Practice Guidelines for Perioperative Blood Transfusion and Adjuvant Therapies

An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies

PRACTICE guidelines are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints, and are not intended to replace local institutional policies. In addition, practice guidelines developed by the American Society of Anesthesiologists (ASA) are not intended as standards or absolute requirements, and their use cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by a synthesis and analysis of the current literature, expert and practitioner opinion, open forum commentary, and clinical feasibility data.


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Address correspondence to the American Society of Anesthesiologists: 520 N. Northwest Highway, Park Ridge, Illinois 60068-2573. These Practice Guidelines, as well as all ASA Practice Parameters, may be obtained at no cost through the Journal Web site, www.anesthesiology.org.

Methodology

A. Definition of Perioperative Blood Transfusion and Adjuvant Therapies

Perioperative blood transfusion refers to the preoperative, intraoperative, and postoperative administration of blood and blood components (e.g., allogeneic or autologous blood, red blood cells, fresh frozen plasma [FFP], platelets, and cryoprecipitate). Adjuvant therapies refer to drugs and techniques to reduce or prevent blood loss and the need for transfusion of allogeneic blood.

B. Purpose of the Guidelines

The purposes of these updated Guidelines are to improve the perioperative management of blood transfusion and adjuvant therapies and to reduce the risk of adverse outcomes associated with transfusions, bleeding, or anemia.

C. Focus

These Guidelines focus on the perioperative management of patients undergoing surgery or other invasive procedures in which significant blood loss occurs or is expected. This includes but is not limited to: (1) patients undergoing cardiopulmonary bypass or cardiac surgery, urgent or emergent procedures, obstetric procedures, organ transplantation, and non-cardiac surgery; (2) patients with preexisting blood disorders or acquired coagulation deficiency; (3) critically-ill patients undergoing surgical or other interventional procedures; and (4) patients who elect not to undergo perioperative transfusion. Excluded from the focus of these Guidelines are neonates, infants, children weighing less than 35 kg, and patients who are not undergoing procedures.

D. Application

These Guidelines apply to both inpatient and outpatient surgical settings, and to interventional procedures performed in operating rooms as well as in other locations (e.g., interventional radiology, critical care units) where blood transfusion or other adjuvant therapy is indicated. They are directly applicable to care administered by anesthesiologists and individuals
who deliver care under the medical direction or supervision of an anesthesiologist. They are also intended to serve as a resource for other physicians and patient care personnel who are involved in the perioperative care of these patients.

E. Task Force Members and Consultants

In 2012, the ASA Committee on Standards and Practice Parameters requested that the updated Guidelines published in 2006 be re-evaluated. This current update consists of a literature evaluation, and an evaluation of new survey findings of expert consultants and ASA members.

A summary of recommendations is found in Appendix 1.

This update was developed by an ASA appointed Task Force of 10 members, consisting of anesthesiologists in both private and academic practices from various geographic areas of the United States, a pathologist specializing in transfusion medicine, and two consulting methodologists from the ASA Committee on Standards and Practice Parameters.

The Task Force developed the Guidelines by means of a seven-step process. First, they reached consensus on the criteria for evidence of effective blood transfusion and adjuvant therapies. Second, original published research studies from peer-reviewed journals relevant to the perioperative management of patients undergoing blood transfusions were reviewed. Third, a panel of expert consultants was asked to (1) participate in opinion surveys on the effectiveness of various perioperative management strategies and (2) review and comment on a draft of the Guidelines developed by the Task Force. Fourth, survey opinions about the Guideline recommendations were solicited from a random sample of active members of the ASA. Fifth, the Task Force held open forums at two major national meetings to solicit input on its draft recommendations. National organizations representing specialties whose members typically care for patients undergoing perioperative transfusion were invited to participate in the open

forums. Sixth, the consultants were surveyed to assess their opinions on the feasibility of implementing the Guidelines. Seventh, all available information was used to build consensus within the Task Force to finalize the Guidelines.

F. Availability and Strength of Evidence

Preparation of these updated Guidelines followed a rigorous methodological process. Evidence was obtained from two principal sources: scientific evidence and opinion-based evidence (Appendix 2).

Scientific Evidence:

Scientific evidence used in the development of these updated Guidelines is based on cumulative findings from literature published in peer-reviewed journals. Literature citations are obtained from PubMed and other healthcare databases, direct internet searches, Task Force members, liaisons with other organizations and from manual searches of references located in reviewed articles.

Findings from the aggregated literature are reported in the text of the Guidelines by evidence category, level, and direction. Evidence categories refer specifically to the strength and quality of the research design of the studies. Category A evidence represents results obtained from randomized controlled trials (RCTs), and Category B evidence represents observational results obtained from non-randomized study designs or RCTs without pertinent controls. When available, Category A evidence is given precedence over Category B evidence in the reporting of results. These evidence categories are further divided into evidence levels. Evidence levels refer specifically to the strength and quality of the summarized study findings (i.e., statistical findings, type of data, and the number of studies reporting/replicating the findings) within the two evidence categories. For this document, only the highest level of evidence is included in the summary report for each intervention, including a directional designation of benefit, harm, or
equivocality for each outcome.

Category A: RCTs report comparative findings between clinical interventions for specified outcomes. Statistically significant (p < 0.01) outcomes are designated as either beneficial (B) or harmful (H) for the patient; statistically non-significant findings are designated as equivocal (E).

Level 1: The literature contains a sufficient number of RCTs to conduct meta-analysis,§ and meta-analytic findings from these aggregated studies are reported as evidence.

Level 2: The literature contains multiple RCTs, but the number of RCTs is not sufficient to conduct a viable meta-analysis for the purpose of these updated Guidelines. Findings from these RCTs are reported as evidence.

Level 3: The literature contains a single RCT, and findings from this study are reported as evidence.

Category B: Observational studies or RCTs without pertinent comparison groups may permit inference of beneficial or harmful relationships among clinical interventions and outcomes. Inferred findings are given a directional designation of beneficial (B), harmful (H) or equivocal (E). For studies that report statistical findings, the threshold for significance is p < 0.01.

Level 1: The literature contains observational comparisons (e.g., cohort, case-control research designs) between clinical interventions for a specified outcome.

Level 2: The literature contains observational studies with associative statistics (e.g., relative risk, correlation, sensitivity/specificity).

Level 3: The literature contains non-comparative observational studies with descriptive statistics (e.g., frequencies, percentages).

Level 4: The literature contains case reports.

§ All meta-analyses are conducted by the ASA methodology group. Meta-analyses from other sources are reviewed but not included as evidence in this document.
Insufficient Literature: The lack of sufficient scientific evidence in the literature may occur when the evidence is either unavailable (i.e., no pertinent studies found) or inadequate. Inadequate literature cannot be used to assess relationships among clinical interventions and outcomes, since such literature does not permit a clear interpretation of findings due to methodological concerns (e.g., confounding in study design or implementation) or does not meet the criteria for content as defined in the “Focus” of the Guidelines.

Opinion-Based Evidence:

All opinion-based evidence (e.g., survey data, open-forum testimony, internet-based comments, letters, and editorials) relevant to each topic was considered in the development of these updated Guidelines. However, only the findings obtained from formal surveys are reported.

Opinion surveys were developed for this update by the Task Force to address each clinical intervention identified in the document. Identical surveys were distributed to expert consultants and a random sample of ASA members.

Category A: Expert Opinion. Survey responses from Task Force-appointed expert consultants are reported in summary form in the text, with a complete listing of consultant survey responses reported in Appendix 2.

Category B: Membership Opinion. Survey responses from active ASA members are reported in summary form in the text, with a complete listing of ASA member survey responses reported in Appendix 2.

Survey responses from expert and membership sources are recorded using a 5-point scale and summarized based on median values.**

Strongly Agree: Median score of 5 (At least 50% of the responses are 5)
Agree: Median score of 4 (At least 50% of the responses are 4 or 4 and 5)

**When an equal number of categorically distinct responses are obtained, the median value is determined by calculating the arithmetic mean of the two middle values. Ties are calculated by a predetermined formula.
Equivocal: Median score of 3 (At least 50% of the responses are 3, or no other response category or combination of similar categories contain at least 50% of the responses)

Disagree: Median score of 2 (At least 50% of responses are 2 or 1 and 2)

Strongly Disagree: Median score of 1 (At least 50% of responses are 1)

Category C: Informal Opinion. Open-forum testimony obtained during development of the original Guidelines, Internet-based comments, letters and editorials are all informally evaluated and discussed during the formulation of Guideline recommendations. When warranted, the Task Force may add educational information or cautionary notes based on this information.

Guidelines

I. Patient Evaluation

Preoperative evaluation of a patient to identify risk factors for requiring a blood transfusion or adjuvant therapy includes: (1) reviewing previous medical records, (2) conducting a patient or family interview, (3) reviewing existing laboratory test results, and (4) ordering additional laboratory tests when indicated.

Although it is well accepted clinical practice to review medical records and conduct a patient interview, comparative studies are insufficient to evaluate the impact of these practices. Observational studies and case reports indicate that certain congenital or acquired conditions (e.g., sickle-cell anemia, clotting factor deficiency, hemophilia, and liver disease) may be associated with blood transfusion complications (Category B3/B4-H evidence). In addition, observational studies indicate that findings from pertinent preoperative laboratory tests (e.g., hemoglobin, hematocrit, coagulation tests) may be predictive of perioperative blood loss, the risk of transfusion, or other adverse events (e.g., acute kidney injury) associated with transfusion (Category B2-B evidence).
The consultants and ASA members both strongly agree to (1) a review of previous medical records and interview the patient or family to identify prior blood transfusion, history of drug-induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischemia and (2) a review available laboratory test results including hemoglobin, hematocrit, and coagulation profiles and order additional laboratory tests depending on a patient’s medical condition (e.g., coagulopathy, anemia). The ASA members agree and the consultants strongly agree regarding (1) informing patients of the potential risks versus benefits of blood transfusion and elicit their preferences and (2) conducting a physical examination of the patient (e.g., ecchymoses, petechiae, pallor).

