A Compendium of Transfusion Practice Guidelines
First Edition  2010

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Users of this brochure should refer to the Circular of Information regarding the approved indications, contraindications, and risks of transfusion, and for additional descriptions of blood components.

Copies of the Circular of Information can be obtained from your American Red Cross Blood Services region or the AABB (aabb.org). The complete text of the side effects and hazards of blood transfusion from the current Circular of Information appears in the appendix section of the brochure.

Users must also refer to the current Circular of Information and AABB Standards for regulatory requirements.
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INTRODUCTION

The art of transfusion has historically been based on personal experience, local practice, expert opinion, and consensus conference recommendations, frequently without a sound foundation in evidence-based medicine. Increasingly, the assumptions and practices of the past are being challenged by improvements in hemovigilance data that document the adverse effects of transfusion, randomized controlled trials (RCT) demonstrating both the benefits and risks of transfusion, and growing debates regarding alternate therapies. Current controversies include the potential advantages of leukoreduction and fresh whole blood transfusion, and the disadvantages of prolonged blood storage. The field of Transfusion Medicine is evolving rapidly, and transfusionists are rightfully demanding sound evidence upon which to base decisions before making substantial changes that may have a significant impact on practice, cost, and the availability of blood products.

The importance of optimum transfusion practice is increasingly under the purview of accrediting and regulatory agencies. Blood transfusion is acknowledged to be a therapy that involves risks, so that the organization’s performance monitoring and improvement program must address the use of blood and blood components, requiring that hospitals institute a cross-functional group of medical and support staff charged with the responsibility of oversight. Transfusion-related fatalities and ABO-incompatible transfusions have long been reportable sentinel events; however, the Joint Commission has seen the need for further standards to assess hospital transfusion practices, and is in the process of promulgating appropriate accreditation criteria.
Blood transfusion is life-saving when used appropriately, and dangerous if abused. Optimum patient care requires that the medical staff agree to a set of practice guidelines for ordering and administering blood products. Ideally, practice guidelines would be grounded in well-designed clinical trials that clearly establish efficacy and quantify risk in at least the most common settings in which therapy is applied. The current literature does provide guidelines for some of the more commonly encountered clinical situations. However, variability in transfusion practice often still reflects hospital tradition, as well as local and community practice.

This compendium is a review of the current blood usage guidelines published in English in peer-reviewed journals. Whenever possible, RCTs are included, but all too often the discussion is informed by expert panels and retrospective cohort studies. We have, when possible, avoided single institutional studies and controversial retrospective studies whose analysis and conclusions appear to be confounded, until prospective RCT data are available (for example, fresh versus old blood). The authors, all of whom are physician staff for the American Red Cross, have made every attempt to fairly reproduce the advice and lessons contained in these publications. They hope that this brochure will be a valuable resource to hospital staff who obtain blood and blood components from the American Red Cross as they develop and update their blood usage guidelines to help improve transfusion safety.
Components

Approved name: Red Blood Cells.

Also referred to as packed cells, red cells, packed red blood cells, RBCs.

Whole blood is rarely required and is, therefore, not addressed.

Description of Components

Red Blood Cells (RBCs) consist of erythrocytes concentrated from whole blood donations by centrifugation or collected by apheresis. The component is anticoagulated with citrate and may have had one or more preservative solutions added.

Depending on the preservative-anticoagulant system used, the hematocrit (Hct) of RBCs is ~55-65% (for example, AS-1, AS-3, AS-5) to ~65-80% (for example, citrate-phosphate-dextrose-adenine solution [CPDA]-1, CPD, CP2D). RBCs contain 20-100 mL of donor plasma with an average of ~50 mL, in addition to the preservative and anticoagulant solution. The typical volume of AS RBCs after addition of the additive solution is 300-400 mL.

Each unit contains approximately 42.5-80 g of hemoglobin (Hgb) or 128-275 mL of pure red cells, depending on the Hgb level of the donor, the starting whole blood collection
volume, and the collection methodology or further processing. When leukoreduced, RBC units must retain at least 85% of the red cells in the original component.

Each unit of RBCs contains approximately 250 mg of iron, mostly in the form of Hgb.

**Selection and Preparation**

RBCs must be compatible with ABO antibodies present in the recipient plasma and must be crossmatched (serologically or electronically, as applicable) to confirm compatibility with ABO and other clinically significant antibodies prior to routine transfusion. Units must be negative for the corresponding antigens.

Rh-positive units may be transfused in an emergency to Rh-negative males and females with non-childbearing potential who have not made anti-D or whose D antigen type is unknown. The D-negative frequency is 15% in Caucasians, 8% in African-Americans and 1% in Asians. The incidence of anti-D production after transfusion of Rh-positive blood to an Rh-negative individual is ~30.4%.

Transfusion services should develop policies on using Rh-positive blood in Rh-negative individuals; this may include switching to Rh-positive units in males and females with non-childbearing potential based on inventory.

Extended storage preservative-anticoagulant preparations, such as AS-1 and AS-3, are appropriate for nearly all patients. Physicians concerned about preservative-anticoagulant in neonates may elect to use a different preparation
(for example, CPD or CPDA-1) or to remove preservative-anticoagulant from transfusion aliquots prior to administration—for example, by centrifugation and volume reduction or washing.

RBCs are capable of transmitting cytomegalovirus, mediating graft-vs-host disease, and causing febrile nonhemolytic reactions. For recipients at particular risk from these transfusion-related complications, use of CMV reduced-risk (that is, CMV-seronegative or leukocyte-reduced), irradiated and leukoreduced preparations, respectively, should be considered.

**Dosing**

RBCs should be transfused based on clinical need.

In the absence of acute hemorrhage, RBC transfusion should be given as single units.

Transfusion of a unit of RBCs should be completed within four hours. Smaller aliquots of the unit can be prepared if the time for transfusion will exceed four hours.
Response

In a stable, non-bleeding or hemolyzing adult transfused with compatible RBCs:
• Hemoglobin (Hgb) equilibrates in 15 minutes after RBC transfusion.
• One unit will increase the Hgb level in an average-sized individual by approximately 1 g/dL and the Hct by 3%.
• The posttransfusion Hgb can be accurately predicted from the patient’s estimated blood volume, baseline red cell volume (blood volume X venous Hct X 0.91), and transfusion volume.

In neonates, a dose of 10-15 mL/kg is generally given, and AS-1 or AS-3 packed red cells with an Hct of approximately 60% will increase the Hgb by about 3 g/dL.

Transfused red cells have a half-life of approximately 30 days in the absence of other processes that would result in red cell loss or premature removal.

Indications and Contraindications

RBCs are indicated for patients with a symptomatic deficiency of oxygen-carrying capacity or tissue hypoxia due to an inadequate circulating red cell mass. They are also indicated for exchange transfusion (for example, for hemolytic disease of the fetus and newborn) and red cell exchange (for example, for acute chest syndrome in sickle cell disease).

Patients must be evaluated individually to determine the proper transfusion therapy, with care taken to avoid
inappropriate over- or under-transfusion. Transfusion decisions should be based on clinical assessment and not on laboratory values alone.

RBCs may be used for patients with acute blood loss that is refractory to crystalloid infusions. RBCs should not be used to treat anemia that can be corrected with a non-transfusion therapy (for example, iron therapy). They also should not be used as a source of blood volume, to increase oncotic pressure, to improve wound healing, or to improve a person’s sense of well being.

For side effects and hazards, see Appendix 1.
RED BLOOD CELLS | UTILIZATION GUIDELINES

Perioperative/Periprocedural

The function of an RBC transfusion is to augment oxygen delivery to tissues. Hemoglobin levels during active bleeding are imprecise measures of tissue oxygenation. Adequate or inadequate fluid resuscitation can significantly alter the measured Hgb concentration. In addition, a number of factors must be considered besides the blood Hgb level, such as oxygenation in the lungs, blood flow, Hgb oxygen affinity and tissue demands for oxygen. The use of only Hgb level as a transfusion trigger should be avoided.

The adequacy of oxygen delivery must be assessed in individual patients, particularly in patients with limited cardiac reserve or significant atherosclerotic vascular disease. If available, mixed venous O₂ levels, O₂ extraction ratios, or changes in oxygen consumption may be helpful in assessing tissue oxygenation. Other factors to consider, in addition to the above, include anticipated degree and rate of blood loss and the effect of body temperature or drugs/anesthetics on oxygen consumption. Notwithstanding the above, the American Society of Anesthesiologists Task Force recommends the following:

- RBCs should usually be administered when the Hgb concentration is low (for example, <6 g/dL in a young, healthy patient), especially when the anemia is acute. RBCs are usually unnecessary when the Hgb concentration is >10 g/dL. These guidelines may be altered in the presence of anticipated blood loss.
• The determination of whether intermediate Hgb concentrations (that is, 6-10 g/dL) justify or require RBC transfusion should be based on any ongoing indication of organ ischemia, potential or actual ongoing bleeding (rate and magnitude), the patient’s intravascular volume status, and the patient’s risk factors for complications of inadequate oxygenation. These risk factors include a low cardiopulmonary reserve and high oxygen consumption.

The use of alternative measures to reduce allogeneic red blood cell use should be considered, including intraoperative and postoperative autologous blood recovery, acute normovolemic hemodilution, and operative and pharmacologic measures that reduce blood loss. In select cases preoperative autologous donation may be considered.

**General Critical Care**

The same considerations regarding individualization of red cell transfusions apply to critical care as well as to perioperative patients (see above). The effects of anemia must be separated from those of hypovolemia, although both can impede tissue oxygen delivery. Blood loss of greater than 30% of blood volume generally causes significant clinical symptoms; but in young, healthy patients, resuscitation with crystalloid alone is usually successful with blood loss of up to 40% of blood volume (for example, 2 liters blood loss in an average adult male). Beyond that level of acute blood loss, even after adequate volume resuscitation, acute normovolemic anemia will exist. However, oxygen delivery in healthy adults is maintained with Hgb levels even as
low as 6-7 g/dL. Consider RBC transfusion in critically ill trauma patients after the immediate resuscitation phase if the Hgb level is <7 g/dL. RBC transfusion is indicated in patients with evidence of hemorrhagic shock and should be considered in patients with Hgb <7 g/dL who are on mechanical ventilation.

There are limited prospective studies of RBC transfusions in the critically ill patient to provide definitive guidance for transfusion, and most of the evidence to either support or refute an RBC transfusion in these patients is based on retrospective studies. In support of a conservative RBC transfusion policy in critical care are several prospective studies demonstrating a higher mortality rate in patients receiving RBCs than in those not receiving RBCs. The TRICC (Transfusion Requirements in Critical Care) trial, a multicenter, randomized, controlled trial compared a transfusion trigger of 7 g/dL with a trigger of 9 g/dL in normovolemic critically ill patients. Overall, 30-day mortality was similar in the two groups and in the subset of more seriously ill patients, but the restrictive group received significantly fewer RBC transfusions. However, in less acutely ill or younger patients, the restrictive strategy resulted in lower 30-day mortality and decreased RBC transfusions.

