

## Patient Blood Management

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**B**LOOD management has been defined as “the appropriate use of blood and blood components, with a goal of minimizing their use.”‡ This goal has been motivated historically by (1) known blood risks; (2) unknown blood risks; (3) preservation of the national blood inventory; and (4) constraints from escalating costs.<sup>1</sup> Known risks of blood include transmissible infectious disease, transfusion reactions, and potential effects of immunomodulation (*e.g.*, postoperative infection or tumor progression). Unknown risks include emerging pathogens transmissible by blood (*e.g.*, new variant Creutzfeldt-Jakob disease and West Nile virus).<sup>2–4</sup> In addition, several studies have linked allogeneic blood transfusions with occurrence of unfavorable outcomes including increased risk of mortality and various morbidities.<sup>5–7</sup> For example, studies have

indicated that the risk of postoperative infections such as sepsis are as much as two to four times higher in transfused patients compared with untransfused cohorts.<sup>8–9</sup> Taken together, these lines of evidence support the implementation of blood management as a means to improve the clinical outcomes of the patients. Blood management was cited recently as 1 of the 10 key advances in transfusion medicine over the past 50 yr.<sup>10</sup>

Patient-focused blood management<sup>11</sup> is described in the Circular of Information§ as “a professional judgment based on clinical evaluation that determines the selection of components, dosage, rate of administration....” Patient blood management therefore encompasses an evidence-based medical and surgical approach that is multidisciplinary (transfusion medicine specialists, surgeons, anesthesiologists, and critical care specialists) and multi-professional (physicians, nurses, pump technologists and pharmacists). Preventive strategies are emphasized to identify, evaluate, and manage anemia<sup>12–14</sup> (*e.g.*, pharmacologic therapy<sup>15</sup> and reduced iatrogenic blood losses from diagnostic testing)<sup>16</sup>; to optimize hemostasis (*e.g.*, pharmacologic therapy<sup>17</sup> and point of care testing<sup>18</sup>); and to establish decision thresholds (*e.g.*, guidelines) for the appropriate administration of blood therapy.<sup>5,19</sup>

Patient blood management has recently been recognized by the World Health Organization (World Health Alliance Resolution A63.R12) as a means to “promote the availability of transfusion alternatives.”|| To achieve these goals, health care institutions and accreditation and regulatory agencies have focused on blood utilization to improve clinical outcomes and patient safety. In the United States, The Joint Commission developed Patient Blood Management Performance Measures and submitted these to the National Quality Forum for endorsement. The National Quality Forum did not endorse these submitted Performance Measures, citing lack of data on the outcomes proposed; as a result, they currently do not carry consequences if not met. Because these Performance Measures were process-based rather than outcomes-based, data on proposed outcomes are difficult to retrieve. The Joint Commission has placed these Performance Measures in their Topic Library where they are to be used as additional patient safety activities and/or quality improvement projects by provider institutions as accreditation

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‡ Society for the Advancement of Blood Management (SABM). Available at <http://www.sabm.org/>. Accessed February 22, 2011.

§ Circular of Information for the Use of Human Blood and Blood Components, 2009, p. 9. Available at <http://www.fda.gov/Biologics/BloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Blood/ucm074940.htm>. Accessed February 10, 2011.

|| World Health Organization (WHO) 63rd World Health Assembly. Availability, safety and quality of blood products. Available at [http://apps.who.int/gb/ebwha/pdf\\_files/WHA63/A63\\_R12-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA63/A63_R12-en.pdf). Accessed January 19, 2012.

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**Table 1.** Patient Blood Management

| TJC* Performance Measures  | Principles   |
|--|--|
| 1. Preoperative anemia screening   | A. Formulate a plan of proactive management for avoiding and controlling blood loss tailored to the clinical management of individual patients, including anticipated procedures |
| 2. Preoperative blood type and antibody screen (blood compatibility testing) | B. Employ a multidisciplinary treatment approach to blood management using a combination of interventions (e.g., pharmacologic, therapy, point of care testing)                  |
| 3. Transfusion consent   | C. Promptly investigate and treat anemia   |
| 4. Blood administration  | D. Exercising clinical judgment, be prepared to modify routine practices (e.g., transfusion triggers) when appropriate   |
| 5. RBC transfusion indication  | E. Restrict blood drawing for unnecessary laboratory tests   |
| 6. Plasma transfusion indication   | F. Decrease or avoid the perioperative use of anticoagulants and antiplatelet agents   |
| 7. Platelet transfusion indication   |  |

\* The Joint Commission.

goals.<sup>#</sup> The principles of these performance indicators are summarized in table 1. We review recent advances in patient blood management to identify for physicians and healthcare institutions opportunities for process improvement blood utilization and patient safety.