**Recommendations for patient evaluation:**

- Review previous medical records and interview the patient or family to identify:
  - Prior blood transfusion
  - History of drug-induced coagulopathy (e.g., warfarin, clopidogrel, aspirin and other anticoagulants, as well as vitamins or herbal supplements that may affect coagulation [*Appendix 3*])
  - The presence of congenital coagulopathy
  - History of thrombotic events (e.g., deep vein thrombosis, pulmonary embolism)
  - Risk factors for organ ischemia (e.g., cardiorespiratory disease) which may influence the ultimate transfusion trigger for red blood cells (e.g., hemoglobin level)
- Inform patients of the potential risks *versus* benefits of blood transfusion and elicit their preferences.
- Review available laboratory test results including hemoglobin, hematocrit and
coagulation profiles.

- Order additional laboratory tests depending on a patient’s medical condition (e.g., coagulopathy, anemia).
- Conduct a physical examination of the patient (e.g., ecchymosis, petechiae, pallor).
- If possible, perform the preoperative evaluation well enough in advance (e.g., several days to weeks) to allow for proper patient preparation.

II. Preadmission Patient Preparation

Preadmission patient preparation includes (1) treatment of anemia, (2) discontinuation of anticoagulants and antiplatelet agents, (3) preadmission autologous blood collection.

**Treatment of anemia:** The World Health Organization identifies anemia as hemoglobin thresholds of 11.0 g/dl for children 0.50-4.99 years,† † 11.5 g/dl for children 5.00-11.99 years, 12.0 g/dl for children 12.00-14.99 years, and non-pregnant women \( \geq \) 15.00 years, 11.0 g/dl for pregnant women and 13.0 g/dl for men \( \geq \) 15.00 years. The World Health Organization identifies anemia as hemoglobin thresholds of 11.0 g/dl for children 0.50-4.99 years,† † 11.5 g/dl for children 5.00-11.99 years, 12.0 g/dl for children 12.00-14.99 years, and non-pregnant women \( \geq \) 15.00 years, 11.0 g/dl for pregnant women and 13.0 g/dl for men \( \geq \) 15.00 years.42,43 Preadmission treatment of anemia includes the administration of erythropoietin and/or iron to improve preoperative hemoglobin levels.

Meta-analyses of placebo-controlled RCTs indicate that erythropoietin with or without iron is effective in reducing the volume of allogeneic blood transfused as well as reducing the number of patients requiring allogeneic transfusions (Category A1-B evidence).44-58 The literature is insufficient to evaluate the efficacy of erythropoietin with iron compared with erythropoietin without iron. RCTs report equivocal findings when preadmission oral iron is compared with either placebo or no iron regarding preoperative hemoglobin levels or perioperative allogeneic blood transfused (Category A2-E evidence).59-61

Both the consultants and ASA members agree that erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in select patient

† † Neonates, infants, and children weighing less than 35 kg are excluded from the focus of these ASA Guidelines.
populations (e.g., renal insufficiency, anemia of chronic disease, refusal of transmission); and both the consultants and ASA members strongly agree regarding the administration of iron to patients with iron deficiency anemia if time permits.

**Discontinuation of anticoagulants and antiplatelet agents:** One nonrandomized comparative observational study is equivocal regarding the effect of discontinuing warfarin and replacing it with low-molecular weight heparin on blood transfusion requirements when compared with patients not on warfarin. Observational studies report blood loss volumes ranging from 265-756 ml, and blood transfusion requirements ranging from 0.08-0.5 units when clopidogrel is discontinued preoperatively. The literature is insufficient to evaluate the effects of discontinuing aspirin before surgery, although two RCTs comparing the administration of aspirin with placebo before surgery report equivocal findings (p > 0.01) for perioperative blood loss, transfusion requirements or postoperative adverse events (e.g., myocardial infarction, major bleeding or death).

Both the consultants and ASA members strongly agree regarding (1) discontinuing anticoagulation therapy (e.g., warfarin, anti-Xa drugs, anti-thrombin agents) for elective surgery, in consultation with an appropriate specialist; (2) if clinically possible, discontinuing non-aspirin antiplatelet agents (e.g., thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions; and (3) that the risk of thrombosis versus the risk of increased bleeding should be considered when altering anticoagulation status.

**Preadmission autologous blood donation:** RCTs indicate that the preadmission donation of autologous blood reduces the volume of allogeneic blood transfused per patient and the number of patients requiring allogeneic transfusions (*Category A2-B evidence*).

†† The Task Force notes that certain adverse outcomes (e.g., transfusion reaction due to clerical errors, bacterial contamination) may still occur with the use of autologous blood.
The consultants and ASA members both strongly agree regarding assuring that blood and blood components are available for patients when significant blood loss or transfusion is expected; they both agree that when autologous blood is preferred, the patient should be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution.

**Recommendations for preadmission patient preparation:**

- Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in selected patient populations (e.g., renal insufficiency, anemia of chronic disease, refusal of transfusion).§§

- Administer iron to patients with iron deficiency anemia if time permits.

- In consultation with an appropriate specialist, discontinue anticoagulation therapy (e.g., warfarin, anti-Xa drugs, antithrombin agents) for elective surgery.
  - Transition to a shorter acting drug (e.g., heparin, low molecular weight heparin) may be appropriate in selected patients.

- If clinically possible, discontinue non-aspirin antiplatelet agents (e.g., thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions.***
  - Aspirin may be continued on a case-by-case basis.

- The risk of thrombosis versus the risk of increased bleeding should be considered when altering anticoagulation status.

- Assure that blood and blood components are available for patients when significant

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§§ The Task Force recognizes that erythropoietin administration is perceived as being expensive and requires time (in weeks) to induce a significant increase in hemoglobin concentration.

*** The Task Force cautions that clopidogrel and aspirin should not be stopped prior to surgery in patients with coronary stents placed in the last 3 months for bare metal stents and 1 year for drug eluting stents due to the risk of perioperative myocardial infarction. See “American Society of Anesthesiologists Committee on Standards and Practice Parameters: Practice alert for the perioperative management of patients with coronary artery stents: a report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology. 2009; 110:22-23.”
blood loss or transfusion is expected.

- When autologous blood is preferred, the patient may be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution.†††

**III. Preprocedure Preparation**

Preprocedure patient preparation includes the following strategies for reducing intraoperative allogeneic transfusion: (1) use of blood management protocols, (2) reversal of anticoagulants, (3) antifibrinolytics to minimize blood loss, (4) acute normovolemic hemodilution (ANH), and (5) empiric pre-procedure transfusion of red blood cells.

**Blood management protocols:** Protocols for perioperative blood management include: (1) multimodal protocols or algorithms, (2) liberal versus restrictive transfusion criteria, (3) avoidance of transfusion (i.e., bloodless surgery), (4) a massive (i.e., hemorrhagic) transfusion protocol, and (5) a maximal surgical blood order schedule.

**Multimodal protocols or algorithms:** Multimodal protocols are strategies that typically consist of a predetermined “bundle” of interventions intended to reduce blood loss and transfusion requirements. The bundle components may include consultation with multiple medical specialties, institutional support, transfusion algorithms, and point-of-care testing in addition to other perioperative blood conservation interventions. Algorithms are intended to identify decision points or “pathways” during a procedure whereby certain interventions should be administered.

RCTs comparing multimodal protocols or algorithms using coagulation tests or hemoglobin concentrations with routine blood management practices report variable findings regarding blood and blood product transfusions when such protocols are implemented (Category A2-E

††† The Task Force cautions that preadmission blood donation may induce preoperative anemia, increase total intraoperative (autologous or allogeneic) transfusions, and increase costs.
RCTs report reduced blood transfusions and percentage of patients transfused when TEG-guided protocols or algorithms are compared with standard laboratory coagulation testing in cardiac surgery patients. (Category A2-B evidence). An RCT reports reductions in allogeneic blood product requirements when comparing a ROTEM-guided algorithm with no algorithm for bleeding burn patients. (Category A1-B evidence). The above studies report protocols or algorithms that contain a large variety of interventional components and the impact of any single component on outcome is not reported.

The consultants and ASA members both strongly agree regarding employment of multimodal protocols or algorithms as strategies to reduce the utilization of blood products.

Restrictive versus liberal transfusion strategy: Definitions for a restrictive versus liberal strategy for blood transfusion vary in the literature, although hemoglobin criteria for transfusion below 8 g/dL and hematocrit values below 25% are typically reported as restrictive. Meta-analysis of RCTs comparing restrictive with liberal transfusion criteria report fewer red blood cell transfusions when restrictive transfusion strategies are employed (Category A1-B evidence). RCT findings for cardiac, neurologic or pulmonary complications, length of hospital stay, and mortality were equivocal (Category A2-E evidence).

The ASA members agree and the consultants strongly agree that a restrictive red blood cell transfusion strategy may be used to reduce transfusion requirements.

Avoidance of transfusion: A protocol to avoid transfusion or to reduce the volume of blood lost, sometimes referred to as “bloodless surgery,” may be preferred in certain selected cases. Studies with observational findings report low blood loss volumes for certain cardiac or other major procedures when these protocols are implemented (Category B3-B evidence).
Both the consultants and ASA members strongly agree that a protocol for avoidance of transfusion (i.e., bloodless surgery) may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible.

**Massive transfusion protocols:** Massive transfusion protocols are implemented in cases of life-threatening hemorrhage after trauma and/or during a procedure, and are intended to minimize the adverse effects of hypovolemia and dilutional coagulopathy. These protocols require large amounts of allogeneic blood and blood products. They often prescribe the transfusion of fresh frozen plasma and platelets in a 1:1 ratio with the transfusion of red blood cells. An observational study indicates that the ratio of fresh frozen plasma to RBCs is higher following the implementation of a massive transfusion protocol (*Category B3-E evidence*). The consultants and ASA members both strongly agree regarding use of a massive transfusion protocol when available as a strategy to optimize the delivery of blood products to massively bleeding patients.

**Maximal surgical blood order schedule:** Observational studies indicate that implementing a maximal surgical blood order schedule or surgical blood order equation may improve the efficiency of blood ordering practices (*Category B2-B evidence*). An RCT comparing a surgical blood order equation with a maximal surgical blood order schedule reports an improved crossmatch-to-transfusion ratio for SBOE (*Category A3-B evidence*). The consultants and ASA members both agree regarding the use of a maximal surgical blood order schedule, when available and in accordance with institutional policy, as a strategy to improve the efficiency of blood ordering practices.