In support of considering cardiovascular status in the decision to transfuse red cells is a retrospective study of transfusion in elderly patients with acute myocardial infarction that showed lower short-term mortality when patients with an Hgb as high as 10 g/dL were transfused. However, a meta-analysis of retrospective studies involving patients with acute coronary syndrome demonstrated that 30-day mortality, myocardial infarction, and death/myocardial
infarction as a composite end-point were all higher for patients who had received an RBC transfusion. In addition, a study among patients with non-ST segment elevated acute coronary syndromes demonstrated that patients receiving RBCs had a significantly greater risk of death or reinfarction as a combined measure than did patients not receiving blood. Several studies have also demonstrated that transfusion of RBCs in patients undergoing cardiac surgery is an independent predictor of mortality with one study reporting a 70% increase compared to the non-transfused group and another reporting an association between RBC transfusion and perioperative morbidity.

In general, RBC transfusions may be beneficial in patients with acute coronary syndromes who have an Hgb level <8 g/dL on hospital admission, and a transfusion should be considered in critically ill patients with stable cardiac disease and an Hgb level <7 g/dL.

Thus, transfusion triggers for red cells in critical care must be customized to defined patient groups, and the decision to transfuse must be based on individual patient characteristics. Unfortunately, the availability of carefully performed clinical trials to assist the clinician is extremely limited.

**Pediatrics Critical Care**

Infants may require simple or exchange transfusions for hemolytic disease of the fetus and newborn (HDFN) or symptomatic anemia in the first months of life.
The American Academy of Pediatrics has published guidance on specific indications for exchange transfusion for newborn infants at 35 or more weeks of gestation with hyperbilirubinemia, including that caused by HDFN. Infants with jaundice caused by HDFN are at greater risk of bilirubin encephalopathy and are treated more intensively than infants with “physiologic” jaundice at any given serum unconjugated bilirubin concentration.

Apart from HDFN, neonatal anemia occurs in many preterm infants because of iatrogenic blood loss for laboratory tests, concurrent infection or illness, and inadequate hematopoiesis in the first weeks of life. Transfusion thresholds for preterm infants and critically ill children have been widely debated for years, but recent randomized studies support the use of a restrictive strategy (for example, transfusion at lower Hgb thresholds) compared to more liberal criteria (for example, transfusion at higher Hgb thresholds).

In the multicenter PINT (Premature Infants in Need of Transfusion) study, 451 very low birthweight infants were randomly assigned to receive red cell transfusions by either restrictive or liberal criteria. Infants in the restrictive transfusion group had lower mean Hgb values than those in the liberal group, and more infants avoided transfusion completely in the restrictive group (11%) compared to the liberal group (5%). There was no difference between the two groups in the composite outcome (death, severe retinopathy, bronchopulmonary dysplasia, and brain injury), supporting the use of restrictive transfusion criteria. In a smaller, single-center trial, Bell et al. randomized 100 preterm infants to either restrictive or liberal transfusion criteria and found a reduction in the number of transfusions
in the restrictive group. However, infants in the restrictive group were noted as having more apnea episodes and neurologic events than infants in the liberal group. In conclusion, the documented benefits of restrictive transfusion practice are a decrease in the number of transfusions and exposure to fewer RBC donors, if a limited-donor program is not used. It is possible that the higher Hgb values maintained in the liberal transfusion group in the study of Bell et al. compared with the corresponding group in the PINT trial may have decreased the risk of apnea and brain injury.

These two studies suggest that transfusion thresholds can be lowered, but identify the need for additional clinical studies. General guidelines for transfusion must take into consideration the infants’ cardiorespiratory status, but transfusion decisions must be tailored to the individual patient.

### General Guidelines for Small-Volume (10-15 mL/kg) Transfusion to Infants

<table>
<thead>
<tr>
<th>Maintain Hct between:</th>
<th>Clinical Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-45%</td>
<td>Severe cardiopulmonary disease* (for example, mechanical ventilation &gt;0.35 FiO₂)</td>
</tr>
<tr>
<td>30-35%</td>
<td>Moderate cardiopulmonary disease (for example, less intensive assisted ventilation, such as nasal CPAP or supplemental oxygen)</td>
</tr>
<tr>
<td>30-35%</td>
<td>Major surgery</td>
</tr>
<tr>
<td>20-30%</td>
<td>Stable anemia, especially if unexplained breathing disorder or unexplained poor growth</td>
</tr>
</tbody>
</table>

*Must be defined by institution

Less controversial are the results from the TRIPICU (Transfusion Requirements in the Pediatric Intensive Care Unit) study, which demonstrated that an Hgb threshold of 7 g/dL for RBC transfusion is not inferior to a treatment strategy using an Hgb threshold of 9.5 g/dL among critically ill but stable children being treated in ICUs. A higher threshold may be indicated for patients with cardiovascular disease or for children with severe hypoxemia, hemodynamic instability, active blood loss, or cyanotic heart disease.

**Chronic Anemia**

**Asymptomatic Chronic Anemia**

Treat with pharmacologic agents based on the specific diagnosis (for example, vitamin B12, folic acid, recombinant erythropoietin, iron).

**Symptomatic Chronic Anemia**

Transfuse to minimize symptoms and risks associated with anemia. Transfusion is usually required when Hgb is <6 g/dL.

**Anemia in Patients Receiving or Awaiting Chemo- or Radiotherapy**

Nearly 50% of all cancer patients experience anemia associated either with the disease itself or with the cancer treatment regimen. Anemia (defined as Hgb <11 g/dL) has been shown to have an effect on tumor hypoxemia and thus on the tumor’s response to chemotherapy or radiotherapy, as well as on the quality of life for the patient. However, in general Hgb levels >12 g/dL are also associated with
increased morbidity and mortality. Meta-analyses of recent clinical studies indicate that the transfusion triggers differ, depending upon the type of cancer being treated; thus the Hgb goals are cancer specific. Patients’ needs should be evaluated in light of the institution’s oncology guidelines.

**Sickle Cell Disease**

Evidence-based clinical guidelines and consensus statements have outlined indications for transfusion in sickle cell disease (SCD). SCD patients should be transfused with leukocyte-reduced blood. Recent clinical practice guidelines propose that extended red cell antigen phenotype (ABO, Rh, Kell, Kidd, Duffy, Lewis, and MNSs blood group systems) be determined for all patients with SCD before they start transfusion therapy, and that they should receive ABO/Rh type-specific units that are phenotypically matched for C, E, and K to reduce the frequency of transfusion reactions and the development of red cell antibodies. The choice between simple transfusion and exchange transfusion is often based on clinical judgment and available resources, with few clinical studies to guide decisions. In preparation for surgery requiring general anesthesia, however, simple transfusion to increase Hgb to 10 g/dL was as effective as exchange transfusion in preventing perioperative complications in patients with sickle cell anemia and was associated with less blood usage and a lower rate of red cell alloimmunization.

Chronic transfusion therapy to maintain the HbS below 30% of the total Hgb prevents first stroke in high-risk children with abnormal transcranial Doppler studies and prevents recurrent stroke in those with a history of infarctive stroke. The treatment goal for prevention of recurrent stroke may be relaxed to less than 50% HbS after several complication-free
years, but treatment cannot be safely discontinued at any point. Similarly, prophylactic transfusion cannot be safely discontinued in children with sickle cell anemia who have abnormalities on transcranial Doppler studies and are at a high risk of stroke (STOP 2, Stroke Prevention Trial in Sickle Cell Anemia). In contrast to simple transfusion, exchange transfusion can prevent iron accumulation and may reverse iron overload in chronically transfused patients.

In general, patients with SCD should not be transfused to an Hgb level >10 g/dL.

**Accepted Indications for Transfusion in Sickle Cell Disease**

<table>
<thead>
<tr>
<th>Episodic or Acute Complications of SCD</th>
<th>Chronic Complications of SCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe anemia</td>
<td>Prevention of stroke in children with abnormal transcranial Doppler studies*</td>
</tr>
<tr>
<td>Acute splenic sequestration</td>
<td>Prevention of stroke recurrence*</td>
</tr>
<tr>
<td>Transient red cell aplasia</td>
<td>Chronic debilitating pain</td>
</tr>
<tr>
<td>Preparation for general anesthesia</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Sudden severe illness*</td>
<td>Anemia associated with chronic renal failure</td>
</tr>
<tr>
<td>Acute chest syndrome*</td>
<td></td>
</tr>
<tr>
<td>Stroke*</td>
<td></td>
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<tr>
<td>Acute multiorgan failure*</td>
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</tbody>
</table>

*Managed with simple transfusion or exchange transfusion.
**Controversial Indications**

- Priapism
- Leg ulcers
- Pregnancy
- Preparation for infusion of contrast media
- “Silent” cerebral infarct and/or neurocognitive damage

**Inappropriate Indications and Contraindications**

- Chronic, steady-state, asymptomatic anemia
- Uncomplicated pain episodes
- Infection
- Minor surgery that does not require general anesthesia
- Aseptic necrosis of the hip or shoulder (unless indicated for surgery)
- Uncomplicated pregnancy

**Severe Thalassemia**

Transfuse to help prevent symptomatic anemia and to suppress endogenous erythropoiesis by maintaining Hgb at 9.5-10.5 g/dL.
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Components

Approved names: Platelets, Pooled Platelets, Apheresis Platelets.

Platelets are also referred to as whole blood-derived platelets, random donor platelets, randoms, or RDPs.

Pooled Platelets are also referred to as Prestorage Pooled Platelets, and Platelets Pooled.

Apheresis Platelets are also referred to as single donor platelets, or SDPs.

Description of Components

Platelets (RDP): derived from whole blood; should contain $5.5 \times 10^{10}$ platelets (average content approximately $8.5 \times 10^{10}$) per bag in 40-70 mL of plasma. Anticoagulant is the same as that used for whole blood collection, usually CPD or CP2D. Prestorage Pooled Platelets should contain ($5.5 \times 10^{10}$ platelets) x number of RDPs in the pool (usually 4-6).

Apheresis Platelets (SDP): obtained using automated instrumentation; should contain $3.0 \times 10^{11}$ platelets (generally $3.5-4.0 \times 10^{11}$) per bag in 100-500 mL of plasma. Anticoagulant is ACD.
Selection and Preparation

Four to six RDPs are pooled at the blood center (prestorage pools) or at the hospital (poststorage pools) prior to transfusion to prepare an adult dose. Prestorage Pooled Platelets, Leukocytes Reduced, and Apheresis Platelets/Apheresis Platelets Leukocytes Reduced are ready for transfusion.

Donor plasma should be ABO-compatible with the recipient’s red cells when one transfuses infants or large volumes to adults to avoid the possibility of hemolysis. Higher platelet increments may result with ABO-identical units.