## Anemia Management

Guidelines for detection, evaluation, and management of anemia in elective surgery patients have been published (fig. 1).<sup>12,13</sup> Predictors of blood transfusion for patients have long been identified, with the most important being the preoperative circulating erythrocyte mass,<sup>20</sup> as estimated by the patient's hemoglobin concentration. In addition to being a risk factor for blood transfusions, preoperative anemia is also an independent predictor of morbidity and mortality postoperatively.<sup>21–24</sup> Evaluation of anemia\*\* should begin with an initial assessment of iron-restricted erythropoiesis, which can occur in either the presence or absence of inflammation. Absorption of oral iron is inhibited in the presence of hepcidin due to inflammation, whereas chronic blood loss (e.g., menses) is an important cause of iron deficiency in the absence of inflammation.<sup>25,26</sup> Iron-restricted erythropoiesis can cause anemia due to an absolute deficiency of storage iron, an iron sequestration syndrome due to inflammation, or a functional iron deficiency due to erythropoietin-stimulated erythropoiesis.<sup>27</sup> The evaluation of unexpected anemia must in addition consider unexpected diagnoses including

chronic kidney disease or occult malignancy. To facilitate this, screening and detection of anemia should occur as far as possible in advance (up to 30 days) of an electively scheduled surgery.<sup>13,28</sup> This requires close collaboration among the patients' primary care physicians, surgeons, anesthesiologists, and the medical directors of the institution's preadmission testing program.

## Blood Availability and Compatibility Testing

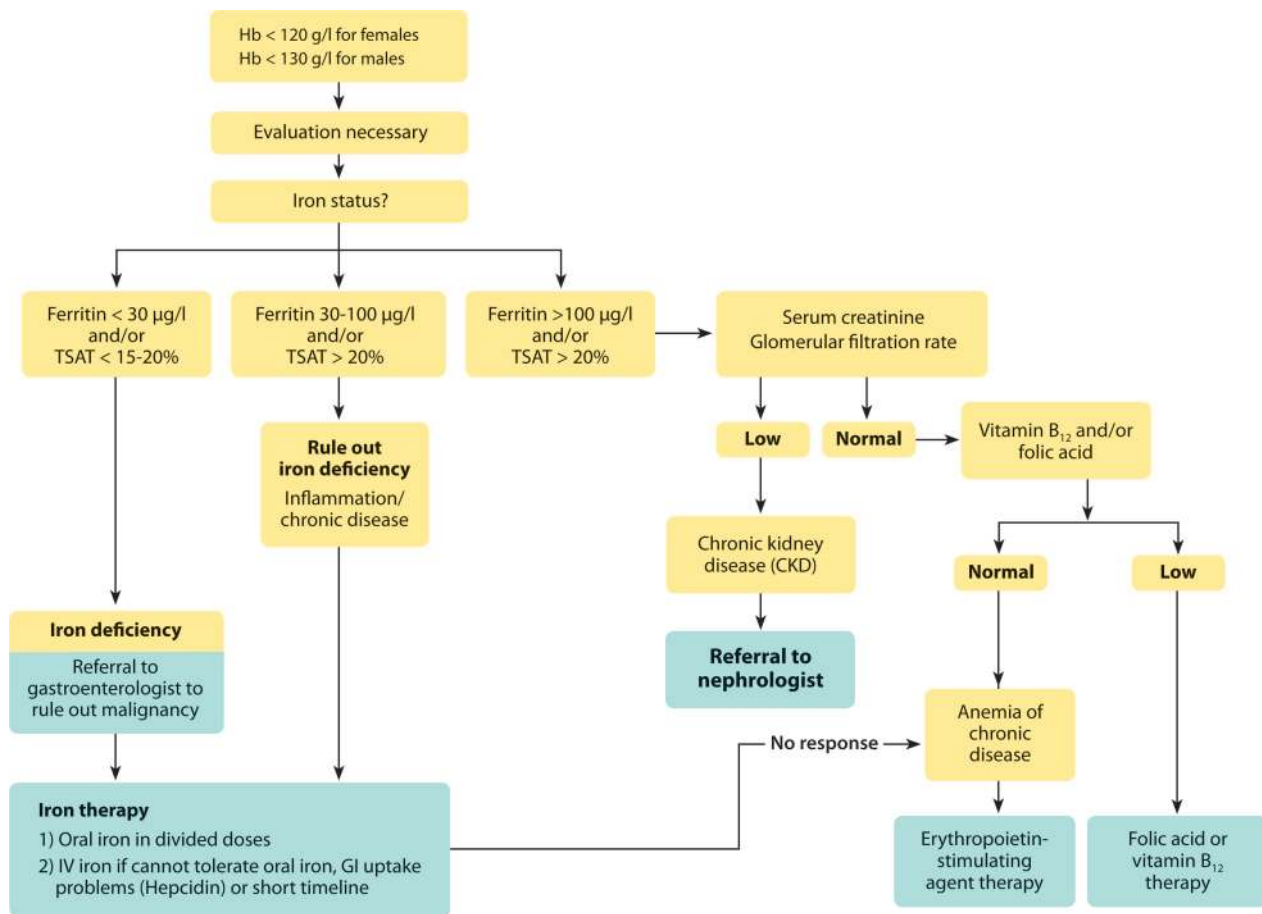
Successful completion of diagnostic testing pretransfusion (blood type/screen crossmatch) must overcome barriers associated with changes in practices for patients undergoing elective surgeries and for the availability of cross-matched blood. A College of American Pathology survey found that 35% of approximately 9,000 patients had type/screen specimens collected only on day of surgery; one-fourth of these tests were not completed (and cross-matched blood was not available) until after surgery had begun.<sup>29</sup> To address these barriers, we implemented a number of steps for process improvement at one of our own institutions<sup>30</sup>:

- An operating room policy was implemented: "All patients with a potential need for blood transfusion will have a type and screen/crossmatch; if the results are positive for antibodies, a completed type and crossmatch is required before the patient can proceed into the operating room."
- A surgical safety checklist†† was implemented that included confirmation that requested blood was available before commencement of anesthesia/surgery.
- The elective surgery schedule was reviewed by the transfusion service each night before surgery. A patient log, for a patient for whom no diagnostic specimens had been received by the Transfusion Service, was faxed to the operating room at 5:00 AM each morning of surgery.
- An extended specimen policy was implemented by the institution, allowing for antibody screen results to be valid for up to 30 days. To ensure compliance with American Association of Blood Banks (AABB) Standards,<sup>31</sup> verification that patients had not been pregnant or transfused within the previous

# Implementation Guide for the Joint Commission Patient Blood Management Performance Measures 2011. Available at [http://www.jointcommission.org/assets/1/6/PBM\\_Implementation\\_Guide\\_20110624.pdf](http://www.jointcommission.org/assets/1/6/PBM_Implementation_Guide_20110624.pdf). Accessed January 19, 2012.

\*\* Iron deficiency anaemia: assessment, prevention, and control. A guide for programme managers. Geneva, World Health Organization, 2001 (WHO/NHD/01.3). Available at [http://whqlibdoc.who.int/publications/2008/9789241596657\\_eng.pdf](http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf). Accessed January 19, 2012.

†† World Health Organization (WHO). World Health Alliance for Patient Safety progress report 2006–2007. Available at [http://www.who.int/patientsafety/information\\_centre/documents/progress\\_report\\_2006\\_2007.pdf](http://www.who.int/patientsafety/information_centre/documents/progress_report_2006_2007.pdf). Accessed January 19, 2012.



**Fig. 1.** Algorithm for the detection, evaluation, and management of preoperative anemia. SF = serum ferritin; TSAT = transferrin saturation. Modified, with permission, from Goodnough LT. *Br J Anaesth* 2011;106:13–22.

3 months (to avoid the possibility that a new alloantibody to erythrocytes could appear) was documented at time of laboratory draw, and confirmed again on day of surgery.

After implementation, the incidence of patients undergoing surgery before availability of cross-matched blood was reduced from 1:133 to 1:328. A compliance rate of 100% for the surgical checklist is necessary to achieve our goal in which no patient undergoes elective surgery without cross-matched blood available.

### Blood Administration and Documentation

Documentation of transfusion events including informed consent are the Performance Measures specified by The Joint Commission:

- Patient identification and transfusion order (blood identification number) must be confirmed before the initiation of blood
- Date and time of transfusion
- Blood pressure, pulse, and temperature recorded before, during, and after transfusion

In addition, The Joint Commission Performance Measures specify that appropriate pretransfusion laboratory testing

(e.g., hemoglobin, prothrombin time/international normalized ratio (INR), and platelet count) be documented along with the clinical indications (see next paragraphs) for transfusion of blood components. Adherence to such requirements should be monitored by the hospital's quality department or transfusion committee.

The elements of transfusion consent comprise a discussion of blood transfusion risks (table 2)<sup>2,3</sup> and benefits; alternatives to blood; an opportunity to ask questions; and patient consent.<sup>32</sup> Current estimates of risk of blood transmission for some known viruses are: 1:280,000 to 1:357,000 for hepatitis B; 1:1,149,000 for hepatitis C; and 1:1,467,000 for human immunodeficiency virus (HIV).<sup>32,33</sup> Consent should occur as far in advance of transfusion as possible, so that alternatives to allogeneic blood such as autologous blood can be made available. As an example, California Health and Safety Code Section 1645 (Paul Gann Blood Safety Act) mandates that alternatives to allogeneic blood are made available for patients and “applies whenever there is a reasonable possibility that a blood transfusion may be necessary as a result of a medical or surgical procedure.” It should also be noted that blood transfusion has been legislated to be a medical ser-