**Reversal of anticoagulants:** Reversal of anticoagulants includes the topics of: (1) preprocedure administration of prothrombin complex concentrates (PCCs), (2) pre-procedure administration of vitamin K, and (3) administration of fresh frozen plasma.
Observational studies and case reports indicate that PCCs (i.e., Beriplex) administered preoperatively are followed by a reduction in INR values, with thromboembolic events reported at 0.003% following patient infusions (*Category B3/4-B evidence*). One retrospective study comparing vitamin K administered immediately before surgery with no vitamin K administered reports equivocal findings for transfusion requirements.

Both the consultants and ASA members strongly agree that for urgent reversal of warfarin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer fresh frozen plasma (FFP). The ASA members agree and the consultants strongly agree regarding administration of vitamin K for non-urgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required.

**Antifibrinolytics to minimize blood loss:**

**ε-Aminocaproic acid:** Meta-analysis of placebo-controlled RCTs indicate that the use of ε-aminocaproic acid administered before and/or during a procedure is effective in reducing total perioperative blood loss and the number of patients transfused in major cardiac, orthopedic, or liver surgery (*Category A1-B evidence*); equivocal findings are reported for the volume of blood transfused (*Category A1-E evidence*).

**Tranexamic acid:** Meta-analysis of placebo-controlled RCTs indicate that tranexamic acid administered before and/or during a procedure is effective in reducing perioperative blood loss, the volume of blood products transfused, and the number of patients transfused (*Category A1-B evidence*). Randomized trials comparing tranexamic acid with placebo or no tranexamic acid controls report no differences for stroke, myocardial infarction, renal failure, reoperation for bleeding, or mortality (*Category A2-B evidence*).

The consultants and ASA members both agree regarding use of antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass. They also
both agree regarding the consideration of using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding.

**Acute normovolemic hemodilution:** Meta-analyses of RCTs indicate that acute normovolemic hemodilution is effective in reducing the volume of allogeneic blood transfused and the number of patients transfused with allogeneic blood for major cardiac, orthopedic, thoracic, or liver surgery (*Category A1-B evidence*). Additional meta-analyses of RCTs indicate that acute normovolemic hemodilution combined with intraoperative red blood cell recovery compared with intraoperative red blood cell recovery alone is effective in reducing the volume of allogeneic blood transfused (*Category A1-B evidence*) and is equivocal regarding the number of patients transfused with allogeneic blood (*Category A1-E evidence*).

Both the consultants and ASA members agree regarding use of acute normovolemic hemodilution (ANH) to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (*e.g.*, major cardiac, orthopedic, thoracic, or liver surgery), if possible.

**Recommendations for preprocedure preparation:**

**Blood management protocols:**

- Multimodal protocols or algorithms may be employed as strategies to reduce the utilization of blood products. However, no single algorithm or protocol can be recommended at this time.

- A restrictive red blood cell transfusion strategy may be safely used to reduce transfusion requirements.
  - Transfusion of red blood cells is rarely necessary when the hemoglobin concentration is more than 10 g/dl.‡‡‡
  - The determination of whether hemoglobin concentrations between 6 and 10 g/dl justify or require red blood cell transfusion should be based on potential

‡‡‡ Red blood cells refers to all red blood cell containing components.
or actual ongoing bleeding (rate and magnitude), intravascular volume status, signs of organ ischemia, and inadequate cardiopulmonary reserve.

- Red blood cells should be administered unit-by-unit, when possible, with interval reevaluation.

- A protocol for avoidance of transfusion (i.e., bloodless surgery) may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible.

- A massive (i.e., hemorrhagic) transfusion protocol may be used when available as a strategy to optimize the delivery of blood products to massively bleeding patients.

- Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices.

Reversal of anticoagulants:

- For urgent reversal of warfarin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer fresh frozen plasma (FFP).

- Administer vitamin K for non-urgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required.

Antifibrinolytics to minimize blood loss:

- Use antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass.

  - Consider using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding.

Acute normovolemic hemodilution:
- Use acute normovolemic hemodilution (ANH) to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (e.g., major cardiac, orthopedic, thoracic, or liver surgery), if possible.\\

IV. Intraoperative and Postoperative Management of Blood Loss and Transfusions

Intraoperative and postoperative interventions include: (1) allogeneic red blood cell transfusion, (2) autologous blood cell transfusion, (3) intraoperative and postoperative patient monitoring, and (4) management of coagulopathy and excessive bleeding.

**Allogeneic red blood cell transfusion:** Transfusion of allogeneic blood includes the topics of (1) the age of stored blood, and (2) leukocyte reduction.

**Age of stored blood:** Nonrandomized comparative studies are equivocal regarding the effects of newer versus older stored blood on infectious complications, in-hospital mortality, 30 days postdischarge mortality, and length of stay in the ICU or hospital (Category B1-E evidence). The consultants are equivocal and ASA members disagree regarding the administration of blood without consideration of duration of storage.

**Leukocyte reduction:** RCTs are equivocal regarding postoperative infections and infectious complications when leukocyte RBC depletion is compared with non-leukocyte depletion (Category A2-B evidence). The ASA members agree and the consultants strongly agree that leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion.

**Reinfusion of recovered red blood cells:**

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\\ ANH may not be possible due to preexisting patient factors such as small blood volume, low hemoglobin, or presence of ischemic disease.
Intraoperative red blood cell recovery: Meta-analyses of RCTs indicate that intraoperative red blood cell recovery compared with conventional transfusion is effective in reducing the volume of allogeneic blood transfused (*Category A1-B evidence*).\(^{194-205}\)

Postoperative red blood cell recovery: RCTs indicate that postoperative blood recovery and reinfusion with recovered red blood cells reduces the frequency of allogeneic blood transfusions (*Category A2-B evidence*) in patients undergoing major orthopedic surgery.\(^{206-208}\)

The consultants and ASA members both strongly agree regarding the reinfusion of recovered red blood cells as a blood-sparing intervention in the intraoperative and/or postoperative period.

**Intraoperative and postoperative patient monitoring:**

Intraoperative and postoperative monitoring consists of monitoring for: (1) blood loss, (2) perfusion of vital organs, (3) anemia, (4) coagulopathy, and (5) adverse effects of transfusion.

Monitoring for blood loss: Blood loss monitoring consists of visual assessment of the surgical field, including the extent of blood present, presence of microvascular bleeding, surgical sponges, clot size and shape, and volume in suction canister.

The literature is insufficient to evaluate the impact of periodically assessing the surgical field for the extent of blood present, the presence of excessive microvascular bleeding (*i.e.*, coagulopathy) or observing surgical sponges, clot size and shape, or the volume of blood in the suction canister to measure blood loss.****

Both the consultants and ASA members strongly agree regarding: (1) periodically conducting a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (*i.e.*, coagulopathy) or surgical bleeding and (2) use of standard methods for quantitative measurement of blood loss including checking suction canisters, surgical sponges, and surgical drains.

**** New methods of measuring blood loss include assessing the blood content of sponges and improved volumetric measures.
Monitoring for perfusion of vital organs: Monitoring for perfusion of vital organs includes standard ASA monitoring. Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (i.e., cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation. The literature is insufficient to evaluate the efficacy of the above monitoring techniques on clinical outcomes associated with blood transfusion.

Both the consultants and ASA members strongly agree regarding: (1) monitoring for perfusion of vital organs using standard ASA monitors (i.e., blood pressure, heart rate, oxygen saturation, electro-cardiography) in addition to observing clinical symptoms and physical exam features and (2) that additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (i.e., cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation.

Monitoring for anemia: Monitoring for anemia includes hemoglobin/hematocrit monitoring. The literature is insufficient to evaluate the efficacy of perioperative monitoring for anemia. The consultants and ASA members both strongly agree that if anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs.

Monitoring for coagulopathy: Monitoring for coagulopathy includes standard coagulation tests (e.g., international normalization ratio (INR), activated partial thromboplastin time (aPTT), fibrinogen concentration), as well as platelet count. Additional monitoring for coagulopathy may include tests of platelet function, viscoelastic assays (e.g., thromboelastoography [TEG] and rotational thromboelastometry [ROTEM]).

An observational study examining point-of-care measurement of activated partial thromboplastin time and prothrombin time by a portable laser photometer reports shorter times for obtaining test results with point-of-care monitoring (Category B2-B evidence). Significant
correlations were reported between photometer and traditional laboratory test findings. An observational study examining platelet count during cardiopulmonary bypass to predict excessive blood loss reports a sensitivity value of 83% and a specificity value of 58% (Category B2 evidence).\(^{210}\) An RCT reported equivocal findings for blood loss and transfusion requirements when TEG is compared with standard laboratory coagulation tests (Category A3-E evidence).\(^ {211}\) An RCT reported equivocal findings with ROTEM versus no fibrinolysis monitoring for RBC, FFP and platelet transfusion requirements (Category A3-E evidence).\(^ {212}\) Note that TEG and ROTEM-guided algorithms are shown to be effective in reducing blood transfusion requirements (see multimodal protocols or algorithms above). For ROTEM, a sensitivity finding for blood loss was reported to be 13%, specificity values ranged from 52%-80%, and a positive predictive value of 45% (Category B2 evidence).\(^ {213,214}\) Nonrandomized correlational studies reported significant correlations (p < 0.01) with standard coagulation tests for fibrinogen level and platelet count, while correlations between ROTEM and PT and aPTT measures were not statistically significant (Category B2 evidence).\(^ {215-220}\)

Both the consultants and ASA members agree that if coagulopathy is suspected, obtain viscoelastic assays (e.g., thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), when available, as well as platelet count. They both strongly agree that if viscoelastic assays are not available, obtain standard coagulation tests (e.g., international normalization ratio [INR], aPTT, fibrinogen concentration), as well as platelet count for monitoring.

**Monitoring for adverse effects of transfusions:** Monitoring for adverse effects of transfusions includes periodic checking for signs of ABO incompatibility such as hyperthermia, hemoglobinuria, or microvascular bleeding; signs of transfusion-related acute lung injury (TRALI) or transfusion-associated circulatory overload (TACO) such as hypoxemia, respiratory
distress, elevated peak airway pressure; signs of bacterial contamination such as hyperthermia; allergic reaction such as urticaria, hypotension; and signs of citrate toxicity such as hypocalcemia (Appendix 4).