Rh-negative recipients should receive Rh-negative platelets when possible, particularly in women with childbearing potential. Consider administering Rh immune globulin if Rh-positive platelets need to be administered, especially when whole blood-derived platelets are used. Apheresis Platelets contain minimal quantities of red cells, but they are usually insufficient to provoke an alloimmune response in immunosuppressed patients.

Patients at risk for transfusion-associated graft-vs-host disease (TA-GVHD) should receive irradiated platelets.

Dosing

Four to ten units of pooled RDPs, one to two units of Prestorage Pooled Platelets, or one to two SDPs are generally transfused to thrombocytopenic or thrombocytopenic patients. To help prevent or treat bleeding, transfuse as needed to maintain target platelet count.
Response

Measure platelet count from 10-60 minutes after transfusion. Generally, expect an average-sized adult (70 kg) platelet count increment of approximately 5,000-10,000/μL for each RDP given, or 20,000-60,000/μL for each SDP given. In neonates and infants, a dose of 5-10 mL/kg of RDPs should result in a 50,000-100,000/μL increment. A dose of 10 mL/kg is most often used. Similar dosing regimens have been used with SDP aliquots, although evaluation of posttransfusion increments have not been studied.

At least 7,100 platelets/μL are consumed daily in endothelial support functions, the equivalent of approximately one RDP per day for a 70 kg adult with marrow failure.

Response to platelet transfusion is adversely affected by the presence of fever, sepsis, splenomegaly, severe bleeding, consumptive coagulopathy, HLA alloimmunization, and treatment with certain drugs (for example, amphotericin B).

Indications and Contraindications

Use to treat bleeding due to critically decreased circulating platelet counts or functionally abnormal platelets.

Use prophylactically to prevent bleeding at prespecified low platelet counts. In general, maintain platelet count at >10,000/μL in stable, non-bleeding patients, at >20,000/μL in unstable, non-bleeding patients, and at >50,000/μL in patients who are actively bleeding or undergoing invasive procedures/surgery. The avoidance of low hematocrits in patients with thrombocytopenia reduces the risk of hemorrhage.
Do not use in patients with autoimmune thrombocytopenia, thrombotic thrombocytopenic purpura, or heparin-induced thrombocytopenia with thrombosis except for life-threatening hemorrhage and, possibly, before invasive procedures/surgery in patients without thrombotic manifestations.

*For side effects and hazards, see Appendix 1.*
PLATELETS | UTILIZATION GUIDELINES

Cardiothoracic Surgery

• When coagulation parameters are not significantly abnormal, counts <100,000/μL accompanied by major unexpected microvascular bleeding are appropriately treated with platelet transfusion.
• Routine prophylactic transfusions do not alter bleeding or postoperative transfusion requirements and are not recommended, even in patients on thienopyridines (for example, clopidogrel), who are known to be at higher risk for bleeding and reoperation.

**Point of care (POC) testing** devices, which measure activated clotting time (ACT) and perform thromboelastography (TEG) and similar functions, are now available to better assess hemostatic function in bleeding surgical patients. These tests can guide optimal administration of blood products and reduce inappropriate component utilization.

Other Surgical Procedures

• Intraoperative platelet counts should be obtained to guide transfusion. Microvascular bleeding in the setting of potential dilutional thrombocytopenia may require empiric transfusion before counts are available.
• Prophylactic preoperative transfusion is rarely required for counts >100,000/μL, is usually required for counts <50,000/μL, and is guided by risk factors for intermediate counts.
• Procedures with insignificant blood loss or vaginal deliveries can be performed at counts <50,000/μL without prophylactic transfusion.
• Neurologic or ophthalmologic procedures may require a platelet count near 100,000/μL.
• Transfusion may be required with apparently adequate counts when known or suspected platelet dysfunction results in microvascular bleeding.

Specific Procedures

• When prophylactic transfusion is deemed necessary, a posttransfusion count should be obtained to assure an appropriate increment before performance of the procedure.
• In the absence of coagulopathy or thrombocytopathy, major invasive procedures require functional platelet counts of at least 40,000-50,000/μL (including central venous catheter placement, paracentesis/thoracentesis, respiratory tract/gastrointestinal [GI] biopsies, closed liver biopsy, lumbar puncture, sinus aspiration, and dental extraction).
• A threshold of 80,000/μL has been proposed for spinal epidural anesthesia.
• Fiberoptic bronchoscopy or GI endoscopy without biopsy may be safely performed by experienced operators in the presence of a platelet count <20,000/μL.

Platelet Function Defects

Patients with congenital or acquired defects in platelet function may be transfused for critical bleeding or before major surgery regardless of the platelet count. Transfusion is gener-
ally not indicated when platelet dysfunction is extrinsic to the platelet (for example, uremia, certain types of von Willebrand disease, hyperglobulinemia) since transfused platelets function no better than the patient’s own platelets. When platelet surface glycoproteins are missing (for example, with Glanzmann thrombasthenia, Bernard-Soulier syndrome), transfusion should be undertaken only when more conservative efforts to manage bleeding have failed since alloimmunization may cause future life-threatening refractoriness.

**Antiplatelet Agents**

Thienopyridine platelet ADP receptor inhibitors and direct glycoprotein IIb/IIIa inhibitors impair platelet function. Platelets should not be transfused prophylactically without thrombocytopenia, but high dose therapeutic transfusion may be required for life-threatening hemorrhage in patients on these drugs.

**Massive Transfusion**

Massive transfusion is defined as transfusing one complete blood volume or 10 units of red blood cells within a 24-hour period. A transfusion target of 50,000/μL is recommended for acutely bleeding patients and 100,000/μL for those with multiple trauma or CNS injury. The platelet count may fall below 50,000/μL when >1.5-2 blood volumes have been replaced with red cells. In the presence of microvascular bleeding, transfusion may be appropriate when counts are known or suspected to be <100,000/μL. Early aggressive platelet therapy has been associated with improved survival in retrospective studies. The role of algorithms that
essentially provide reconstituted whole blood has not yet been determined in prospective randomized controlled studies.

**Disseminated Intravascular Coagulation (DIC)**

Transfusion is appropriate in children and adults with platelet counts <50,000/µL who have active bleeding, require an invasive procedure, or are otherwise at risk for bleeding complications.

**Pediatrics**

Neonates undergoing invasive procedures/surgery or experiencing clinically significant bleeding may be transfused at <50,000/µL.

A prophylactic transfusion trigger of <20,000/µL for stable neonates at term, or <30,000/µL for stable premature neonates, is justified. High-risk neonates (those with extremely low birthweight, perinatal asphyxia, sepsis, ventilatory assistance with an FIO₂>40%, or clinical instability) may be transfused at <30,000/µL at term or at <50,000/µL if premature, due in part to an increased risk of intraventricular hemorrhage.

Infants on extracorporeal membrane oxygenators (ECMO) are usually transfused to maintain a platelet count >100,000/µL.
Acute Leukemia and Following High-Dose Chemotherapy

A prophylactic transfusion trigger of 10,000/μL may be used for stable patients, except as noted below. Patient-specific clinical data may increase the threshold at which prophylactic transfusion is desirable (for example, major/minor bleeding, coagulopathy, drug-induced platelet dysfunction, fever/sepsis, hyperleukocytosis, planned procedures, use of antithymocyte globulin, serious mucositis or cystitis, acute graft-vs-host disease, liver dysfunction/veno-occlusive disease, or rapid decline in counts). Prophylactic platelets may also be given at higher counts when availability of compatible platelet products is reduced.

Higher-than-usual doses of platelets result in longer intervals between transfusions, which may be of value in the outpatient setting.

Therapeutic transfusion for major bleeding should maintain counts 50,000/μL.

Chemotherapy for Solid Tumors

The usual prophylactic transfusion trigger is 10,000/μL. The greater risk of bleeding from bladder neoplasms/necrotic tumors and the serious impact of even minor bleeding in patients with limited physiologic reserves may warrant a transfusion trigger of 20,000/μL.
Transfusion Refractoriness

Posttransfusion platelet counts at 10-60 minutes after infusion should be obtained whenever possible (successful transfusion defined as a corrected count increment [CCI] 7,500/μL per m² per 10¹¹ platelets infused). The 10-60 minute postinfusion count measures transfusion recovery, which is most sensitive to immune platelet destruction. Postinfusion counts at 24 hours assess platelet survival, which is sensitive to non-immune factors such as sepsis, splenomegaly, and DIC, as well as immune factors.

The American Society of Clinical Oncology recommends that additional products be given if counts do not rise appropriately after transfusion.

Alloimmune refractoriness is more likely in the setting of at least two consecutive poor platelet increments at 10-60 minutes after transfusion. Alloimmunization should be confirmed by demonstration of antibodies to platelets (that is, human leukocyte antigens [HLA] or human platelet antigens [HPA]). Single donor products identified either by HLA/HPA matching and/or antibody compatibility or by crossmatching should be transfused. When HLA/HPA typing, antibody identification data, and crossmatched platelets are unavailable, fresh ABO-compatible units are preferred.

The incidence of HLA alloimmunization has been shown to be reduced by the use of leukoreduced blood products (platelets and RBCs) in any patient expected to receive multiple platelet transfusions during the course of therapy.
Severely alloimmunized patients who do not respond to available matched products do not benefit from unmatched prophylactic platelet transfusions. For active bleeding, these patients may benefit from high-dose or continuous platelet transfusion.

**Idiopathic Thrombocytopenic Purpura (ITP)**

Patients who experience major, life-threatening bleeding or intraoperative hemorrhage should receive high-dose platelet transfusions.

Prophylactic transfusions are usually inappropriate since transfused platelets do not survive any longer than patients’ native platelets. Transfusion may be considered before elective splenectomy with platelet counts ≤10,000/μL.

**Thrombotic Thrombocytopenic Purpura (TTP) and Heparin-Induced Thrombocytopenia with Thrombosis (HITT)**

Due to the significant risk of fatal thrombosis, platelets should be transfused only for life-threatening hemorrhage or, possibly, before invasive procedures in patients without thrombotic manifestations.

**Posttransfusion Purpura (PTP)**

Platelets may be used therapeutically for severe bleeding. Transfusion of randomly selected platelets is usually ineffective. Though efficacy is not well documented, human platelet antigen (HPA)-1a (PlA1)-negative platelets are fre-
quently given empirically while specific alloantibody testing is in progress. High-dose intravenous immunoglobulin (IVIG) is the treatment of choice for PTP.

**Neonatal Alloimmune Thrombocytopenia (NAIT)**

IVIG is effective in approximately 75% of affected infants. Platelet transfusions are indicated for severe thrombocytopenia and/or bleeding. Platelets should lack the HPA recognized by circulating maternal antibodies, although platelets from random donors may be effective when matched platelets are unavailable. If maternal platelets are used, they should be washed or volume-reduced and irradiated.

**Aplastic Anemia**

Transfuse stable patients prophylactically at counts 5,000/μL and patients with fever or minor hemorrhage at counts 6,000-10,000/μL.
PLASMA
FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY

25 mL from
500 mL CPD
Whole Blood.
Store at -18°C or colder.