**Table 2.** Potential Risks of Blood Transfusion

|   |
|---|
| I. Infectious Agents  |
| Transfusion-transmitted disease for which donors are tested*  |
| Hepatitis B virus (HBV; 1970 [surface antigen]; 1986–1987 [core antibody]; 2009 [nucleic acid])     |
| Human immunodeficiency virus (HIV; 1985 [antibody]; 2000 [nucleic acid])                            |
| Hepatitis C virus (HCV; 1986–1987 [alanine aminotransferase]; 1990 [antibody]; 1999 [nucleic acid]) |
| Human T-cell lymphotropic virus (HTLV; 1988 [antibody])   |
| West Nile virus (WNV; 2003 [nucleic acid])  |
| Bacteria (in platelets only; 2004)  |
| Trypanosomacruzi (2007 [antibody])  |
| Cytomegalovirus (CMV)   |
| Syphilis  |
| Transfusion-transmitted disease for which donors are not routinely tested                           |
| Hepatitis A virus (HAV)   |
| Parvovirus B19  |
| Dengue fever virus (DFV)  |
| Malaria   |
| Babesia sp  |
| Plasmodium sp   |
| Leishmania sp   |
| Brucella sp   |
| New variant Creutzfeldt-Jakob disease (nvCJD) prions  |
| Unknown pathogens   |
| II. Transfusion reactions   |
| III. Medical errors: (e.g., patient misidentification and ABO mismatch)                             |
| IV. Transfusion associated acute lung injury (TRALI)  |
| V. Volume overload  |
| VI. Iron overload   |
| VII. Immunomodulation   |

\* The target of the screening assay (antibody, microbial antigen, or microbial nucleic acid) and the year of assay implementation are indicated in parentheses.

Modified from Vamvakas *et al.* Blood 2009;113:3406–17.<sup>2</sup>

vice not subject to commerce and trade laws, thus excluding the principle of implied warranty and granting blood banks immunity from strict product liability.<sup>34</sup>

## Alternatives to Allogeneic Blood

When feasible, the patient's own (autologous) blood can serve to reduce or eliminate the need for allogeneic blood. In preoperative autologous donation, the patients donate their own blood over a period of a few weeks preceding the elective procedure.<sup>35</sup> In acute normovolemic hemodilution, the donation takes place in the operating room before the surgery and reinfusion occurs before the patient leaves the operating room. In cell salvage, the reinfusion occurs during or after the surgery as patients' blood is collected and reinfused.

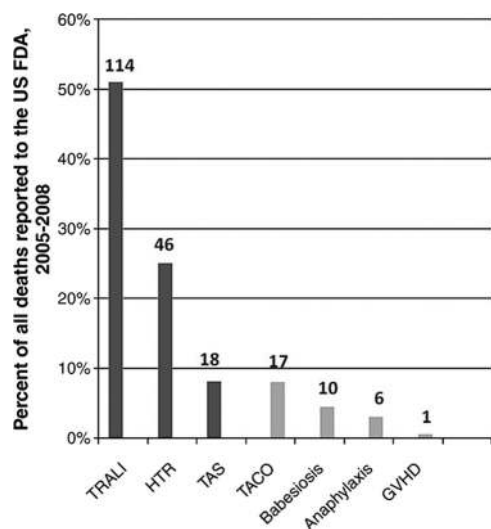
Preoperative autologous donation has some limitations.<sup>15</sup> As with allogeneic blood units, autologous blood is suscep-

ble to acquired storage lesions, such as depletion of 2,3-diphosphoglycerate and impaired ability for erythrocytes to unload oxygen to tissues. Many predonated blood units may be wasted rather than transfused. In addition, preoperative autologous donation induces anemia preoperatively, with an attendant increased subsequent likelihood of blood transfusion with the associated risks, including errors in blood administration. Thus, preoperative autologous donation is generally not cost-effective but may be of value in selected patient populations, such as in patients previously alloimmunized with erythrocyte antibodies.<sup>36</sup>

Acute normovolemic hemodilution causes blood losses during surgery to be diluted, thus reducing actual total blood losses. Acute normovolemic hemodilution offers several advantages compared with preoperative autologous donation, including avoidance of blood storage lesions; no risk of blood labeling or patient identification errors; and adaptability for patients undergoing nonelective procedures.<sup>37</sup> However, evidence on efficacy of acute normovolemic hemodilution is mixed.<sup>38–40</sup> Reasons for low acceptance include lack of standardized protocols, variations in the target hemoglobin, types of fluids used, heterogeneity in surgical blood losses by procedure, and patient selection criteria. Acute normovolemic hemodilution is most effective in procedures associated with large blood loss. Publications addressing the efficacy of acute normovolemic hemodilution have used mathematical modeling that does not take into account individual patient vascular and hemostatic compensation. Because some large blood loss surgical procedures may not result in significant blood loss, benefit of acute normovolemic hemodilution may not be realized. Regardless, the risk of monitored acute normovolemic hemodilution is extremely low and this rare loss of benefit still favors acute normovolemic hemodilution.<sup>41</sup>

Autologous blood cell salvage and reinfusion has been demonstrated to be safe and effective in reducing allogeneic blood transfusions in a variety of patient populations.<sup>42,43</sup> The procedure requires the collected shed blood to be washed, resulting in loss of platelets and plasma, which could potentially cause dilutional coagulopathy or thrombocytopenia with large blood volumes processed. However, reinfusion of the yielded autologous blood is still preferred rather than allowing the shed blood to be completely wasted, or using allogeneic blood that is also devoid of platelets and plasma and carries the same if not more risks at large volumes. The use of cell salvage in situations such as cancer and obstetric and bowel (contaminated) surgeries with introduction of unwanted materials into the circulation has been considered a relative contraindication for cell salvage<sup>44</sup>; nevertheless, this technique has been used successfully in these circumstances.<sup>45</sup> AABB has Standards for Perioperative Autologous Blood Collection and Administration<sup>46</sup> to provide guidance on quality management for facilities who seek accreditation for these activities.