Nonrandomized comparative studies report higher risk of infection after RBC transfusion (Category B1-H evidence), and case reports indicate that adverse outcomes including TRALI and delayed hemolytic transfusion reaction may occur after transfusion (Category B4-H evidence). The literature is insufficient to recommend specific monitoring practices to identify these adverse transfusion effects.

Both the consultants and ASA members strongly agree that (1) during and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension, and signs of hypocalcemia and (2) before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing.

Prophylaxis and treatment of excessive bleeding:

Intraoperative and postoperative prophylaxis and treatment of excessive bleeding includes:

(1) transfusion of platelets, (2) transfusion of fresh frozen plasma (FFP), (3) transfusion of cryoprecipitate, and (4) pharmacologic prophylaxis and treatment of excessive bleeding.

Transfusion of platelets: Recent literature is insufficient to evaluate the impact of platelet transfusion on resolution of coagulopathy.

The consultants and ASA members both agree regarding obtaining a platelet count before transfusion of platelets, if possible; however, the ASA members agree and the consultants are equivocal regarding obtaining a test of platelet function, if available, in patients with suspected or drug-induced (e.g., clopidogrel) platelet dysfunction.
Transfusion of fresh frozen plasma: RCTs report inconsistent findings regarding blood loss and RBC transfusion requirements when FFP transfusion is compared with non-FFP transfusion, *(Category A2-E evidence).*228,229

The consultants and ASA members both agree that, in patients with excessive bleeding, obtain coagulation tests *(i.e., PT or INR and aPTT)* before transfusion of FFP, if possible.

Transfusion of cryoprecipitate: The literature is insufficient to evaluate the intraoperative or postoperative transfusion of cryoprecipitate to manage actual or potential coagulopathy.

The ASA members agree and the consultants strongly agree that, in patients with excessive bleeding, assess fibrinogen levels before the administration of cryoprecipitate, if possible.

Pharmacologic prophylaxis and treatment of excessive bleeding: Pharmacologic treatments for excessive bleeding include: (1) desmopressin, (2) antifibrinolytics *(i.e., ε-aminocaproic acid, tranexamic acid)*, (3) topical hemostatics *(i.e., fibrin glue, thrombin gel)*, (4) prothrombin complex concentrates, (5) coagulation factor concentrates (recombinant factor VIIa), and (6) treatments for hypofibrinogenemia (cryoprecipitate, fibrinogen concentrate).

Desmopressin: Meta-analysis of placebo-controlled RCTs indicate that desmopressin is effective in reducing the volume of postoperative blood loss *(Category A1-B evidence).*230-236

Both the consultants and ASA members agree that, in patients with excessive bleeding and platelet dysfunction, consider the use of desmopressin.

Antifibrinolytics: An RCT comparing ε-aminocaproic acid with placebo reports less blood loss and lower RBC transfusion requirements when prophylactic ε-aminocaproic acid is administered before tourniquet deflation after total knee replacement surgery *(Category A3-B evidence).*237 Meta-analysis of the prophylactic administration of tranexamic acid compared with placebo reported lower blood loss volumes after knee and hip arthroplasty *(Category A1-B evidence).*
PRACTICE GUIDELINES

One RCT did not show efficacy when tranexamic acid was administered after cardiac surgery and continued for 12 hours (Category A3-E evidence). The consultants and ASA members both agree that, in patients at risk for excessive bleeding, use prophylactic antifibrinolytic therapy to reduce the bleeding and risk of transfusion. They also both agree that, in patients with excessive bleeding, consider the use of antifibrinolytics (i.e., ε-aminocaproic acid, tranexamic acid), if not already being used.

Topical hemostatics: Meta-analysis of RCTs indicates that fibrin glue is effective in reducing the volume of perioperative blood loss and the number of patients transfused when compared with no fibrin glue (Category A1-B evidence). RCTs indicate that thrombin gel is effective in reducing perioperative blood loss and time to hemostasis (Category A2-B evidence).

The consultants and ASA members both agree that, in patients with excessive bleeding, consider topical hemostatics such as fibrin glue or thrombin gel.

PCCs: Observational studies and case reports indicate that intraoperative administration of PCCs (i.e., Beriplex) are followed by a reduction in blood loss and normalization of INR values. (Category B3/4-B evidence).

The consultants and ASA members both agree that, in patients with excessive bleeding and elevated INR, consider the use of prothrombin complex concentrates.

Coagulation factor concentrates: Meta-analysis of placebo-controlled RCTs of recombinant activated factor VII reports equivocal findings regarding the volume of blood loss, the volume of blood transfused, and the number of patients transfused (Category A1-E evidence).

Both the consultants and ASA members agree that, when traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider administering recombinant activated factor VII.
Treatments for hypofibrinogenemia: The literature is insufficient to evaluate the intraoperative or postoperative transfusion of cryoprecipitate to manage hypofibrinogenemia. RCTs comparing fibrinogen concentrate with placebo report a lower volume of RBC transfusion and a reduced frequency of patients transfused when fibrinogen concentrate is administered intraoperatively (Category A2-B evidence).\textsuperscript{271,272} The consultants and ASA members both agree that, in patients with excessive bleeding, consider the use of fibrinogen concentrate.

**Recommendations for Intraoperative and Postoperative Management of Blood Loss and Transfusions:**

**Allogeneic red blood cell transfusion:**
- Administer blood without consideration of duration of storage.
- Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion.

**Reinfusion of recovered red blood cells:**
- Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative period, when appropriate.

**Intraoperative and postoperative patient monitoring:**
- Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (i.e., coagulopathy) or surgical bleeding.
- Use standard methods for quantitative measurement of blood loss, including checking suction canisters, surgical sponges, and surgical drains.
• Monitor for perfusion of vital organs using standard ASA monitors (i.e., blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical exam features.††††

  o Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (i.e., cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation.

• If anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs.

• If coagulopathy is suspected, obtain viscoelastic assays (e.g., thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), when available, as well as platelet count.

  o If viscoelastic assays are not available, obtain standard coagulation tests (e.g., international normalization ratio [INR], aPTT, fibrinogen concentration), as well as platelet count for monitoring.

• During and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension and signs of hypocalcemia.

  o Before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing.

**Prophylaxis and treatment of excessive bleeding:**

• In patients at risk for excessive bleeding, use prophylactic antifibrinolytic therapy to reduce the bleeding and risk of transfusion.

†††† American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring (last amended October 20, 2010, effective date July 1, 2011).
In patients with excessive bleeding, obtain a platelet count before transfusion of platelets, if possible (see Table 1 for suggested transfusion criteria for platelets). In addition, obtain a test of platelet function, if available, in patients with suspected or drug-induced (e.g., clopidogrel) platelet dysfunction.

In patients with excessive bleeding, obtain coagulation tests (i.e., PT or INR and aPTT) before transfusion of FFP, if possible (see Table 1 for suggested transfusion criteria for FFP).

In patients with excessive bleeding, assess fibrinogen levels before the administration of cryoprecipitate, if possible (see Table 1 for suggested transfusion criteria for cryoprecipitate).

- Transfusion of cryoprecipitate is rarely indicated if fibrinogen concentration is greater than 150 mg/dl in non-pregnant patients.

In patients with excessive bleeding and platelet dysfunction, consider the use of desmopressin.

In patients with excessive bleeding, consider topical hemostatics such as fibrin glue or thrombin gel.

In patients with excessive bleeding, consider the use of antifibrinolytics (i.e., ε-aminocaproic acid, tranexamic acid) if not already being used.

- In patients with excessive bleeding and elevated INR, consider the use of prothrombin complex concentrates.

- In patients with excessive bleeding, consider the use of fibrinogen concentrate.‡‡‡‡

- When traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider recombinant activated factor VII. §§§§

‡‡‡‡ Fibrinogen concentrate is now available in the United States.
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The Task Force cautions that there may be a risk of arterial thrombosis with the use of activated factor VII that can result in a myocardial infarction, especially in older patients.
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40


Table 1: Suggested Criteria for Perioperative Transfusion of Non-RBC Blood Products

### Platelets

- Platelet transfusion may be indicated despite an apparently adequate platelet count or in the absence of a platelet count if there is known or suspected platelet dysfunction (e.g., the presence of potent antiplatelet agents, cardiopulmonary bypass, congenital platelet dysfunction) and bleeding.†††††
- In surgical or obstetric patients, platelet transfusion is rarely indicated if the platelet count is known to be greater than $100 \times 10^9$ /L and is usually indicated when the count is below $50 \times 10^9$ /L in the presence of excessive bleeding.

### Fresh Frozen Plasma

- FFP is indicated:
  - For correction of excessive microvascular bleeding (i.e., coagulopathy) in the presence of an INR greater than 2.0, in the absence of heparin
  - For correction of excessive microvascular bleeding secondary to coagulation factor deficiency in patients transfused with more than one blood volume (approximately 70ml/kg) and when PT or INR and aPTT cannot be obtained in a timely fashion
  - For urgent reversal of warfarin therapy when PCCs are not available
  - For correction of known coagulation factor deficiencies for which specific concentrates are unavailable.
- FFP is not indicated:
  - If PT or INR and aPTT are normal.
  - Solely for augmentation of plasma volume or albumin concentration.
- Administer FFP in doses calculated to achieve a minimum of 30% of plasma factor concentration. Four to five platelet concentrates, 1 unit single-donor apheresis platelets, or 1 unit fresh whole blood‡‡‡‡‡ provide a quantity of coagulation factors similar to that contained in one unit FFP.

### Cryoprecipitate

- Cryoprecipitate is indicated:
  - When a test of fibrinogen activity indicates a deficiency.
  - When the fibrinogen concentration is less than 80-100 mg/dl in the presence of excessive bleeding.
  - As an adjunct in massively transfused patients when fibrinogen concentrations cannot be measured in a timely fashion.
  - For patients with congenital fibrinogen deficiencies.