VOLUNTEER DONOR
The product may contain infectious agents. Use only
PROPERLY IDENTIFY INTENDED RECIPIENT

Rh POSITIVE
THE AMERICAN NATIONAL RED CROSS
Washington, D.C. 20006
U.S. License #190

Collected and Processed by
American Red Cross Blood Services
Arizona Region
Tucson, AZ 85711

Collection Date: 07GE 40468
Expires: 08/13/10
Barcodes: 38A4R3307E, FM09D17015

Registration #: 2072599

Form 56225A 04/05/08
**Components**

Approved names: Fresh Frozen Plasma; Plasma Frozen Within 24 Hours After Phlebotomy; Plasma Cryoprecipitate Reduced.

Also referred to as FFP, FP24, or cryo poor plasma, respectively.

Preparation variations include: Thawed Plasma, Liquid Plasma.

**Description of Components**

Plasma consists of the noncellular portion of blood that is separated and frozen after donation. It may be prepared from whole blood or collected by apheresis. The anticoagulant solution used and the volume are indicated on the label. The volume of the unit is approximately 250 mL, but variation may be expected depending on the method of collection. FFP is frozen at -18°C or colder within 6-8 hours of collection (depending upon the anticoagulant), and it contains functional quantities of all coagulation factors. Plasma Frozen Within 24 Hours (FP24) and Thawed Plasma may contain variably reduced levels of Factor V and Factor VIII. Despite these differences, FP24, Thawed Plasma and FFP are generally used for the same indications, and are referred to as Plasma in this brochure.
After removal of cryoprecipitate, Plasma Cryoprecipitate Reduced has decreased factor levels, including fibrinogen (40-70% of FFP), Factor VIII and von Willebrand factor (~20% of FFP), fibronectin, and Factor XIII. Proteins such as albumin and other coagulation factors remain at approximately the same levels as in FFP.

FFP, FP24 and Plasma Cryoprecipitate Reduced have equivalent levels of ADAMTS13, the protein that is thought to be deficient in thrombotic thrombocytopenic purpura (TTP). Its activity should remain stable for the duration of the shelf life of thawed products.

Coagulation factor half-life should be considered when plasma is given prior to invasive procedures. For example, with reduced levels of Factor VII, its 5-hour in vivo half-life mandates transfusion as close as possible to the time of the procedure to achieve hemostatic factor levels.

By convention, one unit of a coagulation factor is defined as that activity present in each mL of plasma.

**Selection and Preparation**

Plasma for transfusion must be ABO-compatible with the recipient’s red cells: for example, group A Plasma is suitable for group A and group O patients. Group AB Plasma is suitable for all blood types. Frozen plasma must be thawed, usually in a water bath or in an FDA-cleared device, and infused immediately or stored at 1-6°C for up to 24 hours. Alternatively, onced thawed, FFP and FP24 may be
relabeled as Thawed Plasma and used as a source of stable coagulation factors for up to 5 days, unless it was collected by apheresis in an open collection system. If collected in a closed system, Plasma Cryoprecipitate Reduced can be used for up to 5 days postthaw if relabeled Thawed Plasma Cryoprecipitate Reduced.

Dosing

The dose of Plasma is determined by patient size and clinical condition. When used to correct multiple coagulation factor deficiencies, plasma transfusion should be guided by coagulation testing. A prothrombin time (PT) greater than 1.5 times the mid-range of normal, an activated partial thromboplastin time (aPTT) greater than 1.5 times the top of the normal range, or a factor assay of less than 25%, can be used as thresholds at which therapeutic or prophylactic replacement may be indicated in an appropriate clinical setting. When such testing is not readily available, clinical evidence of bleeding may be used to direct transfusion decisions. Plasma should be administered in doses calculated to achieve a minimum of 30% of plasma factor concentration. This is usually achieved with the administration of 10-20 mL/kg, though more may be required depending upon the clinical situation.

When used to correct isolated coagulation factor deficiencies for which no concentrated preparation is available (for example, Factor V or XI), dosing will depend on the half-life of the specific factor, the pretransfusion level of the factor, the desired posttransfusion level, and the duration of raised levels required.
TTP initially requires the exchange of 1-1.5 plasma volumes daily; this may need to be increased to twice daily single plasma volume exchanges in refractory patients. The volume and/or frequency of exchange may be tapered as disease activity declines.

**Response**

Plasma used to correct coagulation abnormalities should stop bleeding and bring the aPTT and PT within the hemostatic range; but transfusion will not always correct these values, or the correction may be transient.

Plasma used to treat TTP should result in an increasing platelet count associated with a decrease in serum lactate dehydrogenase.

**Indications and Contraindications**

Plasma is indicated for use in patients with the following conditions:
- Active bleeding or risk of bleeding due to deficiency of multiple coagulation factors.
- Severe bleeding due to warfarin therapy or urgent reversal of warfarin effect.
- Massive transfusion with coagulopathic bleeding.
- Bleeding or prophylaxis of bleeding for a known single coagulation factor deficiency for which no concentrate is available.
- Thrombotic thrombocytopenic purpura (Plasma or Plasma Cryoprecipitate Reduced).
- Rare specific plasma protein deficiencies for which no concentrate is available.
Plasma should not be used for the following:

- Increasing blood volume or albumin concentration.
- Coagulopathy that can be corrected with administration of Vitamin K.
- Normalizing abnormal coagulation screen results in the absence of bleeding.

*For side effects and hazards, see Appendix 1.*
Liver Disease

Plasma may be used to replace multiple coagulation factors (for example, with liver disease) in a patient who is actively bleeding or prior to an invasive procedure that would create a risk of bleeding. However, the response may be unpredictable and complete normalization of the hemostatic defect may not occur. Patients with liver disease may safely undergo operative or invasive procedures when the PT is 1.5 times the mid-range of normal.

Warfarin

Patients on warfarin who experience serious bleeding are treated with Vitamin K (at a dose determined by the INR) and Plasma or prothrombin complex concentrates as clinically warranted. Urgent reversal of warfarin effect may necessitate Plasma transfusion. As with liver disease, patients on warfarin may safely undergo operative or invasive procedures when the PT is 1.5 times the mid-range of normal.

Massive Transfusion and Cardiopulmonary Bypass

Plasma may be used to treat excessive microvascular bleeding, as determined on joint visual assessment of the operative field by the anesthesiologist and surgeon when the coagulation screening test results are abnormal or are not available in a timely fashion. However, microvascular bleeding may be a result of hypofibrinogenemia or residual heparin effect.
For massive transfusion, recent trends in the literature based on retrospective studies advocate using a high Plasma-to-RBC ratio to improve survival.

**Disseminated Intravascular Coagulation**

Addressing the underlying cause is the foundation of treatment, and the patient is supported with transfusion of Plasma in combination with platelets and cryoprecipitate. Transfusion of Plasma should be reserved for patients who are actively bleeding or non-bleeding patients with abnormal coagulation tests awaiting an invasive procedure.

**Thrombotic Thrombocytopenic Purpura**

If plasma exchange is not immediately available, simple transfusion of plasma can be a useful alternative until exchange can be started. Having equivalent levels of ADAMTS13, Plasma, and Plasma Cryoprecipitate Reduced are equally efficacious in the treatment of TTP and newly diagnosed TTP. If ADAMTS13 is used to diagnose and/or monitor the response, a level should be obtained prior to initiation of treatment.
Specific Plasma Protein/Factor Deficiencies

Deficiencies of other isolated plasma proteins and factors in a setting where concentrates are not readily available are also treated with Plasma:

• Prophylactic correction of a known factor deficiency for which specific concentrates are unavailable is guided by recommended perioperative hemostatic levels for each type of procedure.
• Treatment or prophylaxis of thromboembolism in antithrombin, protein C, and protein S deficiencies.
• Heparin resistance (antithrombin deficiency) in a patient requiring heparin.
• Therapy of acute angioedema or preoperative prophylaxis in hereditary C1-inhibitor deficiency.
• Factor V deficiency (no plasma concentrate available).
• Factor XI deficiency (factor concentrate not available in the U.S.).

Pediatrics

The indications for transfusion of Plasma in children are essentially the same as for adults. In infants of less than 6 months of age, the levels of vitamin K dependent coagulants, anticoagulants, and fibrinolytic proteins are decreased resulting in prolongation of coagulation assays as compared to older children and adults. Despite these differences, hemostatic balance is maintained in the healthy newborn, and spontaneous bleeding or thrombosis are rarely observed. The reserve capacity to respond to pathologic insults in a sick premature infant during the first week of life, however, may be limited.

Ref. 1, 2, 11, 15, 23, 26, 40, 41, 42, 54, 57, 68, 74, 76, 84, 86, 91, 92, 96, 97, 104, 105, 107, 108, 111, 116, 137
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Components

Approved names: Cryoprecipitated AHF; Pooled Cryoprecipitated AHF.

Also referred to as cryoprecipitate, cryo, cryoprecipitate pool, and pooled cryo, respectively.

Description of Components

A cryoprecipitate unit is prepared by thawing one unit of FFP at 1-6°C and recovering the cold insoluble precipitate. The cryoprecipitate is refrozen within 1 hour.

If the label indicates “Cryoprecipitated AHF Pooled,” several units of cryoprecipitate have been pooled into one bag, and the volume of the pool is indicated on the label.

Cryoprecipitate contains concentrated levels of fibrinogen, Factor VIII:C, Factor VIII:vWF (von Willebrand factor), Factor XIII, and fibronectin. Each unit of cryoprecipitate should contain a minimum of 80 IU of Factor VIII:C and 150 mg of fibrinogen in 5-20 mL of plasma. Mean American Red Cross single/pool of five content for blood group O: Factor VIII:C 140/650 IU and fibrinogen 420/2000 mg/dL, respectively. Cryoprecipitate from other ABO blood group plasma contains ~30% higher levels of Factor VIII:C.
Selection and Preparation

Cryoprecipitate is considered to be an acellular blood component. Compatibility testing is unnecessary, though cryoprecipitate that is ABO-compatible with recipient red cells is preferred. Rh type need not be considered.

CMV testing and leukoreduction are not required. Frozen cryoprecipitate is thawed in a protective plastic overwrap in a waterbath at 30-37°C up to 15 minutes or in an approved microwave. Thawed cryoprecipitate should be kept at room temperature and transfused as soon as possible. If it is from a closed single unit or has been pooled using an FDA-approved sterile connecting device, it should be transfused within 6 hours of thawing.* If it is an open system or if units have been pooled after thawing by entering the containers, it should be transfused within 4 hours.

For pooling, the precipitate in each unit should be mixed well with 10-15 mL of diluent (0.9% Sodium Chloride Injection, USP) to ensure complete removal of all material from the container. Cryoprecipitate pooled prior to freezing requires no extra diluent.