**Fig. 2.** Percent of all transfusion-attributed deaths reported to the U.S. Food and Drug Administration (FDA), 2005–2008. The three leading causes of allogeneic blood transfusion (ABT)-related deaths, along with all other causes of ABT-related deaths reported to the US FDA for the last 4 yr (2005–2008). The figure shows the proportion of all deaths reported to the US FDA in 2005 to 2008 that was attributed to each cause of transfusion-related mortality. The actual number of deaths from each cause is shown above the corresponding column. GVHD = graft-versus-host disease; HTR = hemolytic transfusion reaction; TACO = transfusion-associated circulatory overload; TAS = transfusion-associated sepsis; TRALI = transfusion-related acute lung injury. Reproduced, with permission, from Vamvakas EC. *Transfus Med Rev* 2010;24:77–124.

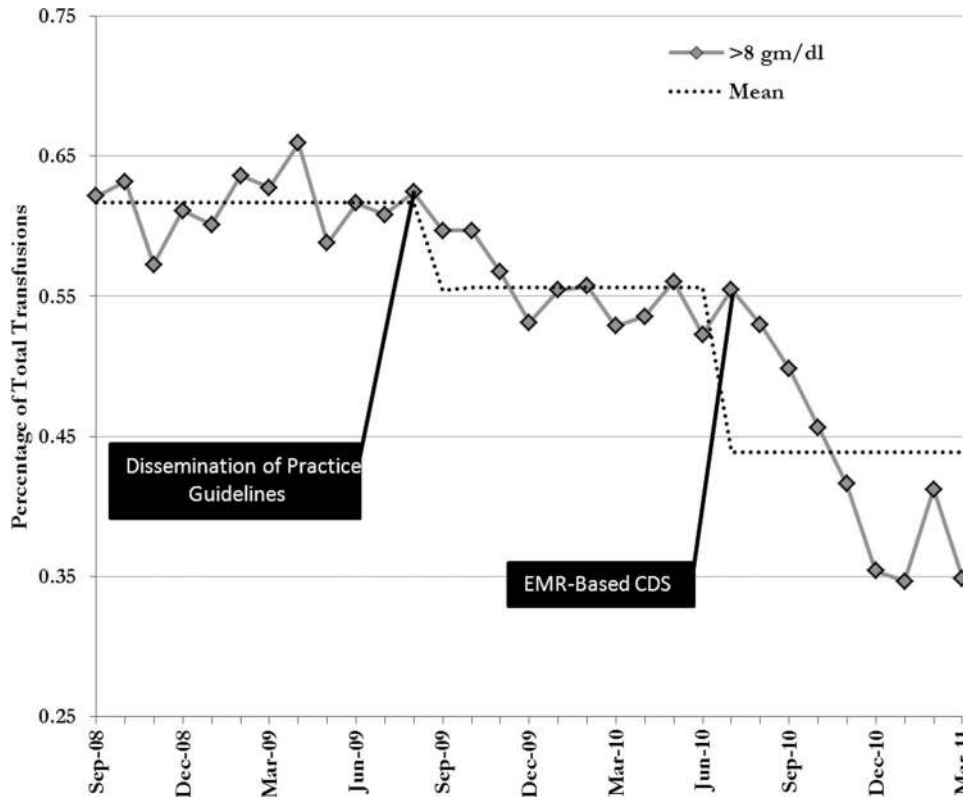
### Indications for Blood Transfusion

Of the estimated 39 million discharges in the United States in 2004, 5.8% (2.3 million) were associated with blood transfusion.<sup>47</sup> Blood transfusion occurred in more than 10% of all hospital stays that included a procedure and was the most frequently performed procedure in 2009. The rate of blood transfusion more than doubled from 1997 to 2009.<sup>‡‡</sup> Increased provider awareness of the costs associated with blood transfusion<sup>4</sup> and recognition of the potential negative outcomes have stimulated multidisciplinary, multiprofessional, and institution-based approaches to patient blood management. For the 4-yr period 2005–2008, 212 fatalities reported to the Food and Drug Administration<sup>48</sup> were deemed to be transfusion related (fig. 2); the leading causes of death were transfusion-related acute lung injury ( $n = 114$ ), hemolytic transfusion reactions ( $n = 46$ ), transfusion-associated sepsis ( $n = 18$ ), transfusion-associated cardiac overload ( $n = 17$ ), and babesiosis ( $n = 10$ ). As discussed previously, a greater number of patients could have potentially had worse clinical outcomes (increased morbidity and mortality) associated with unnecessary transfusions in the same period.