***** This table displays some transfusion criteria that may suggest when to transfuse with the above blood products. The decision to apply some or all of the criteria shown in this table is dependent upon the clinical context and judgment of the practitioner. The table is not intended as a mandatory or exhaustive list. Scientific evidence is insufficient to evaluate the perioperative benefit of applying the above suggested criteria.
††††† The proper dose of platelets should be based on recommendations of the local institutional transfusion committee.
‡‡‡‡‡ Many institutions in the United States no longer have fresh whole blood available from the blood bank.
Whenever possible, decisions regarding patients with congenital fibrinogen deficiencies should be made in consultation with the patient's hematologist.

- Transfusion of cryoprecipitate is rarely indicated if fibrinogen concentration is greater than 150 mg/dl in non-pregnant patients.
- Treat bleeding patients with von Willebrand disease types 1 and 2A with desmopressin and subsequently with specific VWF/FVIII concentrate, if available. Cryoprecipitate should be administered if there is no response to or availability of desmopressin or VWF/FVIII concentrate.
- Treat bleeding patients with von Willebrand disease types 2B, 2M, 2N and 3 with specific VWF/FVIII concentrate, if available. If VWF/FVIII concentrate is not available, cryoprecipitate is indicated.
Appendix I: Summary of Recommendations

I. Patient Evaluation

- Review previous medical records and interview the patient or family to identify:
  - Prior blood transfusion.
  - History of drug-induced coagulopathy (e.g., warfarin, clopidogrel, aspirin and other anticoagulants, as well as vitamins or herbal supplements that may affect coagulation.
  - The presence of congenital coagulopathy.
  - History of thrombotic events (e.g., deep vein thrombosis, pulmonary embolism).
  - Risk factors for organ ischemia (e.g., cardiorespiratory disease) which may influence the ultimate transfusion trigger for red blood cells (e.g., hemoglobin level).
- Inform patients of the potential risks versus benefits of blood transfusion and elicit their preferences.
- Review available laboratory test results including hemoglobin, hematocrit and coagulation profiles.
- Order additional laboratory tests depending on a patient’s medical condition (e.g., coagulopathy, anemia).
- Conduct a physical examination of the patient (e.g., ecchymoses, petechiae, pallor).
- If possible, perform the preoperative evaluation well enough in advance (e.g., several days to weeks) to allow for proper patient preparation.

II. Preadmission Patient Preparation

- Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in selected patient populations (e.g., renal insufficiency, anemia of chronic disease, refusal of transfusion).§§§§§
- Administer iron to patients with iron deficiency anemia if time permits.
- In consultation with an appropriate specialist, discontinue anticoagulation therapy (e.g., warfarin, anti-Xa drugs, antithrombin agents) for elective surgery.
  - Transition to a shorter acting drug (e.g., heparin, low molecular weight heparin) may be appropriate in selected patients.
- If clinically possible, discontinue non-aspirin antiplatelet agents (e.g., thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions.
  - Aspirin may be continued on a case-by-case basis.
- The risk of thrombosis versus the risk of increased bleeding should be considered

§§§§§ The Task Force recognizes that erythropoietin administration is perceived as being expensive and requires time (in weeks) to induce a significant increase in hemoglobin concentration.
****** The Task Force cautions that clopidogrel and aspirin should not be stopped prior to surgery in patients with coronary stents placed in the last 3 months for bare metal stents and 1 year for drug eluting stents due to the risk of perioperative myocardial infarction. See “American Society of Anesthesiologists Committee on Standards and Practice Parameters: Practice alert for the perioperative management of patients with coronary artery stents: a report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters. Anesthesiology. 2009; 110:22-23.
when altering anticoagulation status.

- Assure that blood and blood components are available for patients when significant blood loss or transfusion is expected.
- When autologous blood is preferred, the patient may be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution.††††††

**III. Preprocedure Preparation**

**Blood management protocols:**

- Multimodal protocols or algorithms may be employed as strategies to reduce the utilization of blood products. However, no single algorithm or protocol can be recommended at this time.
- A restrictive red blood cell transfusion strategy may be safely used to reduce transfusion requirements.
  - Transfusion of red blood cells is rarely necessary when the hemoglobin concentration is more than 10 g/dl.‡‡‡‡‡‡
  - The determination of whether hemoglobin concentrations between 6 and 10 g/dl justify or require red blood cell transfusion should be based on potential or actual ongoing bleeding (rate and magnitude), intravascular volume status, signs of organ ischemia, and inadequate cardiopulmonary reserve.
  - Red blood cells should be administered unit-by-unit, when possible, with interval reevaluation.
- A protocol for avoidance of transfusion (i.e., bloodless surgery) may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible.
- A massive (i.e., hemorrhagic) transfusion protocol may be used when available as a strategy to optimize the delivery of blood products to massively bleeding patients.
- Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices.

**Reversal of anticoagulants:**

- For urgent reversal of warfarin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer fresh frozen plasma (FFP).
- Administer vitamin K for non-urgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required.

**Antifibrinolytics to minimize blood loss:**

- Use antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass.
  - Consider using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding.

†††††† The Task Force cautions that preadmission blood donation may induce preoperative anemia, increase total intraoperative (autologous or allogeneic) transfusions, and increase costs.
‡‡‡‡‡‡ Red blood cells refers to all red blood cell containing components.
Acute normovolemic hemodilution:

- Use acute normovolemic hemodilution (ANH) to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (e.g., major cardiac, orthopedic, thoracic, or liver surgery), if possible. §§§

IV. Intraoperative and Postoperative Management of Blood Loss and Transfusions

Allogeneic red blood cell transfusion:

- Administer blood without consideration of duration of storage.
- Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion.

Reinfusion of recovered red blood cells:

- Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative period, when appropriate.

Intraoperative and postoperative patient monitoring:

- Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (i.e., coagulopathy) or surgical bleeding.
- Use standard methods for quantitative measurement of blood loss, including checking suction canisters, surgical sponges, and surgical drains.
- Monitor for perfusion of vital organs using standard ASA monitors (i.e., blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical exam features. *******
- Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (i.e., cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation.
- If anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs.
- If coagulopathy is suspected, obtain viscoelastic assays (e.g., thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), when available, as well as platelet count.
  - If viscoelastic assays are not available, obtain standard coagulation tests (e.g., international normalization ratio (INR), aPTT, fibrinogen concentration), as well as platelet count for monitoring.
- During and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension and signs of hypocalcemia.
  - Before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing.

§§§§§§ ANH may not be possible due to preexisting patient factors such as small blood volume, low hemoglobin, or presence of ischemic disease.

******* American Society of Anesthesiologists: Standards for Basic Anesthetic Monitoring (last amended October 20, 2010, effective date July 1, 2011).
Prophylaxis and treatment of excessive bleeding:

- In patients at risk for excessive bleeding, use prophylactic antifibrinolytic therapy to reduce the bleeding and risk of transfusion.
- In patients with excessive bleeding, obtain a platelet count before transfusion of platelets if possible. In addition, obtain a test of platelet function, if available, in patients with suspected or drug-induced (e.g., clopidogrel) platelet dysfunction.
- In patients with excessive bleeding, obtain coagulation tests (i.e., PT or INR and aPTT) before transfusion of FFP, if possible.
- In patients with excessive bleeding, assess fibrinogen levels before the administration of cryoprecipitate, if possible.
- In patients with excessive bleeding and platelet dysfunction, consider the use of desmopressin.
- In patients with excessive bleeding, consider topical hemostatics such as fibrin glue, or thrombin gel.
- In patients with excessive bleeding, consider the use of antifibrinolytics (i.e., ε-aminocaproic acid, tranexamic acid) if not already being used.
- In patients with excessive bleeding and elevated INR, consider the use of prothrombin complex concentrates.
- In patients with excessive bleeding, consider the use of fibrinogen concentrate.
- When traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider recombinant activated factor VII.

††††††† Fibrinogen concentrate is now available in the United States.
‡‡‡‡‡‡‡ The Task Force cautions that there may be a risk of arterial thrombosis with the use of activated factor VII that can result in a myocardial infarction, especially in older patients.
Appendix 2: Methods and Analyses

A. State of the Literature.

For these updated Guidelines, a review of studies used in the development of previous update was combined with studies published subsequent to approval of the update in 2005. The scientific assessment of these Guidelines was based on evidence linkages or statements regarding potential relationships between clinical interventions and outcomes. The interventions listed below were examined to assess their relationship to a variety of outcomes related to the perioperative blood transfusion and adjuvant therapies.

Patient Evaluation:

- Reviewing medical records (checking for acquired or congenital conditions, previous lab tests)
- Conducting a patient interview
- Conducting/ordering new laboratory tests when indicated
  - Hemoglobin or hematocrit (to identify preoperative anemia)
  - Coagulation profile (PT, aPTT, ACT, TEG)
  - Type and cross versus type and screen
  - Maximum surgical blood ordering schedule for elective procedures

Preadmission Patient Preparation:

- Prevention or reduction of perioperative anemia
  - Erythropoietin
  - Iron
- Discontinuation of anticoagulants
  - Warfarin
- Discontinuation of anti-thrombotic agents
  - Clopidogrel, Ticagralor, Prasugrel or other thienopyridines
  - Aspirin
- Preadmission autologous blood donation (PAD)
  - PAD versus allogeneic blood or blood products
  - PAD versus preprocedure acute normovolemic hemodilution (ANH)
  - PAD versus intraoperative or postoperative blood recovery

Preprocedure preparation:

- Blood management protocol
  - Multimodality protocol or algorithm
  - Liberal versus restrictive transfusion protocol

PRACTICE GUIDELINES

Non-transfusion protocol (i.e., bloodless surgery)
- Massive transfusion protocol
- Maximum surgical blood ordering schedule for elective procedures

Reversal of anticoagulants
- Prothrombin complex concentrates (PCC)
  - Bebulin
  - Profilnin
  - Kcentra (Beriplex, Confidex)
- Vitamin K

Antifibrinolytics to minimize blood loss
- \( \varepsilon \)-Aminocaproic acid
- Tranexamic acid

Acute normovolemic hemodilution (ANH)
- ANH versus no ANH
- ANH combined with intraoperative blood recovery (ICSB) versus either ANH or ICSB

Intraoperative and Postoperative Interventions:

Allogeneic red blood cell transfusion:
- Age of stored RBCs
- Leukocyte reduction