**Dosing**

For hypo/dysfibrinogenemia, cryoprecipitate units can be estimated by the following:

- Weight (kg) x "Factor"/kg = blood volume (mL)
- Blood volume (mL) x (1.0-hematocrit) = plasma volume (mL)
- Fibrinogen required (mg) = (desired fibrinogen level [mg/dL] - initial fibrinogen level [mg/dL] multiplied by plasma volume [mL] divided by 100)
- Bags of cryo required = mg fibrinogen required divided by 420 mg fibrinogen per bag of cryo (or 2000 per cryo pool)

"Factor": 65 mL, average adult female; 70 mL, average adult male; 100 mL, preterm neonate; 85 mL, term neonate; 75 mL, one (1) month.

The frequency of dosing depends on the recovery and half-life of the coagulation factor that is being replaced (check factor levels). The half-life of fibrinogen is approximately 4 days in the absence of consumption.

**Response**

Pretransfusion and posttransfusion coagulation factor levels should be determined to assess the adequacy of the cryoprecipitate dose.

Adult: 1 pool (5 bags) raises the fibrinogen ~50 mg/dL in the absence of continued consumption.

Child: fibrinogen replacement, dosed at 1 bag/10 kg, should increase the fibrinogen level by 60 to 100 mg/dL in children. In neonates, 1 bag may increase the fibrinogen level by more than 100 mg/dL.
Indications and Contraindications

Cryoprecipitate is indicated for bleeding associated with fibrinogen deficiencies. Alternative uses in Factor XIII deficiency, hemophilia A, or von Willebrand disease should be considered only when the specific factor concentrate is not available. Use of this component may be considered for uremic bleeding after other modalities have failed.

For side effects and hazards, see Appendix 1.
Acquired Fibrinogen Deficiency and Bleeding

Cardiac surgery is the most common surgical circumstance for cryoprecipitate transfusion. Excessive bleeding associated with worsened morbidity and mortality may result from coagulopathy due to exposure of the blood to artificial surfaces, hemodilution, hypothermia, and/or acidosis. Established guidelines recommend maintaining fibrinogen levels above 100 mg/dL in bleeding patients, although this number is not based on clinical trials; and some recent laboratory guided protocols suggest that clot structure may be improved at even higher levels (that is, >200 mg/dL). Further clinical validation is required.

Fibrin Sealant

Commercially produced, virus-inactivated fibrin sealant is preferable to cryoprecipitate with respect to safety and efficacy.

Massive Transfusion

Transfuse for bleeding in massively transfused patients when the fibrinogen level is documented to be <100 mg/dL. This will usually occur after one or more blood volumes (4,000-5,000 mL in an adult) have been replaced.
Uremic Bleeding

May offer some efficacy during active bleeding; however, 1-deamino-8-D-arginine vasopressin (DDAVP) and other modalities are preferred.

Disseminated Intravascular Coagulation (DIC)

Although transfusion in DIC is not based on lab values, severe hypo fibrinogenemia (<100 mg/dL) that persists despite FFP replacement may be treated with cryoprecipitate.

Fibronectin Replacement

Cryoprecipitate has been shown to increase fibronectin levels in trauma and surgery patients, a population in whom fibronectin deficiency has been correlated with increased infection rates and poorer survival. However, whether replacement is clinically relevant is still unknown.

Congenital Factor Deficiencies

Congenital Fibrinogen Deficiency

For spontaneous bleeding, prior to surgery, or to prevent fetal loss throughout pregnancy, recommendations are to keep fibrinogen levels above 100 mg/dL. After surgical or spontaneous bleeding is stopped, levels above 50 mg/dL should be maintained until wound healing is complete.

In 2009, human-derived, virus-inactivated fibrinogen concentrate became FDA approved and is now considered first line treatment for congenital fibrinogen deficiency.
Hemophilia A and von Willebrand Disease (vWD)

Cryoprecipitate is appropriate only if recombinant or virus-inactivated Factor VIII or Factor VIII:vWF concentrates are not available. DDAVP is the treatment of choice for type 1 vWD.

Factor XIII Deficiency

Deficiency of Factor XIII presents risk for severe bleeding, spontaneous abortion, and spontaneous intracranial hemorrhage (25-40%). Cryoprecipitate is appropriate only if virus-inactivated Factor XIII concentrates are not available.

Due to the high incidence of intracranial hemorrhage, newborns and some adults receive prophylactic dosing.
1. Leukocyte-Reduced Components

Description and Preparation of Components

Alternative terminology: leukocyte reduction, leukoreduction, leukoreduced, LR, leukocyte-poor, leuko-poor.

Leukoreduction is a process by which white blood cells are removed from the blood component. This may be accomplished by prestorage filtration in the laboratory (generally within 72 hours of collection of red blood cells or random platelets), bed-side filtration, or in-process for some apheresis blood product collections. Prestorage filtration is preferred over bedside filtration because it is conducted soon after blood product collection, removing leukocytes prior to the release of cytokines, cellular debris, or possibly intracellular viruses. These latter components may, in turn, contribute to erythrocyte storage induced damage, transfusion reactions, and/or infections, respectively.


The average RBC unit contains $1 \times 10^9$ leukocytes. To meet quality standards, a leukoreduced component must have a final white blood cell count of $<5 \times 10^6$ per each unit of RBC and apheresis/prestorage pooled WBD platelets.
Individual WBD platelet units require a final leukocyte count of $<8.3 \times 10^5$ per unit. The shelf life of leukoreduced products remains unchanged.

Leukoreduction does not prevent transfusion-associated graft-vs-host disease (TA-GVHD). For such at-risk patients, cellular products must be irradiated.

Apheresis Granulocytes (granulocytes pheresis) must not be leukoreduced.

**Indications**

- Recurrent febrile nonhemolytic reaction (FNHR): may decrease the incidence of FNHR by as much as 60%.
- Alloimmunization and platelet refractoriness: may reduce platelet refractoriness by 50-80%.
- Intracellular pathogens: reduces transfusion transmission of cytomegalovirus (see Blood Component Modifications, Section 2). Transmission reduction of other intracellular viruses, such as HTLV-I/II, HIV-1/2, and Epstein-Barr Virus (EBV), is still unproven.
2. Cytomegalovirus (CMV)-Reduced-Risk Components

Description and Preparation of Components

CMV may be transmitted by cellular blood components with the exception of frozen, deglycerolized red blood cells.

CMV-reduced-risk components include:
• CMV-seronegative components from donors who have tested negative by an FDA-approved screening test for CMV antibodies (CMV seroprevalence is estimated to be 20-80% in the U.S.).
• Leukoreduced (LR) cellular components (either by prestorage LR processes or by apheresis collection), frozen deglycerolized red blood cells, and frozen plasma components, irrespective of the CMV-serologic status of the blood donor.

Use of CMV-seronegative or leukoreduced cellular components decreases the risk of CMV transmission to 1-4%.

Factors contributing to this residual risk include:
• For CMV-seronegative cellular blood products: window-period donors (6-8 weeks of initial infection), failure to seroconvert or donors previously infected whose antibodies have disappeared and/or decreased in titer.
• For leukoreduced blood products: leukoreduction failure in reducing white blood cells (WBCs), high levels of WBC associated virus or a theoretical risk of cell-free virus in the plasma.
Indications

- Premature newborns (<1200 g) during infancy.
- Patients requiring intrauterine transfusion (IUT).
- Transplant patients: CMV-seronegative or CMV-unknown organ, bone marrow and stem cell transplant candidates, and CMV-seronegative organ, bone marrow and stem cell transplant recipients of CMV-seronegative grafts or graft of unknown status.
- Immune deficient or immune suppressed patients: AIDS or HIV infected patients, patients who have congenital immune deficiency, and immunosuppressed patients who are CMV-seronegative or have CMV results pending.
- Pregnant women who are CMV-seronegative or of unknown CMV status.

Notes

- For recipients requiring CMV-reduced-risk granulocyte transfusions, the donor should be CMV-seronegative since these products cannot undergo leukoreduction.
- The CMV serostatus of chronically transfused infants should be checked monthly if initially seronegative.
- CMV-reduced-risk components are not considered necessary for patients receiving chemotherapy unless they are severely immunosuppressed.
3. Irradiated Components

Description and Preparation of Components

Blood products must be exposed to 25 Gy (2500 cGy) delivered to the central portion of the container; the minimum dose at any point in the components shall be 15 Gy (1500 cGy). Irradiation may be in the form of gamma or x-rays, which destroy the lymphocyte’s ability to divide and thereby prevent TA-GVHD.

All cellular products (RBCs, Apheresis Granulocytes, WBD Platelets, Apheresis Platelets) require irradiation as does any plasma product that has never been frozen. TA-GVHD has not been reported from transfusion of cryoprecipitate or frozen plasma; thus these components do not require irradiation.

Irradiation induces erythrocyte membrane damage and an increase in supernatant potassium levels, compared to non-irradiated red cells. Removal of residual supernatant plasma prior to transfusion may reduce the risk associated with elevated plasma potassium. The expiration date of irradiated RBCs is changed to 28 days postirradiation if available shelf life exceeds 28 days. Irradiation has no deleterious effect on platelets, and the expiration date remains unchanged.
**Indications**

- Intrauterine transfusion.
- Infants who have received intrauterine transfusion.
- Known or suspected congenital cellular immunodeficiency (for example, severe combined immunodeficiency-SCID).
- Neonatal exchange transfusion.
- Granulocytes transfusion.
- Components from biologic relatives (any degree).
- Hematopoietic progenitor cell (HPC) recipients (allogeneic, autologous).
- HPC donors requiring allogeneic transfusions prior to completing the collection.
- HLA selected or crossmatched platelet units.
- Hodgkin disease.
- Patients who are undergoing or have received treatment with fludarabine, other purine analogues, or alemtuzumab.

Some programs irradiate all units for newborns who have not had the opportunity to demonstrate immune competence. Routine irradiation for all newborns is, however, controversial.

Aggressive chemotherapy regimens producing profound impairment of cellular immunity may require the use of irradiated blood products.
4. Washed Cellular Components

Description and Preparation of Components

Cellular blood components are washed repetitively, preferably in an automated device, with 1 to 2 liters of normal saline solution (0.9% Sodium Chloride Injection, USP) removing the majority of plasma proteins as well as metabolites and cellular debris accumulated during storage. This method uses an open system, which increases the risk of bacterial contamination, and shortens the expiration date of the washed cellular products to the following: RBCs to 24 hours at 1-6 C, and Platelets (WBD or Apheresis) to 4 hours at room temperature.

Washing may result in a 10-20% loss of product in RBC units. Alternatively, a reduction of 33% of product can occur from platelet units.