‡‡ AHRQ HCUP 2009 report. Available at [http://www.hcup-us.ahrq.gov/reports/factsandfigures/2009/section3\\_TOC.jsp](http://www.hcup-us.ahrq.gov/reports/factsandfigures/2009/section3_TOC.jsp). Accessed January 19, 2012.

Guidelines for blood transfusion attest to the inadequacy of discrete hemoglobin concentrations as ‘triggers’ for transfusion, and in addition to recommending transfusion of one blood unit each treatment event, they also acknowledge the necessity of considering other more physiologic criteria.<sup>49</sup> It is generally agreed that transfusion is not of benefit when hemoglobin concentrations are greater than 10 g/dl, and are beneficial when hemoglobin concentrations are less than 6 g/dl.<sup>50,51</sup> The variability in transfusion outcomes in patients undergoing cardiothoracic surgery continues to persist even after adjusting for patient- and institution-related factors.<sup>52,53</sup> Moreover, prospective randomized trials in patients undergoing cardiac<sup>54</sup> and noncardiac<sup>55,56</sup> surgery have each demonstrated that such patients can tolerate perioperative anemia without transfusion to hemoglobin concentrations between 7 and 8 g/dl, and have equivalent clinical outcomes comparable with transfusions to hemoglobin concentrations of greater than 10 g/dl. It is noteworthy that the recently published FOCUS trial found that elderly (mean age older than 80 yr), high-risk (factors for coronary artery disease) patients who have undergone hip fracture surgery tolerate a hemoglobin trigger as low as 8 g/dl (or higher if symptomatic).<sup>56</sup> A Cochrane meta-analysis of prospective randomized trials<sup>57</sup> comparing “high” versus “low” hemoglobin thresholds on more than 3,700 patients found that (1) “low” hemoglobin thresholds were well tolerated; (2) erythrocyte transfusions were reduced (approximately 37%) significantly in patients randomized to the “low” hemoglobin cohorts; (3) infections were reduced by 34% in patients in the “low” hemoglobin cohorts; and (4) a hemoglobin concentration of 7g/dl was sufficient for most patients. More recently, a randomized controlled trial of 2,016 elderly patients with history or risk factors of cardiovascular disease who underwent hip surgery demonstrated that mortality rates, inability to walk independently, and in-hospital morbidity rates were similar in liberal- versus restrictive-transfused patients, despite significant fewer transfusions in the restrictive group.<sup>56</sup>

Patient blood management strategies for patients undergoing cardiac surgery have been shown to be safe and effective in reducing transfusion, while at the same time delivering high-quality outcomes. One of our institutions<sup>58</sup> reported that only 11% of patients undergoing cardiac surgeries received blood transfusions, in which the program ranked first in their state for lowest risk-adjusted mortality. Other single-center initiatives using laboratory-guided transfusion algorithms in both operating rooms and intensive care units have reported a 50% reduction in transfusions of blood components (personal communication, September 9, 2011, by Mark Erath M.D., Professor of Anesthesiology, in the Department of Anesthesiology at the Mayo Clinic in Rochester, Minnesota, as presented at the Mayo Clinic Symposium (February 2011) on Patient Blood Management). Both the pediatric<sup>59</sup> and adult hospitals at one of our own medical centers have reduced blood utilization using computerized physician order entry: hemoglobin



**Fig. 3.** Percent of erythrocyte transfusions administered to patients with hemoglobin concentration more than 8 g/dl. Blood utilization at Stanford Hospital and Clinics (SHC) improved after a clinical effectiveness (CE) team instituted physician education and electronic medical records (EMR)-based clinical decision support (CDS). Horizontal axis: percentage of total erythrocyte transfusions for inpatients on medical/surgical units at SHC whose last recorded hemoglobin concentration was greater than 8 g/dl; vertical axis: monthly intervals, September 2008 - March 2011. Reproduced, with permission, from *Compass* 2011; Stanford Hospital and Clinics (SHC) Quality and Clinical Effectiveness Newsletter, third Quarter.

threshold for blood transfusion decreased in our adult hospital after a clinical effectiveness team instituted physician education and clinical decision support *via* electronic physician order entry (fig. 3).