Autologous red blood cell transfusion:
- Intraoperative blood recovery
  - Cell salvage
  - Whole blood (WB)
- Postoperative blood recovery
  - Cell salvage
  - Whole blood (WB)

Intraoperative and postoperative patient monitoring:
- Monitoring blood loss:
  - Visual assessment of the surgical field
    - Extent of blood present
    - Presence of microvascular bleeding
    - Surgical sponges
    - Clot size and shape
    - Volume in suction canister
  - Monitoring for inadequate perfusion and oxygenation of vital organs
    - Cardiac monitoring (blood pressure, heart rate, oxygen saturation)
    - Renal monitoring (urine output)
    - Cerebral monitoring
      - Cerebral oximetry
      - Near infrared spectroscopy (NIRS)
    - Arterial blood gas measurement
    - Mixed venous oxygen saturation
  - Monitoring for non-RBC transfusion – coagulopathy
    - Platelet function monitoring
    - Viscoelastic haemostatic assays (VHA)
      - Thromboelastography (TEG)
• Rotational thromboelastometry (ROTEM)
  o Monitoring (periodic checking) for adverse effects of transfusions
    ▪ Transfusion-related acute lung injury (TRALI)
    ▪ Hemolytic (ABO incompatibility) transfusion reactions
    ▪ Citrate toxicity (hypocalcemia)
    ▪ Transfusion-associated circulatory overload (TACO)
    ▪ Bacterial contamination
    ▪ Immunomodulation (e.g., graft versus host disease [GVHD], infection)
• Prophylaxis and treatment of excessive bleeding
  o Transfusion treatments:
    ▪ Platelet transfusion
    ▪ Fresh frozen plasma transfusion
    ▪ Cryoprecipitate
  o Pharmacologic treatments:
    ▪ Desmopressin (DDAVP)
    ▪ Antifibrinolytics
      ▪ $\varepsilon$-Aminocaproic acid
      ▪ Tranexamic acid
    ▪ Topical hemostatics
      ▪ Fibrin glue
      ▪ Thrombin gel
    ▪ Prothrombin complex concentrates (PCC)
      ▪ PCC versus FFP
      ▪ Bebulin
      ▪ Profilnin
      ▪ Kcentra (Beriplex, Confidex)
    ▪ Coagulation factor concentrates
      ▪ Recombinant Factor VIIa
    ▪ Treatments for hypofibrinogenemia:
      ▪ Cryoprecipitate
      ▪ Fibrinogen concentrate (Riastap)

For the literature review, potentially relevant clinical studies were identified via electronic and manual searches of the literature. The updated searches covered an 11-year period from 2004 through 2014. Over 1800 new citations that addressed topics related to the evidence linkages were identified. These articles were reviewed and those meeting the appropriate criteria as outlined in the “Focus” section above were combined with pre-2005 articles used in the previous update, resulting in a total of 521 articles that contained direct linkage-related evidence. A complete bibliography used to develop these Guidelines, organized by section, is available as Supplemental Digital Content 2, http://links.lww.com/ALN/____.
Initially, each pertinent study finding was classified and summarized to determine meta-analysis potential. Literature pertaining to ten evidence linkages contained enough studies with well-defined experimental designs and statistical information sufficient for meta-analyses. These linkages were (1) erythropoietin versus placebo, (2) \( \varepsilon \)-aminocaproic acid versus placebo; (3) tranexamic acid versus placebo administered before or during surgery, (4) acute normovolemic hemodilution (ANH) versus no acute normovolemic hemodilution; (5) ANH with intraoperative red blood cell recovery versus red blood cell recovery alone, (6) restrictive versus liberal transfusion strategy, (7) intraoperative red blood cell recovery versus conventional transfusion, (8) desmopressin versus placebo, (9) tranexamic acid versus placebo administered after surgery, (10) fibrin glue versus no fibrin glue, and (11) recombinant activated factor VII versus placebo (Table 2).

General variance-based effect-size estimates or combined probability tests were obtained for continuous outcome measures, and Mantel-Haenszel odds-ratios were obtained for dichotomous outcome measures. Two combined probability tests were employed as follows: (1) the Fisher combined test, producing chi-square values based on logarithmic transformations of the reported P values from the independent studies, and (2) the Stouffer combined test, providing weighted representation of the studies by weighting each of the standard normal deviates by the size of the sample. An odds-ratio procedure based on the Mantel-Haenszel method for combining study results using 2 x 2 tables was used with outcome frequency information. An acceptable significance level was set at \( P < 0.01 \) (one-tailed). Tests for heterogeneity of the independent studies were conducted to assure consistency among the study results. DerSimonian-Laird random-effects odds ratios were obtained when significant heterogeneity was found (\( P < 0.01 \)). To control for potential publishing bias, a "fail-safe n" value was calculated. No search for unpublished studies was conducted, and no reliability tests for locating research results were
done. To be accepted as significant findings, Mantel-Haenszel odds-ratios must agree with combined test results whenever both types of data are assessed. In the absence of Mantel-Haenszel odds-ratios, findings from both the Fisher and weighted Stouffer combined tests must agree with each other to be acceptable as significant.

For the previous update, interobserver agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a kappa (k) statistic for two-rater agreement pairs were as follows: (1) type of study design, $k = 0.82-1.00$; (2) type of analysis, $k = 0.82-1.00$; (3) evidence linkage assignment, $k = 0.93-1.00$; and (4) literature inclusion for database, $k = 0.76-1.00$. Three-rater chance-corrected agreement values were: (1) study design, $Sav = \_\_\_$, Var $(Sav) = \_\_.\_\_\_$; (2) type of analysis, $Sav = \_\_\_$, Var $(Sav) = \_\_.\_\_\_$; (3) linkage assignment, $Sav = \_\_\_\_$, Var $(Sav) = \_\_.\_\_\_$; (4) literature database inclusion, $Sav = \_\_\_\_$ Var $(Sav) = \_\_.\_\_\_\_\_\_\_\_\_$ These values represent moderate to high levels of agreement.

B. Consensus-Based Evidence.

For the previous update, consensus was obtained from multiple sources, including: (1) survey opinion from consultants who were selected based on their knowledge or expertise in perioperative blood transfusion and adjuvant therapies, (2) survey opinions from a randomly selected sample of active members of the ASA, (3) testimony from attendees of two publicly-held open forums at two national anesthesia meetings, ******* (4) Internet commentary, and (5) Task Force opinion and interpretation. The survey rate of return was 31% ($n = 21$ of 67) for consultants, and 29% ($n = 87$ of 300) for membership respondents. Survey results are reported in Tables 3 and 4, and summarized in the text of the Guidelines.

For the previous update, the consultants were asked to indicate which, if any, of the evidence linkages would change their clinical practices if the Guidelines were instituted. The rate of

return was 24% (n = 16 of 67). The percent of responding consultants expecting no change
associated with each linkage were as follows: preoperative evaluation - 75%; discontinuation of
anticoagulation and delay of surgery- 94%; drugs to manage perioperative anemia - 75%; drugs
to promote coagulation and minimize blood loss - 81%; preoperative autologous blood collection
- 88%; monitoring for inadequate perfusion and oxygenation - 94%; monitoring for transfusion
indications - 88%; transfusion of allogeneic red blood cells - 94%, transfusion of autologous
blood - 100%; transfusion of platelets - 88%; transfusion of FFP - 88%; transfusion of
cryoprecipitate - 94%; treatment of excessive bleeding - 88%; and monitoring and laboratory
testing for transfusion reactions - 88%. Eighty-eight percent of the respondents indicated that the
Guidelines would have no effect on the amount of time spent on a typical case. Two respondents
(12%) indicated that there would be an increase in the amount of time they would spend on a
typical case with the implementation of these Guidelines. The amount of increased time
anticipated by these respondents ranged from 5-10 min.
### Table 2. Meta-Analysis Summary

<table>
<thead>
<tr>
<th>Linkages</th>
<th>N</th>
<th>Fisher Chi-square</th>
<th>p</th>
<th>Weighted Stouffer Zc</th>
<th>p</th>
<th>Effect Size</th>
<th>Mantel-Haenszel OR</th>
<th>CI</th>
<th>Heterogeneity Significance</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preadmission patient preparation</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>Prevent or reduction of perioperative anemia</strong></td>
<td></td>
<td></td>
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<tr>
<td>Erythropoietin vs. placebo</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood volume transfused</td>
<td>8</td>
<td>67.93</td>
<td>0.001</td>
<td>-4.80</td>
<td>0.001</td>
<td>0.21</td>
<td>-</td>
<td>-</td>
<td>0.001</td>
<td>0.003</td>
</tr>
<tr>
<td>Patients transfused</td>
<td>15</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.38</td>
<td>0.27-0.53</td>
<td>-</td>
<td>0.039</td>
</tr>
<tr>
<td>Pts. transfused (without iron)</td>
<td>7</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.45</td>
<td>0.26-0.78</td>
<td>-</td>
<td>0.038</td>
</tr>
<tr>
<td>Pts. transfused (with iron)</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.34</td>
<td>0.23-0.52</td>
<td>-</td>
<td>0.179</td>
</tr>
<tr>
<td><strong>Antifibrinolytics to minimize blood loss (administered before and/or during surgery)</strong></td>
<td></td>
<td></td>
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<tr>
<td>ε-Aminocaproic acid vs. placebo</td>
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</tr>
<tr>
<td>Total blood loss</td>
<td>7</td>
<td>58.34</td>
<td>0.001</td>
<td>-5.35</td>
<td>0.001</td>
<td>-0.28</td>
<td>-</td>
<td>-</td>
<td>0.490</td>
<td>0.597</td>
</tr>
<tr>
<td>Patients transfused</td>
<td>9</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.58</td>
<td>0.33-0.96</td>
<td>-</td>
<td>0.043</td>
</tr>
<tr>
<td>Tranexamic acid vs. placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Intraoperative blood loss</td>
<td>10</td>
<td>68.83</td>
<td>0.001</td>
<td>-4.41</td>
<td>0.001</td>
<td>-0.19</td>
<td>-</td>
<td>-</td>
<td>0.343</td>
<td>0.340</td>
</tr>
<tr>
<td>Postoperative blood loss</td>
<td>12</td>
<td>172.51</td>
<td>0.001</td>
<td>-10.20</td>
<td>0.001</td>
<td>-0.36</td>
<td>-</td>
<td>-</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Total blood loss</td>
<td>13</td>
<td>180.64</td>
<td>0.001</td>
<td>-6.22</td>
<td>0.001</td>
<td>-0.30</td>
<td>-</td>
<td>-</td>
<td>0.051</td>
<td>0.002</td>
</tr>
<tr>
<td>Patients transfused</td>
<td>13</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.29</td>
<td>0.13-0.86</td>
<td>-</td>
<td>0.005</td>
</tr>
<tr>
<td><strong>Acute Normovolemic Hemodilution (ANH)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ANH vs. no ANH</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Volume transfused with allogeneic blood</td>
<td>7</td>
<td>60.84</td>
<td>0.001</td>
<td>-2.79</td>
<td>0.003</td>
<td>-0.21</td>
<td>-</td>
<td>-</td>
<td>0.003</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients transfused with allogeneic blood</td>
<td>11</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.59</td>
<td>0.38-0.90</td>
<td>-</td>
<td>0.308</td>
</tr>
</tbody>
</table>
ANH+intraoperative blood recovery versus intraoperative blood recovery