The risk for transfusion transmission of infectious pathogens is not altered, nor is the risk for TA-GVHD decreased. Leukoreduction is the preferred means of preventing alloimmunization.
Indications

• Febrile non-hemolytic reaction, when leukoreduced products are ineffective.
• Severe hypersensitivity to transfused blood components: caused by donor plasma proteins such as C4, IgA and haptoglobin. Washing provides an alternative blood product source for IgA deficient patients when IgA deficient donors are not readily available.
• Hemolytic Disease of the Fetus and Newborn (HDFN) and Neonatal Alloimmune Thrombocytopenia (NAIT): patients who are to receive maternal components.
• Hyperkalemia: specific patient populations (for example, infants with intra-cardiac catheterization) who are susceptible to the effects of elevated plasma potassium levels as introduced by rapid transfusion and/or large volumes.
• Paroxysmal nocturnal hemoglobinuria (PNH).

Ref. 15, 52, 70, 75, 96, 100
Overview

In an effort to ensure the safety and efficacy of transfusions, several regulatory and accrediting agencies—including the Joint Commission, the AABB, and the College of American Pathologists—require hospitals to monitor blood transfusion practices and adverse events. Further, both the Joint Commission and the Code of Federal Regulations (CFR) require a hospital to develop, implement, and maintain an effective, ongoing, hospital-wide, data-driven quality assessment and performance improvement program, which includes transfusion services. These agencies do not mandate how the hospital should accomplish these tasks, only that they be performed. For this reason, the approach in monitoring transfusion practices may vary: either a multidisciplinary transfusion committee (TC) may be developed or the task may fall under the purview of other departmental specialties, such as quality assurance, surgery, or critical care services. The committee, referred to as TC in this discussion, is an important facet of the overall blood management program at an institution.

Membership

A multidisciplinary approach allows for better quality assessment and performance improvement. The TC should include representatives from the medical staff (such as those from surgery, anesthesia, medicine, hematology, and
pediatrics) and from nursing, quality services, the transfusion service and other interested and applicable parties, such as blood suppliers. The Medical Director of the transfusion service is a vital contributor to the committee and may or may not serve as chairperson. The chairperson should, however, be a physician knowledgeable in transfusion medicine.

**Functions**

The responsible TC should address, through review or audit, the following aspects of transfusion, as incorporated in policies and procedures (list may not be all inclusive):

- Blood ordering practices.
- Blood refusal practices.
- Patient identification.
- Informed consent.
- Sample collection and labeling.
- Pretransfusion testing orders.
- Distribution, handling, and dispensing.
- Blood administration policies.
- Infectious and non-infectious adverse events.
- Appropriate utilization.
- Monitoring of patients for appropriate responses.
- Compliance with peer-review recommendations.
- Medical errors, near misses, and sentinel events.
- Wastage and discard rates.
- Ability of transfusion services to meet patient needs.
- Clinical alternatives to blood transfusion (for example, erythropoietin, perioperative salvage).
- New transfusion therapies.
- Performance improvement measures.
**Process**

TC members should meet regularly to review various aspects of blood transfusion.

A key function of the committee is to establish transfusion guidelines for administering each of the blood components transfused in the institution, using current peer-reviewed medical literature as a resource. The guidelines should be approved by the Medical Staff prior to implementation. Transfusion guidelines are intended to remind ordering physicians of the transfusion practices for which there is general support and clinical trial evidence. Guidelines provide an overview of selected subjects with reference to alternative literature resources, but they cannot be expected to cover every instance in which a transfusion is indicated. In every case, however, the rationale for transfusion should be clearly documented in the medical record. Guidelines should be reviewed periodically and revised as needed.

The review of transfusions can be done prospectively or concurrently by transfusion service personnel (before blood is issued) or retrospectively by the transfusion service and TC (after blood is issued). For certain high-cost blood products, prospective review may be appropriate to prevent unnecessary transfusions. Similarly, potentially inappropriate orders—for example, a request for platelet transfusion to a patient with thrombotic thrombocytopenic purpura or an order for four units of red blood cells for a small child—may also require review prior to blood issue.
Some hospitals have successfully implemented concurrent electronic screening of blood orders. For most transfusions, where large numbers of blood products are utilized, a retrospective review is adequate and more commonly used. These reviews are best conducted immediately after the transfusion event instead of months later.

There are several methods for performing transfusion audits. As an example, trained hospital quality assurance or compliance staff may perform chart or electronic record reviews, using the approved transfusion guidelines developed by the TC. When there are questions about the indications and results of a transfusion, the clinical records should be brought to the attention of the TC, and the TC should follow its policies for further action as needed.

The TC should also review and discuss various quality indicators (see below). In addition, sentinel reports to the Joint Commission and biological product deviations or fatalities reported to the Food and Drug Administration should be reviewed by the committee.

**Monitors**

Various quality indicators may be monitored and tracked. Performance improvement measures should be put in place where indicated.

Examples of indicators that may be tracked include, but are not limited to the following:
• Blood usage parameters as established by the institution, clinical department, physician, diagnosis (Diagnosis-Related Groups), or surgical procedure.
• Wastage of all blood components, both allogeneic and autologous.
• Patient monitoring during transfusion.
• Adverse reactions to blood products.
• Suspected transfusion-transmitted infections.
• Near-miss events defined as deviations from established procedures and recognized before being carried out.
• Sample collection and labeling, including “wrong blood in tube.”
• Turn-around times for emergency requests.
• Crossmatch-to-transfusion ratio.

Finally, the TC should have a mechanism in place to periodically assess its own effectiveness.

**Reports**

A TC member should be designated as secretary to document activities, distributing minutes and reports of the group’s work for submission to other entities of the hospital (for example, clinical departments of the Medical Staff, the Medical Staff Executive Committee, the Clinical Practices Committee, and the Credentials Committee). The intent of these documents is to provide other peer review committees with a record of the actions taken to ensure appropriate transfusion-related patient care. These minutes may be protected from inappropriate legal discovery as a critical component of an institution’s quality monitoring program.
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Trypanosoma cruzi
(Chagas Disease)
Side Effects and Hazards for Whole Blood and All Blood Components

Immunologic Complications, Immediate

1. *Hemolytic transfusion reaction*, the destruction of red cells, is discussed in detail in the section on components containing red cells and in the platelet section.

2. *Immune-mediated platelet destruction*, one of the causes of refractoriness to platelet transfusion, is the result of alloantibodies in the recipient to HLA or platelet-specific antigens on transfused platelets. This is described in more detail in the section on platelets.

3. *Febrile nonhemolytic reaction* is typically manifested by a temperature elevation of ≥ 1 °C or 2 °F occurring during or shortly after a transfusion and in the absence of any other pyrexic stimulus. This may reflect the action of antibodies against white cells or the action of cytokines, either present in the transfused component or generated by the recipient in response to transfused elements. Febrile reactions may occur in approximately 1% of transfusions, and they occur more frequently in patients receiving non-leukocyte-reduced platelets and those previously alloimmunized by transfusion or pregnancy. No routinely available pre- or posttransfusion tests are helpful in predicting or preventing these reactions. Antipyretics usually provide effective symptomatic relief. Patients who experience repeated, se-
vere febrile reactions may benefit from receiving leukocyte-reduced components. If these reactions are caused by cytokines in the component, prestorage leukocyte reduction may be beneficial.

4. **Allergic reactions** frequently occur as mild or self-limiting urticaria or wheezing that usually respond to antihistamines. More severe manifestations including respiratory and cardiovascular symptoms are more consistent with anaphylactoid/anaphylactic reactions and may require more aggressive therapy (see below). No laboratory procedures are available to predict these reactions.

5. **Anaphylactoid/anaphylactic reactions**, characterized by hypotension, tachycardia, nausea, vomiting and/or diarrhea, abdominal pain, severe dyspnea, pulmonary and/or laryngeal edema, and bronchospasm and/or laryngospasm, are rare but dangerous complications requiring immediate treatment with epinephrine. These reactions have been reported in IgA deficient patients who develop IgA antibodies. Such patients may not have been previously transfused and may develop symptoms after infusion of very small amounts of IgA containing plasma, in any blood component. Similar reactions have also been described in patients with haptoglobin deficiency. In certain circumstances, patients might benefit from the use of washed cellular components to prevent or reduce the severity of allergic reactions not minimized by treatment with medication alone.

6. **Transfusion-related acute lung injury** (TRALI) is the acute onset of hypoxemia within 6 hours of a blood or blood component transfusion and is the most commonly reported cause of transfusion-related deaths in the United States. In addition to hypoxemia, criteria for diagnosis include the presence of bilateral infiltrates on frontal chest radiographs and the exclusion of transfusion-associated
circulatory overload (TACO), or preexisting acute lung injury. The exact mechanism of TRALI is not known, but hypotheses include donor antibodies that react against white cell antigens (HLA or human neutrophil antigens) and the sequestration of neutrophils by the pulmonary endothelium (caused by the recipient’s underlying condition) that are subsequently activated by the infusion of substances in the donor plasma such as antibodies or other biologically active substances. In far fewer cases, antibodies in the recipient that may react with antigens on transfused white cells have been implicated. Laboratory testing does not alter management of this reaction, which is diagnosed mainly on clinical and radiographic findings. Treatment of TRALI requires aggressive respiratory support, frequently requiring mechanical ventilation.

Immunologic Complications, Delayed

1. Delayed hemolytic reaction is described in detail in the section on components containing red cells.
2. Alloimmunization to antigens of red cells, white cells, platelets, or plasma proteins may occur unpredictably after transfusion. Blood components may contain certain immunizing substances other than those indicated on the label. For example, platelet components may also contain red cells and white cells. Primary immunization does not become apparent until days or weeks after the immunizing event, and does not usually cause symptoms or physiologic changes. If components that express the relevant antigen are subsequently transfused, there may be accelerated removal of cellular elements from the circulation and/or systemic symptoms. Clinically significant antibodies to red cell antigens will ordinarily be detected by pretransfusion testing. Alloimmunization to antigens of white cells,
platelets, or plasma proteins can be detected only by specialized testing.

3. Posttransfusion purpura (PTP) is a rare syndrome characterized by the development of dramatic, sudden, and self-limited thrombocytopenia, typically 7 to 10 days after a blood transfusion, in a patient with a history of sensitization by either pregnancy or transfusion. Although the immune specificity may be to a platelet-specific antigen the patient lacks, both autologous and allogeneic platelets are destroyed. High-dose Immune Globulin, Intravenous (IGIV) may correct the thrombocytopenia.

4. Transfusion-associated graft-vs-host disease (TA-GVHD) is a rare but extremely dangerous condition that occurs when viable T lymphocytes in the transfused component engraft in the recipient and react against recipient tissue antigens. TA-GVHD can occur if the host does not recognize and reject the foreign transfused cells, and it can follow transfusion of any component that contains even very small numbers of viable T lymphocytes. Recipients with severe cellular immunodeficiency (except for HIV infection) are at greatest risk (eg, fetuses receiving intrauterine transfusions, recipients of hematopoietic progenitor cell transplants, and selected patients with severe immunodeficiency conditions), but TA-GVHD has also been reported in recipients receiving fludarabine for oncologic and rheumatologic diseases, and in immunologically normal recipients who are heterozygous for a tissue antigen haplotype for which the donor is homozygous. Tissue antigen haplotype sharing is most likely to occur when the transfused component is from a blood relative or has been selected for HLA compatibility. TA-GVHD remains a risk with leukocyte-reduced components because they contain sufficient residual T lymphocytes. Irradiation of the component renders T lymphocytes incapable of prolifera-
tion and is presently the only approved means to prevent TA-GVHD.