Data from the American Red Cross on blood usage suggests an estimated decline of 3% over each of the past 2 yr (2009–2010), indicating that physician behavior toward blood transfusions is undergoing change nationally (personal communication, September 9, 2011, Richard Benjamin M.D., Ph.D., Adjunct Associate Professor of Pathology at Georgetown University, Washington, D.C., and Chief Medical Officer for the American Red Cross; as presented at the Food and Drug Administration Blood Products Advisory Committee, June 2011). This trend is accompanied by data from the most recent National Blood Collection and Utilization Survey,<sup>§§</sup> which shows a progressive annual decrease in number of patients and percentage of hospitals who have cancelled elective surgical procedures due to blood inventory constraints (table 3). Current initiatives in research for blood transfusions are reflected in the growing literature on adverse

effects of blood storage and their possible implications for oxygen delivery by blood transfusion.<sup>60</sup>

### Indications for Plasma Transfusion

In a recent evidence-based review the Transfusion Practices Committee of the AABB recommended plasma therapy for only a few clinical indications, based on the available evidence in the literature (which was assessed to be of “weak quality”): trauma patients with substantial hemorrhage, patients undergoing complex cardiovascular surgery, and in patients with intracranial hemorrhage requiring emergency reversal of warfarin-associated coagulopathy.<sup>61</sup> Patients with mild prolongations of the INR (less than 1.7) are not at risk of bleeding and do not need plasma therapy for minor procedures,<sup>62</sup> so that for most clinical settings there is ample evidence that plasma transfusions are inappropriate. However, logistical/technical barriers that prevent effective and timely plasma therapy (possibly resulting in plasma therapies that are “too little, too late”) have probably contributed to the paucity of evidence demonstrating any benefit for plasma therapy.<sup>17</sup>

One of the largest prospective studies<sup>63</sup> of plasma transfusions and their effect on INR and bleeding included both

§§ U.S. Department of Health and Human Services. National Blood Collection and Utilization Survey. Available at <http://www.hhs.gov/ash/bloodsafety/nbcus/index.html>. Accessed January 19, 2012.

**Table 3.** Cancellation of Elective Surgeries by U.S. Hospitals due to Blood Inventory Constraints, 1997–2008

| Year | % Hospitals with Cancellation of ≥1 Day | Range of Days | Median Number of Days | Number of Patients Affected |
|------|---|---------------|-----------------------|-----------------------------|
| 1997 | 8.6                                     | 1–21          | 2                     | Not determined              |
| 1999 | 7.4                                     | 1–150         | 2                     | 568                         |
| 2001 | 12.7                                    | 1–63          | 2                     | 952                         |
| 2004 | 8.4                                     | 1–39          | 2                     | 546                         |
| 2006 | 6.9                                     | 1–120         | 3                     | 412 (721 weighted)          |
| 2008 | 4.4                                     | 1–100         | 2                     | 151 (325 weighted)          |

From The U.S. Department of Health and Human Services 2009 National Blood Collection and Utilization Survey Report.

medical and surgical patients with pretransfusion INR of between 1.1 and 1.85. The authors reported that less than 1% of patients had normalization of their INR and only 15% had at least 50% correction. The median dose of plasma was 2 units (only 5 to 7 ml/kg), and there was no correlation between plasma dose and change in INR. This study had many of the limitations common to other reports<sup>64</sup> in this clinical arena: lack of control groups, only modest prolongation in coagulation tests, poorly defined clinical endpoints (e.g., change in hemoglobin or need for transfusion), and/or an inadequate dose of plasma therapy.

The paucity of evidence for benefit of plasma transfusion therapy has been accompanied by growing evidence that risks of plasma have been underrecognized; in a prospective study, 6% of transfused patients developed transfusion associated cardiac overload<sup>65</sup> which is much higher than previously re-

ported rates in retrospective studies.<sup>66,67</sup> Transfusion-related acute lung injury<sup>68</sup> is a significant cause of morbidity/mortality from blood transfusions, whose incidence has declined subsequently with use of plasma from male donors or female donors who have no history of pregnancy.<sup>69</sup>

### Indications for Platelet Transfusion

A performance indicator for prophylactic platelet transfusions has been developed by The Joint Commission for patients with malignant hematologic diseases or those who undergo stem cell transplantation, in which a platelet count threshold of 10,000/mm<sup>3</sup> is appropriate for prophylactic platelet transfusions.<sup>70</sup>

Current guidelines from the European Union and United States recommend a transfusion trigger of 10 × 10<sup>9</sup>/l for