<table>
<thead>
<tr>
<th>Volume transfused with allogeneic blood</th>
<th>7</th>
<th>64.52</th>
<th>0.001</th>
<th>-5.05</th>
<th>0.001</th>
<th>-0.21</th>
<th>-</th>
<th>-</th>
<th>0.011</th>
<th>0.017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients transfused with allogeneic blood</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.71</td>
<td>0.48-1.05</td>
<td>-</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Intraoperative and postoperative interventions

Restrictive versus liberal transfusion protocol

| Volume transfused with allogeneic blood | 5 | 49.88 | 0.001 | -3.31 | 0.001 | -0.13 | - | - | 0.022 | 0.001 |

Intraoperative blood recovery versus conventional transfusion

<table>
<thead>
<tr>
<th>Volume transfused with allogeneic blood</th>
<th>7</th>
<th>66.07</th>
<th>0.001</th>
<th>-4.16</th>
<th>0.001</th>
<th>-0.26</th>
<th>-</th>
<th>-</th>
<th>0.036</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients transfused with allogeneic blood</td>
<td>9</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.29</td>
<td>0.10-1.22</td>
<td>-</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Drugs to treat excessive bleeding

Desmopressin vs. placebo

<table>
<thead>
<tr>
<th>Postoperative blood loss</th>
<th>6</th>
<th>51.72</th>
<th>0.001</th>
<th>-2.34</th>
<th>0.010</th>
<th>-0.11</th>
<th>-</th>
<th>-</th>
<th>0.001</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients transfused</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.92</td>
<td>0.51-1.66</td>
<td>-</td>
<td>0.125</td>
</tr>
</tbody>
</table>

Antifibrinolytics (administered after surgery)

Tranexamic acid vs. placebo

<table>
<thead>
<tr>
<th>Total blood loss</th>
<th>5</th>
<th>91.77</th>
<th>0.001</th>
<th>-10.84</th>
<th>0.001</th>
<th>-0.59</th>
<th>-</th>
<th>-</th>
<th>0.043</th>
<th>0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients transfused</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.33</td>
<td>0.49-2.38</td>
<td>-</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Topical hemostatics

Fibrin glue vs. no fibrin glue

<p>| Postop/total blood loss | 11 | 145.03 | 0.001 | -4.34 | 0.001 | -0.29 | - | - | 0.001 | 0.001 |</p>
<table>
<thead>
<tr>
<th>Patients transfused</th>
<th>7</th>
<th>-</th>
<th>-</th>
<th>-</th>
<th>-</th>
<th>-</th>
<th>0.58</th>
<th>0.34-0.97</th>
<th>-</th>
<th>0.012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VII vs. no Factor VII (^1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood volume transfused</td>
<td>5</td>
<td>44.55</td>
<td>0.001</td>
<td>-0.01</td>
<td>0.496</td>
<td>-0.21</td>
<td>-</td>
<td>-</td>
<td>0.075</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients transfused (^2)</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.16</td>
<td>0.03-2.85</td>
<td>-</td>
<td>0.001</td>
</tr>
</tbody>
</table>

\(^1\) Double-blind studies only.
\(^2\) DerSimonian-Laird random effects odds ratio.

CI = 99% confidence interval; OR = odds ratio; pts = patients
Table 3. Consultant Survey Responses

<table>
<thead>
<tr>
<th>I. Patient Evaluation:</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Uncertain</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Review previous medical records and interview the patient or family to identify prior blood transfusion, history of drug-induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischemia</td>
<td>74</td>
<td>68.9*</td>
<td>24.3</td>
<td>2.7</td>
<td>4.1</td>
</tr>
<tr>
<td>2. Inform patients of the potential risks versus benefits of blood transfusion and elicit their preferences</td>
<td>74</td>
<td>75.7*</td>
<td>12.2</td>
<td>8.1</td>
<td>4.1</td>
</tr>
<tr>
<td>3. Review available laboratory test results including hemoglobin, hematocrit, and coagulation profiles and order additional laboratory tests depending on a patient’s medical condition (e.g., coagulopathy, anemia)</td>
<td>74</td>
<td>91.9*</td>
<td>6.8</td>
<td>1.4</td>
<td>0.0</td>
</tr>
<tr>
<td>4. Conduct a physical examination of the patient (e.g., ecchymoses, petechiae, pallor)</td>
<td>74</td>
<td>58.1*</td>
<td>29.7</td>
<td>10.8</td>
<td>1.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>II. Preadmission Patient Preparation:</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Uncertain</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in select patient populations (e.g., renal insufficiency, anemia of chronic disease, refusal of transmission)</td>
<td>74</td>
<td>43.2</td>
<td>30.6*</td>
<td>19.4</td>
<td>5.6</td>
</tr>
<tr>
<td>6. Administer iron to patients with iron deficiency anemia if time permits</td>
<td>71</td>
<td>63.4*</td>
<td>31.0</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td>7. In consultation with an appropriate specialist, discontinue anticoagulation therapy (e.g., warafin, anti-Xa drugs, anti-thrombin agents) for elective surgery</td>
<td>71</td>
<td>74.6*</td>
<td>14.1</td>
<td>11.3</td>
<td>0.0</td>
</tr>
<tr>
<td>8. If clinically possible, discontinue non-aspirin antiplatelet agents (e.g., thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions)</td>
<td>71</td>
<td>66.2*</td>
<td>18.3</td>
<td>12.7</td>
<td>2.8</td>
</tr>
<tr>
<td>9. The risk of thrombosis versus the risk of increased bleeding should be considered when altering anticoagulation status</td>
<td>72</td>
<td>88.9*</td>
<td>11.1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

†††††††† N = the number of consultants who responded to each item. An asterisk beside a percentage score indicates the median.
10. Assure that blood and blood components are available for patients when significant blood loss or transfusion is expected

11. When autologous blood is preferred, the patient should be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution

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### III. Preprocedure Preparation:

#### Blood Management Protocols

12. Employ multimodal protocols or algorithms as strategies to reduce the utilization of blood products

13. A restrictive red blood cell transfusion strategy may be used to reduce transfusion requirements

14. A protocol for avoidance of transfusion (i.e., bloodless surgery) may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible

15. Use massive transfusion protocol when available as a strategy to optimize the delivery of blood products to massively bleeding patients

16. Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices

---

#### Reversal of Anticoagulants

17. For urgent reversal of warfarin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer fresh frozen plasma (FFP)

18. Administer vitamin K for non-urgent reversal of warfarin, except when rapid restoration of anticoagulation after surgery is required

---

#### Antifibrinolytics to Minimize Blood Loss

19. Use antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass

20. Consider using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding
Acute Normovolemic Hemodilution
21. Use acute normovolemic hemodilution (ANH) to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (e.g., major cardiac, orthopedic, thoracic, or liver surgery), if possible  

IV. Intraoperative and Postoperative Management of Blood Loss and Transfusions:

Allogeneic Red Blood Cell Transfusion
22. Administer blood without consideration of duration of storage

23. Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion

Reinfusion of Recovered Red Blood Cells
24. Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative and/or postoperative period

Intraoperative and Postoperative Patient Monitoring
25. Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (i.e., coagulopathy) or surgical bleeding

26. Use standard methods for quantitative measurement of blood loss including checking suction canisters, surgical sponges, and surgical drains

27. Monitor for perfusion of vital organs using standard ASA monitors (i.e., blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical exam features

28. Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (i.e., cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation

29. If anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs
30. If coagulopathy is suspected, obtain viscoelastic assays (e.g., thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), when available, as well as platelet count

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</thead>
<tbody>
<tr>
<td>70</td>
<td>48.6</td>
<td>25.7*</td>
<td>14.3</td>
<td>7.1</td>
<td>4.3</td>
</tr>
</tbody>
</table>

31. If viscoelastic assays are not available, obtain standard coagulation tests (e.g., international normalization ratio [INR], aPTT, fibrinogen concentration), as well as platelet count for monitoring

<p>| | | | | | |</p>
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</thead>
<tbody>
<tr>
<td>70</td>
<td>68.6*</td>
<td>28.6</td>
<td>1.4</td>
<td>1.4</td>
<td>0.0</td>
</tr>
</tbody>
</table>

32. During and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension, and signs of hypocalcemia

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</thead>
<tbody>
<tr>
<td>71</td>
<td>73.2*</td>
<td>25.4</td>
<td>1.4</td>
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33. Before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing

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Prophylaxis and Treatment of Excessive Bleeding

34. In patients at risk for excessive bleeding, use prophylactic antifibrinolytic therapy to reduce the bleeding and risk of transfusion

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<td>39.4*</td>
<td>16.9</td>
<td>11.3</td>
<td>4.2</td>
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35. In patients with excessive bleeding:
   a) obtain a platelet count before transfusion of platelets if possible
   b) in addition, obtain a test of platelet function, if available, in patients with suspected or drug-induced (e.g., clopidogrel) platelet dysfunction

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36. In patients with excessive bleeding, obtain coagulation tests (i.e., PT or INR and aPTT) before transfusion of FFP, if possible