Nonimmunologic Complications

1. Because whole blood and blood components are made from human blood, they may carry a risk of transmitting infectious agents [eg, viruses, bacteria, parasites, the variant Creutzfeldt- Jakob disease (vCJD) agent, and, theoretically, the classic CJD agent]. Careful donor selection and available laboratory tests do not totally eliminate the hazard. Also, septic and toxic reactions can result from transfusion of bacterially contaminated blood and blood components. Such reactions are infrequent, but may be life-threatening. This may occur despite careful selection of donors and testing of blood. Donor selection criteria are designed to screen out potential donors with increased risk of infection with HIV, HTLV, hepatitis, and syphilis, as well as other agents (see section on Testing of Donor Blood). These procedures do not totally eliminate the risk of transmitting these agents.

Cytomegalovirus (CMV) may, unpredictably, be present in white-cell-containing components from donors previously infected with this virus, which can persist lifelong despite the presence of serum antibodies. Up to 70% of donors may be anti-CMV positive. Transmission of CMV by transfusion may be of concern in low-birthweight (≤1200 g) premature infants born to CMV-seronegative mothers and in certain other categories of immunocompromised individuals, if they are CMV seronegative. For at-risk recipients, the risk of CMV transmission by cellular components can be reduced by transfusing CMV seronegative or leukocyte-reduced components. For other infectious agents (eg, Babesia spp, Leishmania spp, and Plasmodia spp) there
are no routinely available tests to predict or prevent disease transmission. All potential blood donors are subjected to screening procedures intended to reduce to a minimum the risk that they will transmit infectious agents.

2. *Bacterial sepsis* occurs rarely but can cause acute, severe, sometimes life-threatening effects. Onset of high fever (≥ 2°C or ≥ 3.5°F increase in temperature), severe chills, hypotension, or circulatory collapse during or shortly after transfusion should suggest the possibility of bacterial contamination and/or endotoxin reaction. Although platelet components stored at room temperature have been implicated most frequently, previously frozen components thawed by immersion in a waterbath and red cell components stored for several weeks at 1 to 6°C have also been implicated. Although most apheresis platelets are routinely tested for bacterial contamination, this does not completely eliminate the risk. Both gram-positive and gram-negative organisms have been identified as causing septic reactions. Organisms capable of multiplying at low temperatures (e.g., *Yersinia enterocolitica*) and those using citrate as a nutrient are most often associated with components containing red cells. A variety of pathogens, as well as skin contaminants, have been found in platelet components. Endotoxemia in recipients has resulted from multiplication of gram-negative bacteria in blood components. Prompt recognition of a possible septic reaction is essential, with immediate discontinuation of the transfusion and aggressive therapy with broad-spectrum antimicrobials and vasopressor agents, if necessary. In addition to prompt sampling of the patient’s blood for cultures, investigation should include examination of material from the blood container by Gram’s stain, and cultures of specimens from the container and the administration set. It is important to report all febrile trans-
fusion reactions to the transfusion service. Follow-through from the transfusion service to the blood collection facility may facilitate retrieval of other components associated with the collection.

3. **TACO**, leading to pulmonary edema, can occur after transfusion of excessive volumes or at excessively rapid rates. This is a particular risk in the very young and the elderly and in patients with chronic severe anemia in whom low red cell mass is associated with high plasma volume. Small transfusion volumes can precipitate symptoms in at-risk patients who already have a positive fluid balance. Pulmonary edema should be promptly and aggressively treated, and infusion of colloid preparations, including plasma components and the suspending plasma in cellular components, reduced to a minimum.

4. **Hypothermia** carries a risk of cardiac arrhythmia or cardiac arrest and exacerbation of coagulopathy. Rapid infusion of large volumes of cold blood or blood components can depress body temperature, and the danger is compounded in patients experiencing shock or surgical or anesthetic manipulations that disrupt temperature regulation. A blood warming device should be considered if rapid infusion of blood or blood components is needed. Warming must be accomplished using an FDA-cleared warming device so as not to cause hemolysis.

5. **Metabolic complications** may accompany large-volume transfusions, especially in neonates and patients with liver or kidney disease.

a) Citrate “toxicity” reflects a depression of ionized calcium caused by the presence in the circulation of large quantities of citrate anticoagulant. Because citrate is promptly metabolized by the liver, this complication is rare. Patients with severe liver disease or those with circulatory collapse
that prevents adequate hepatic blood flow may have physiologically significant hypocalcemia after rapid, large-volume transfusion. Citrated blood or blood components administered rapidly through central intravenous access may reach the heart so rapidly that ventricular arrhythmias occur. Standard measurement of serum calcium does not distinguish ionized from complexed calcium. Ionized calcium testing or electrocardiogram monitoring is more helpful in detecting physiologically significant alteration in calcium levels.

b) Other metabolic derangements can accompany rapid or large-volume transfusions, especially in patients with pre-existing circulatory or metabolic problems. These include acidosis or alkalosis (deriving from changing concentrations of citric acid and its subsequent conversion to pyruvate and bicarbonate) and hyper- or hypokalemia.

**Fatal Transfusion Reactions**

When a fatality occurs as a result of a complication of blood or blood component transfusion, the Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research (CBER), should be notified within 1 FDA business day (telephone: 301-827-6220; email: fatalities2@fda.hhs.gov). Within 7 days after the fatality, a written report must be submitted to the Director, Office of Compliance and Biologics Quality, HFM-600, CBER, FDA, 1401 Rockville Pike, Rockville, MD 20852-1448. A copy of the report should be sent to the collecting facility, if appropriate. Updated information about CBER reporting requirements may be found at http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/default.htm.
Appendix 2:
Published Estimates of Transfusion Risks

The incidence of adverse transfusion reactions is not known with certainty and is often widely variable among studies. Transfusion risks depend on a number of factors, including but not limited to, patient characteristics, concurrent medications and underlying illness (for example, immunosuppression), component type and preparation method, intensity of surveillance activities for transfusion reactions, and definitions, recognition, and completeness of reporting transfusion reactions.

Published estimates of the incidence of transfusion risks in the following tables are expressed as a percentage if greater than 0.1% or as a ratio if less than 0.1%. The denominator is the number of transfusions, unless otherwise noted for distributed components. A range is given if possible, and the reader is referred to the selected references for additional information.
## Immunologic Complications, Immediate

<table>
<thead>
<tr>
<th>Description</th>
<th>Estimated incidence</th>
<th>Comment</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hemolytic transfusion reaction (incompatible red cells)</td>
<td>1 per 12,000-38,000</td>
<td>About 2-7% of ABO-mistransfusion events are fatal</td>
<td>27, 62, 68</td>
</tr>
<tr>
<td>Fatal: 1 per 600,000-1.5 million</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute hemolytic transfusion reactions (incompatible plasma)</td>
<td>1 per 46,000</td>
<td>~21% of platelet transfusions were incompatible in a retrospective cohort study</td>
<td>68, 71</td>
</tr>
<tr>
<td>Immune-mediated platelet destruction (refractoriness to platelet transfusion)</td>
<td>4-13%</td>
<td>About 50% of HLA-alloimmunized patients become refractory to prestorage leukoreduced components</td>
<td>105, 112</td>
</tr>
<tr>
<td>Febrile nonhemolytic reaction</td>
<td>RBC: 0.1-0.4%</td>
<td>Prestorage leukoreduced components</td>
<td>27, 59, 62, 135</td>
</tr>
<tr>
<td>WBD Platelets: 0.1%; Apheresis Platelets: 4-8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic reaction (mild)</td>
<td>RBC: 0.1-0.6%</td>
<td></td>
<td>27, 38, 62</td>
</tr>
<tr>
<td>Apheresis Platelets: ~5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma: 1-3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaphylactoid/anaphylactic reactions</td>
<td>1 per 20,000-50,000</td>
<td></td>
<td>27, 38, 62</td>
</tr>
<tr>
<td>Transfusion-related acute lung injury (TRALI)</td>
<td>1 per 5,000-440,000</td>
<td>Plasma collected predominantly from male donors</td>
<td>17, 27, 30, 43, 62, 89, 123</td>
</tr>
<tr>
<td>RBC: 1 per 440,000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma: 1 per 250,000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apheresis Platelets: 1 per 96,000</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Immunologic Complications, Delayed**

<table>
<thead>
<tr>
<th>Description</th>
<th>Estimated Incidence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alloimmunization (red cell antigens)—Delayed hemolytic transfusion reaction</td>
<td>1 per 5,400-62,000 Fatal: 1 per 1.8 million</td>
<td>27, 62, 68, 123</td>
</tr>
<tr>
<td>Alloimmunization (red cell antigens)—Delayed serologic transfusion reaction</td>
<td>1 per 1,500-3,000 0.5% per RBC transfused</td>
<td>27, 33, 62, 102</td>
</tr>
<tr>
<td>Alloimmunization [human leukocyte antigens (HLA), human platelet antigens (HPA)] (prestorage leukoreduced components)</td>
<td>HLA: 10-17% of multiply-transfused patients HPA: 2-10% of multiply-transfused patients</td>
<td>112</td>
</tr>
<tr>
<td>Posttrasfusion purpura (PTP)</td>
<td>Less than 1 in 2,000,000</td>
<td>123</td>
</tr>
<tr>
<td>Transfusion-associated graft-vs-host disease (TA-GVHD)</td>
<td>Exceedingly rare; case reports</td>
<td>27, 62, 123</td>
</tr>
</tbody>
</table>
## Nonimmunologic Complications
(Infectious and Noninfectious)

<table>
<thead>
<tr>
<th></th>
<th>Estimated Incidence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious complications</strong> (see Appendix 5 for infectious diseases for which donations are tested)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>1-4% with CMV reduced-risk components (seronegative donor or leukoreduced component)</td>
<td>62</td>
</tr>
<tr>
<td>Babesiosis (Babesia microti; Babesia spp.)</td>
<td>RBC: 1 per 10&lt;sup&gt;6&lt;/sup&gt; units 3-10 cases/yr in the US</td>
<td>125</td>
</tr>
<tr>
<td>Malaria (Plasmodia spp.)</td>
<td>RBC: &lt; 0.1 per 10&lt;sup&gt;6&lt;/sup&gt;</td>
<td>117</td>
</tr>
<tr>
<td>Leishmaniasis (Leishmania spp.)</td>
<td>Rare case reports</td>
<td>14</td>
</tr>
<tr>
<td>vCJD</td>
<td>4 cases worldwide</td>
<td>87, 120</td>
</tr>
<tr>
<td>CJD</td>
<td>None</td>
<td>22</td>
</tr>
<tr>
<td>Lyme disease (Borrelia bergdorferi)</td>
<td>None</td>
<td>77</td>
</tr>
<tr>
<td>Bacterial sepsis</td>
<td>RBC: 1 per 5,000,000 Platelets: see Appendix 5</td>
<td>27, 62</td>
</tr>
<tr>
<td><strong>Noninfectious complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfusion-associated circulatory overload (TACO)</td>
<td>1-8%</td>
<td>27, 62</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>No published estimates—more likely to occur with massive transfusion or in pediatric and neonatal patients</td>
<td>-</td>
</tr>
<tr>
<td>Metabolic complications (hypocalcemia, acidosis/alkalosis; hyper- or hypokalemia)</td>
<td>No published estimates—more likely to occur with massive transfusion or in pediatric and neonatal patients</td>
<td>-</td>
</tr>
</tbody>
</table>
**Appendix 3: Brief History of Infectious Disease Testing in the United States**