### Patient Blood Management

|                | Optimize erythropoiesis   | Minimize blood loss  | Manage anemia  |
|----------------|---|--|--|
| PREOPERATIVE   | <ul style="list-style-type: none"> <li>Identify, evaluate, and treat underlying anemia</li> <li>Preoperative autologous blood donation</li> <li>Consider erythropoiesis stimulating agents (ESA) if nutritional anemias ruled out/treated</li> <li>Refer for further evaluation if necessary</li> </ul> | <ul style="list-style-type: none"> <li>Identify and manage bleeding risk (past/family history)</li> <li>Review medications (antiplatelet, anticoagulation therapy)</li> <li>Minimize iatrogenic blood loss</li> <li>Procedure planning and rehearsal</li> </ul>  | <ul style="list-style-type: none"> <li>Compare estimated blood loss with patient-specific tolerable blood loss</li> <li>Assess/optimize patient's physiologic reserve (e.g., pulmonary and cardiac function)</li> <li>Formulate patient-specific management plan using appropriate blood conservation modalities to manage anemia</li> </ul> |
| INTRAOPERATIVE | <ul style="list-style-type: none"> <li>Time surgery with optimization of erythrocyte mass (note: unmanaged anemia is a contraindication for elective surgery)</li> </ul>  | <ul style="list-style-type: none"> <li>Meticulous hemostasis and surgical techniques</li> <li>Blood-sparing surgical techniques</li> <li>Anesthetic blood conserving strategies</li> <li>Acute normovolemic hemodilution</li> <li>Cell salvage/reinfusion</li> <li>Pharmacologic/hemostatic agents</li> </ul>  | <ul style="list-style-type: none"> <li>Optimize cardiac output</li> <li>Optimize ventilation and oxygenation</li> <li>Evidence-based transfusion strategies</li> </ul>   |
| POSTOPERATIVE  | <ul style="list-style-type: none"> <li>Manage nutritional/correctable anemia (e.g., avoid folate deficiency, iron-restricted erythropoiesis)</li> <li>ESA therapy if appropriate</li> <li>Be aware of drug interactions that can cause anemia (e.g., ACE inhibitor)</li> </ul>                          | <ul style="list-style-type: none"> <li>Monitor and manage bleeding</li> <li>Maintain normothermia (unless hypothermia indicated)</li> <li>Autologous blood salvage</li> <li>Minimize iatrogenic blood loss</li> <li>Hemostasis/anticoagulation management</li> <li>Be aware of adverse effects of medications (e.g., acquired vitamin K deficiency)</li> </ul> | <ul style="list-style-type: none"> <li>Maximize oxygen delivery</li> <li>Minimize oxygen consumption</li> <li>Avoid/treat infections promptly</li> <li>Evidence-based transfusion strategies</li> </ul>  |

**Fig. 4.** Patient blood management. These principles applied in the perisurgical period enable treating physicians to have the time and tools to provide patient-centered evidenced-based patient blood management to minimize allogeneic blood transfusions. ACE = angiotensin-converting enzyme.



platelets transfused prophylactically.<sup>63,71</sup> These guidelines are based on outcomes from four randomized clinical trials that compared prophylactic triggers of  $10 \times 10^9/l$  versus  $20 \times 10^9/l$  in patients with acute leukemia and in autologous and allogeneic hematopoietic stem cell transplant recipients.<sup>70,72–75</sup> Two additional prospective studies also demonstrated safety with the lower threshold of  $10 \times 10^9/l$  for prophylactic platelet transfusions.<sup>76,77</sup> The effect of these thresholds on numbers of platelet and blood transfusions is variable, however<sup>77</sup>; one study demonstrated a 36% and 16% reduction in platelet and blood transfusions, respectively,<sup>77</sup> whereas another showed no differences.<sup>76</sup>

A recent trial<sup>78</sup> demonstrated that “low-dose” prophylactic platelet transfusions are equally effective as those with “standard” or “high” dose. For therapeutic platelet transfusions, algorithms for platelet transfusions based on point of care testing have demonstrated promise in patients who have platelet-derived bleeding such as in cardi thoracic surgery<sup>18,79</sup> and in trauma.<sup>80</sup> As for the evidence-based literature for plasma therapy, additional studies in platelet transfusion are also needed.<sup>81</sup>

## Conclusion

Blood transfusions carry risks, are costly, and the supply of blood is limited. Blood transfusion outcomes are therefore undergoing renewed scrutiny by healthcare institutions to reduce blood utilization. In addition to accreditation organizations, professional societies are also well positioned to incorporate blood transfusion outcomes as quality indicators in their own guidelines and recommendations.<sup>82</sup>

Quality improvement in health care has been described as undergoing an identity crisis, in which differences in measurable outcomes between quality and safety are unclear; this observation has been characterized by a redefinition of terms: from quality to process improvement; and safety to value or cost-effectiveness.<sup>83</sup> The relationship between quality and safety has always been direct for patients in transfusion medicine: patient blood management improves patient safety by reducing blood transfusions. Medical harm from errors in patient identification and specimen labeling in blood administration<sup>84</sup> exceeds currently known risks from blood-transmissible agents,<sup>2</sup> so that maintaining the status quo is likely to continue to result in harm for patients who receive transfusions unnecessarily. In recognition of this finding, the Department of Human Health Services has announced the formation of a national committee to establish standards for administering blood transfusions.|||| The foundations of patient blood management in the perisurgical period are illustrated in figure 4: (1) optimize erythropoiesis; (2) minimize blood loss; and (3) manage anemia. Strategies begin with preoperative preadmission testing and extend throughout the intraoperative and the postoperative intervals, enabling

treating physicians to minimize allogeneic blood transfusions, while delivering safe and effective healthcare. Physicians and hospital quality/clinical effectiveness departments should incorporate principles of patient blood management into hospital-based process improvement initiatives that improve patient safety and clinical outcomes.

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