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<td>31.0*</td>
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37. In patients with excessive bleeding, assess fibrinogen levels before the administration of cryoprecipitate, if possible

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38. In patients with excessive bleeding and platelet dysfunction, consider the use of desmopressin

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<td>4.3</td>
<td>1.4</td>
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39. In patients with excessive bleeding, consider topical hemostatics such as fibrin glue or thrombin gel

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40. In patients with excessive bleeding, consider the use of antifibrinolytics (i.e., ε-aminocaproic acid, tranexamic acid), if not already being used

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<td>70</td>
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<td>40.0*</td>
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</table>
41. In patients with excessive bleeding and elevated INR, consider the use of prothrombin complex concentrates (PCCs) 70 30.0 38.6* 24.3 1.4 5.7

42. In patients with excessive bleeding, consider the use of fibrinogen concentrate 70 22.9 37.1* 30.0 4.3 5.7

43. When traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider administering recombinant activated factor VII 71 22.5 49.3* 16.9 5.6 5.6

Table 4. ASA Membership Survey Responses

<table>
<thead>
<tr>
<th>I. Patient Evaluation:</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Uncertain</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td></td>
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<tr>
<td>1. Review previous medical records and interview the patient or family to identify prior blood transfusion, history of drug-induced coagulopathy, presence of congenital coagulopathy, history of thrombotic events, and risk factors for organ ischemia 386 54.9* 24.1 14.2 4.9 1.8</td>
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<tr>
<td>2. Inform patients of the potential risks versus benefits of blood transfusion and elicit their preferences 382 47.4 29.3* 17.3 4.2 1.8</td>
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</tbody>
</table>

N = the number of ASA members who responded to each item. An asterisk beside a percentage score indicates the median.
3. Review available laboratory test results including hemoglobin, hematocrit, and coagulation profiles and order additional laboratory tests depending on a patient’s medical condition (e.g., coagulopathy, anemia)  

4. Conduct a physical examination of the patient (e.g., ecchymoses, petechiae, pallor)  

II. Preadmission Patient Preparation:  
5. Erythropoietin with or without iron may be administered when possible to reduce the need for allogeneic blood in select patient populations (e.g., renal insufficiency, anemia of chronic disease, refusal of transmission)  
6. Administer iron to patients with iron deficiency anemia if time permits  
7. In consultation with an appropriate specialist, discontinue anticoagulation therapy (e.g., warafin, anti-Xa drugs, anti-thrombin agents) for elective surgery  
8. If clinically possible, discontinue non-aspirin antiplatelet agents (e.g., thienopyridines such as clopidogrel, ticagrelor, or prasugrel) for a sufficient time in advance of surgery, except for patients with a history of percutaneous coronary interventions)  
9. The risk of thrombosis versus the risk of increased bleeding should be considered when altering anticoagulation status  
10. Assure that blood and blood components are available for patients when significant blood loss or transfusion is expected  
11. When autologous blood is preferred, the patient should be offered the opportunity to donate blood before admission only if there is adequate time for erythropoietic reconstitution  

III. Preprocedure Preparation:  

Blood Management Protocols  
12. Employ multimodal protocols or algorithms as strategies to reduce the utilization of blood products
13. A restrictive red blood cell transfusion strategy may be used to reduce transfusion requirements.

14. A protocol for avoidance of transfusion (i.e., bloodless surgery) may be used as a strategy to reduce blood loss for patients in whom transfusion is refused or is not possible.

15. Use massive transfusion protocol when available as a strategy to optimize the delivery of blood products to massively bleeding patients.

16. Use a maximal surgical blood order schedule, when available and in accordance with your institutional policy, as a strategy to improve the efficiency of blood ordering practices.

Reversal of Anticoagulants

17. For urgent reversal of warafin, administer prothrombin complex concentrates (PCCs) in consultation with the appropriate specialist, or administer fresh frozen plasma (FFP).

18. Administer vitamin K for non-urgent reversal of warafin, except when rapid restoration of anticoagulation after surgery is required.

Antifibrinolytics to Minimize Blood Loss

19. Use antifibrinolytic therapy to reduce allogeneic blood transfusion in patients undergoing cardiopulmonary bypass.

20. Consider using antifibrinolytic therapy in other clinical circumstances at high-risk for excessive bleeding.

Acute Normovolemic Hemodilution

21. Use acute normovolemic hemodilution (ANH) to reduce allogeneic blood transfusion in patients at high-risk for excessive bleeding (e.g., major cardiac, orthopedic, thoracic, or liver surgery), if possible.

IV. Intraoperative and Postoperative Management of Blood Loss and Transfusions:

Allogeneic Red Blood Cell Transfusion

22. Administer blood without consideration of duration of storage.
23. Leukocyte reduced blood may be used for transfusion for the purpose of reducing complications associated with allogeneic blood transfusion

Reinfusion of Recovered Red Blood Cells
24. Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative and/or postoperative period

Intraoperative and Postoperative Patient Monitoring
25. Periodically conduct a visual assessment of the surgical field jointly with the surgeon to assess the presence of excessive microvascular (i.e., coagulopathy) or surgical bleeding
26. Use standard methods for quantitative measurement of blood loss including checking suction canisters, surgical sponges, and surgical drains
27. Monitor for perfusion of vital organs using standard ASA monitors (i.e., blood pressure, heart rate, oxygen saturation, electrocardiography) in addition to observing clinical symptoms and physical exam features
28. Additional monitoring may include echocardiography, renal monitoring (urine output), cerebral monitoring (i.e., cerebral oximetry and near infrared spectroscopy), analysis of arterial blood gasses, and mixed venous oxygen saturation
29. If anemia is suspected, monitor hemoglobin/hematocrit values based on estimated blood loss and clinical signs
30. If coagulopathy is suspected, obtain viscoelastic assays (e.g., thromboelastography [TEG] and rotational thromboelastometry [ROTEM]), when available, as well as platelet count
31. If viscoelastic assays are not available, obtain standard coagulation tests (e.g., international normalization ratio [INR], aPTT, fibrinogen concentration), as well as platelet count for monitoring
32. During and after transfusion, periodically check for hyperthermia, hemoglobinuria, microvascular bleeding, hypoxemia, respiratory distress, elevated peak airway pressure, urticaria, hypotension, and signs of hypocalcemia
33. Before instituting therapy for transfusion reactions, stop the blood transfusion and order appropriate diagnostic testing

Prophylaxis and Treatment of Excessive Bleeding

34. In patients at risk for excessive bleeding, use prophylactic antifibrinolytic therapy to reduce the bleeding and risk of transfusion

35. In patients with excessive bleeding:
   a) obtain a platelet count before transfusion of platelets if possible
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42. In patients with excessive bleeding, consider the use of fibrinogen concentrate

43. When traditional options for treating excessive bleeding due to coagulopathy have been exhausted, consider administering recombinant activated factor VII
Appendix 3. Vitamin and Herbal Supplements that May Affect Blood Loss

Herbal Supplements that Decrease Platelet Aggregation

- Bilberry
- Bromelain
- Don quoi
- Feverfew
- Fish oil
- Flax seed oil
- Garlic
- Ginger
- Ginko biloba
- Grape seed extract
- Saw palmetto

Herbs that Inhibit Clotting

- Chamomile
- Dandelion root
- Dong quoi
- Horse chestnut

Vitamins that Affect Coagulation

- Vitamin K
- Vitamin E
Appendix 4. Adverse effects associated with transfusion

Acute intravascular hemolytic transfusion reactions occur when red cells break down in the intravascular space due to either a complement mediated immune mechanism (usually secondary to ABO incompatibility) or to physical damage to the red cells (osmotic or temperature related). Both mechanisms result in hemoglobinemia and hemoglobinuria. However, the severe, often fatal complications such as shock and DIC are usually only seen in ABO incompatibility. The frequency of fatalities due to ABO incompatibilities, once the major cause of transfusion-associated fatalities, has markedly decreased over the last decade as strict processes for identifying the patient and the blood units being transfused have been put in place. In the operating room, acute intravascular hemolytic transfusion reactions secondary to ABO incompatibility are manifested by intractable bleeding in the operating field, hypotension and shock, fever, and hemoglobinuria. Treatment consists of stopping the blood transfusion, supportive measures to maintain blood pressure, and aggressive transfusion of platelets, FFP, and cryoprecipitate to counteract the consumptive coagulopathy while maintaining oxygen carrying capacity through transfusion of type O Red Blood Cells.

Transfusion-associated acute lung injury (TRALI) is now the leading cause of transfusion-associated fatalities. It is caused by donor antibodies in plasma-containing blood components (usually FFP or platelets, and occasionally Red Blood Cells) interacting with antigens on the patient’s granulocytes (HLA or granulocyte specific) resulting in granulocytes aggregation and complement activation in the lung capillaries. The symptoms (fever, hypoxemia, acute respiratory distress, elevated peak airway pressure) occur within 6 hours after the transfusion. Except for the presence of fever, these symptoms are undistinguishable from those of transfusion-associated circulatory overload (TACO). Treatment consists of stopping the transfusion and instituting critical care supportive measures.
*Bacterial contamination of blood components* is most often associated with platelet transfusion as platelets are stored a 20-24 C which facilitates the growth of bacteria. There has been a significant decrease in the fatalities associated with bacterial contamination since 2001, as processes to detect bacterial contamination in platelets have been put into place. Bacterial contamination is manifested by hyperthermia. Treatment consists of stopping the transfusion and supportive measures.

*Allergic reactions* are caused by IgE antibodies in the patient against proteins in the plasma of the blood component transfused. As very small amounts of allergenic protein is needed to cause a reaction, any blood components can be associated with such a reaction except for washed blood. Symptoms usually are restricted to urticaria and other erythematous skin manifestations and subside spontaneously or with diphenhydramine administration. Occasionally allergic reactions are more severe and result in anaphylaxis.

Citrate is the anticoagulant used to collect blood components and it is present in significant amounts in all blood components. It readily binds calcium and magnesium. When large numbers of blood components are transfused over a short period of time, the metabolism of citrate is overwhelmed and the patient develops *citrate toxicity* (hypocalcemia and hypomagnesemia) which may result in adverse cardiac manifestations.