surgical Aspirator are blood-conserving innovations in hemostasis and dissection, respectively.[1,2,30]
vi. Cell salvage and autotransfusion can be performed effectively by techniques ranging from simple manual scooping of blood from a wound, filtration, and then reinfusion, to use of sophisticated computerized cell salvage machines that return washed blood into the patient.
vii. Other techniques like controlled hypotension and hypothermia may be used cautiously in selected patients.[2,4]

Optimizing tissue oxygenation

Allogeneic blood transfusion has been shown not to improve tissue oxygenation.[19–21] However, tissue oxygenation can be improved by other methods that avoid blood transfusion by considering the equation for oxygen delivery[31]:
$DO_2 = CO \times CaO_2 = CO \times \{(Hb \times SaO_2 \times 1.39) + (PaO_2 \times 0.003)\}$, where DO_2 = oxygen delivery, CO = cardiac output, CaO_2 = arterial O_2 content, Hb = hemoglobin concentration, SaO_2 = fraction of hemoglobin saturated with O_2, and PaO_2 = partial pressure of O_2 dissolved in arterial blood). Thus, even when Hb is low, DO_2 can be improved by improving the CO and CaO_2 (SaO_2 and PaO_2).

a. Volume replacement with crystalloids (*e.g.*, normal saline and Ringer's lactate) or colloids (*e.g.*, Hetastarch, Hemacel, Dextran, and Isoplasma) reduces blood viscosity and improves cardiac output. The crystalloid requirement is 3 times blood volume lost, while colloid requirement is equivalent volume lost.

b. Oxygen therapy increases SaO_2 and PaO_2. Intraoperative hyperoxic ventilation not only improves tissue oxygenation but also can augment acute normovolemic hemodilution and avert allogeneic blood transfusion.[2,4] Hyperbaric oxygen is rarely needed but may be used when indicated and available.[2,4]

c. Minimizing oxygen consumption may be achieved through appropriate interventions, such as adequate analgesia, treatment of sepsis, and mechanical ventilation (to reduce the work of breathing).
d. Causes of tissue hypoxia should be treated promptly (*e.g.*, pneumonia and bronchial asthma).
e. Inotropic and vasoactive agents may be used in extreme cases to improve cardiac output.
f. Artificial oxygen carriers are still largely experimental. They include Perfluorocarbon emulsions and modified hemoglobin-based solutions. They have been used successfully in augmented acute normovolemic hemodilution.[2,4]

Blood Conservation Programs

Blood conservation programs are specialized programs offering nonblood treatment by a committed multidisciplinary staff to a wide variety of registered patients within a hospital setting. There are up to 240 such programs worldwide (2010, www.mybloodsite.com). Depending on the emphasis, institutions have adopted various names for their programs, such as Bloodless Medicine and Surgery Program or Blood Management Program. These programs provide the standard of care for patients without the use of allogeneic blood products. They invariably record superior results.[4]

Conclusion

Blood conservation is not one technique but a combination of techniques tailored to the needs and physiological status of the individual patient in order to avoid transfusion of allogeneic blood. It requires planning and a multidisciplinary team approach, but usually little technology, to achieve the best results. Setting up a blood conservation program (or blood management program) with written protocols standardizes the practice of bloodless medicine and surgery, thus ensuring that patients receive the best care.

Blood conservation is evidence based.[22] It results in faster recovery, lower morbidity, lower mortality, shorter hospital stay, lower cost, and better patient (and physician) satisfaction.[1,4] Furthermore, patient autonomy is respected and the hazards of allogeneic blood transfusion are avoided, in accordance with the principles of nonmaleficence and beneficence in the Hippocratic oath (Spence, 2004, www.orthosupersite.org).[22,32] Understandably then, blood conservation is no longer an ''alternative'' but the current standard of care.[2] Blood conservation may also be considered a crucial step in the journey toward universal ethical, scientific, and evidence-based practice of surgery.

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