<table>
<thead>
<tr>
<th>Disease or Infection</th>
<th>Analyte</th>
<th>Year Introduced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td><em>Treponema pallidum</em> antibodies</td>
<td>1950s</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Hepatitis B surface antigen (HBsAg)</td>
<td>1971</td>
</tr>
<tr>
<td></td>
<td>Anti-HBc</td>
<td>1986</td>
</tr>
<tr>
<td></td>
<td>DNA</td>
<td>2008-2009</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Anti-HCV</td>
<td>1990; 1992; 1997</td>
</tr>
<tr>
<td></td>
<td>RNA</td>
<td>1999</td>
</tr>
<tr>
<td>AIDS; HIV</td>
<td>Anti-HIV-1/2</td>
<td>1985; 1992; 2009</td>
</tr>
<tr>
<td></td>
<td>RNA</td>
<td>1999</td>
</tr>
<tr>
<td>HTLV</td>
<td>Anti-HTLV-I/II</td>
<td>1988; 1998</td>
</tr>
<tr>
<td>WNV</td>
<td>RNA</td>
<td>2003</td>
</tr>
<tr>
<td>Chagas</td>
<td><em>Trypanosoma cruzi</em> (<em>T. cruzi</em>) antibodies</td>
<td>2007 (universal) 2009 (selective, donor-based testing)</td>
</tr>
</tbody>
</table>

Abbreviations: AIDS, acquired immuno deficiency syndrome; HIV, human immunodeficiency virus; HTLV, human T-cell lymphotropic virus; WNV, West Nile virus.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Marker</th>
<th>Assay method</th>
<th>Trade name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>HBsAg (screen)</td>
<td>Chemiluminescent immunoassay (ChLIA)</td>
<td>Abbott PRISM</td>
</tr>
<tr>
<td></td>
<td>HBsAg (neutralization, confirmatory)</td>
<td>ChLIA</td>
<td>Abbott PRISM</td>
</tr>
<tr>
<td></td>
<td>Anti-HBc</td>
<td>ChLIA</td>
<td>Abbott PRISM</td>
</tr>
<tr>
<td></td>
<td>HBV DNA</td>
<td>Nucleic acid test (transcription mediated amplification; TMA)</td>
<td>Novartis PROCLEIX Ultrio (HIV-1/HCV/ HBV)</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Anti-HCV (screen)</td>
<td>Enzyme-linked immunosorbent assay (HCV 3.0 ELISA)</td>
<td>Ortho Summit Processing System</td>
</tr>
<tr>
<td></td>
<td>Hepatitis C Virus Encoded Antigen (Recombinant) c22-3, c200 and NS5</td>
<td>Recombinant immunoblot assay (RIBA)</td>
<td>Novartis (Chiron) RIBA</td>
</tr>
<tr>
<td></td>
<td>Anti-HCV (confirmatory)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HCV RNA*</td>
<td>TMA</td>
<td>Novartis PROCLEIX Ultrio (HIV-1/HCV/ HBV)</td>
</tr>
<tr>
<td>HIV-1, -2</td>
<td>Anti-HIV-1/HIV-2 (screen)</td>
<td>ChLIA</td>
<td>Abbott PRISM</td>
</tr>
<tr>
<td></td>
<td>Anti-HIV-1/HIV-2 (confirmatory and differentiation)</td>
<td>HIV-1 indirect immunofluorescence (IFA); HIV-2 enzyme immunoassay (EIA); Multispot HIV-1/ HIV-2 rapid test</td>
<td>Sanochemia IFA; Bio-Rad EIA and rapid test</td>
</tr>
<tr>
<td></td>
<td>HIV RNA*</td>
<td>TMA</td>
<td>Novartis PROCLEIX Ultrio Assay (HIV-1/ HCV/HBV)</td>
</tr>
</tbody>
</table>
### Appendix 4: Current Test Methods, Infectious Disease, American Red Cross (2010), continued

<table>
<thead>
<tr>
<th>Disease</th>
<th>Marker</th>
<th>Assay method</th>
<th>Trade name</th>
</tr>
</thead>
<tbody>
<tr>
<td>HTLV I/II</td>
<td>Anti-HTLV-I/HTLV-II (screen)</td>
<td>ChLIA</td>
<td>Abbott PRISM</td>
</tr>
<tr>
<td></td>
<td>Anti-HTLV-I/HTLV-II (confirmatory and differentiation)</td>
<td>State of California algorithm involving in-house EIA, IFA, western blot and radio-immunoprecipitation assay (RIPA)</td>
<td>State of California Viral and Rickettsial Diseases Laboratory</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Treponema pallidum</td>
<td>Agglutination</td>
<td>Olympus PK TP PK7200 System</td>
</tr>
<tr>
<td></td>
<td>Antibody (screen)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treponema pallidum</td>
<td>EIA</td>
<td>Captia-G</td>
</tr>
<tr>
<td></td>
<td>Antibody (confirmatory)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WNV</td>
<td>WNV RNA (screen)</td>
<td>TMA</td>
<td>Novartis PROCLEIX WNV</td>
</tr>
<tr>
<td></td>
<td>WNV RNA and Antibody (confirmatory)</td>
<td>TMA, PCR and IgM/IgG antibodies</td>
<td>Novartis PROCLEIX WNV; National Genetics Institute and Focus Diagnostic</td>
</tr>
<tr>
<td>Chagas</td>
<td>T. cruzi Antibody (screen)</td>
<td>ELISA</td>
<td>Ortho</td>
</tr>
<tr>
<td></td>
<td>T. cruzi Antibody (confirmatory)</td>
<td>RIPA</td>
<td>Quest</td>
</tr>
<tr>
<td>Bacteria (apheresis and pooled WBD-platelets)</td>
<td>Bacteria aerobic media</td>
<td>Culture</td>
<td>BacT/ALERT 3D, bioMérieu</td>
</tr>
</tbody>
</table>

*Antibody negative/RNA positive samples are confirmed by polymerase chain reactive (PCR) at National Genetics Institute

**Abbreviations:** WBD, whole blood-derived
Appendix 5: Prevalence of Infectious Markers among Blood Donors and Residual Risk of Transfusion-Transmitted Infections

<table>
<thead>
<tr>
<th>Agent</th>
<th>Prevalence in Blood Donors</th>
<th>Residual Risk for Recipient</th>
<th>Time Period</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV**</td>
<td>1 per 34,883**</td>
<td>1 per 1,467,000***</td>
<td>2007-2008</td>
<td>140, 141</td>
</tr>
<tr>
<td>HCV#</td>
<td>1 per 2,748**</td>
<td>1 per 1,149,000***</td>
<td></td>
<td>140, 141</td>
</tr>
<tr>
<td>HBV</td>
<td>1 per 11,443**</td>
<td>1 per 282,000†</td>
<td>11/2006-07/2008 for residual risk</td>
<td>139, 140</td>
</tr>
<tr>
<td>HTLV-I/II</td>
<td>1 per 40,938**</td>
<td>1 per 4,364,000‡</td>
<td>2007-2008 for residual risk</td>
<td>140</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>1 per 4,054**</td>
<td>No transmissions reported since 1960s</td>
<td>2007-2008</td>
<td>138, 140</td>
</tr>
<tr>
<td>WNV</td>
<td>1 per 16,000 during transmission season</td>
<td>1 per 4,570,000 during transmission season (that is, 11 cases from 9 donations since screening began)</td>
<td>June 2003-Dec 2009 (includes June-Dec for each year or 18.7 million donations total)</td>
<td>120, 140</td>
</tr>
<tr>
<td>Trypanosoma cruzi</td>
<td>1 per 76,560**</td>
<td>No transmissions reported from screened blood; &lt; 1 per 15 million, based on cases of prevalent infections</td>
<td>Jan 2007-Oct 2009 (&gt; 30 million donations screened)</td>
<td>140</td>
</tr>
</tbody>
</table>
Appendix 5: Prevalence of Infectious Markers among Blood Donors and Residual Risk of Transfusion-Transmitted Infections, continued

<table>
<thead>
<tr>
<th>Agent</th>
<th>Prevalence in Blood Donors</th>
<th>Residual Risk for Recipient</th>
<th>Time Period</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria, Apheresis Platelets</td>
<td>1 per 5,000</td>
<td>1 in 109,000 distributed</td>
<td>Dec 2006-July 2008</td>
<td>10, 29</td>
</tr>
<tr>
<td>Bacteria, WBD-Pooled Platelets (5 donors/pool)</td>
<td>1 per 1,200</td>
<td>ND</td>
<td>2008</td>
<td>10, 28</td>
</tr>
</tbody>
</table>

# For HIV and HCV, the data represent results for both antibody testing and viral RNA testing by NAT. (Zou S, Notari EP, Stramer SL, Dodd RY. American Red Cross, personal communication).

*Numbers reflect HIV-1 as the prevalence and residual risk for HIV-2 are too low to calculate in the U.S.

**Among whole blood donations from both first-time and repeat donors in 2008 (Zou S, Notari EP, Stramer SL, Dodd RY. American Red Cross, personal communication).

***Allogeneic donations (whole blood and apheresis) from both first-time and repeat donors (Zou S, Notari EP, Stramer SL, Dodd RY. American Red Cross, personal communication).

Abbreviations: WNV, West Nile Virus; WBD, whole blood-derived; ND, not determined.
References


28. Eder AF, Dy BA, Benjamin RJ. American Red Cross Hemovigilance Program, 2008; personal communication.


128. van de Watering L. What has universal leucodepletion given us: evidence from clinical trials? *Vox Sang* 2004;87(suppl):139-142.


<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ACT</td>
<td>activated clotting time</td>
</tr>
<tr>
<td>aPTT</td>
<td>activated partial thromboplastin time</td>
</tr>
<tr>
<td>AS</td>
<td>additive solution/adenine saline</td>
</tr>
<tr>
<td>CCl</td>
<td>corrected count increment</td>
</tr>
<tr>
<td>cGy</td>
<td>centiGray</td>
</tr>
<tr>
<td>ChLIA</td>
<td>chemiluminescent immunoassay</td>
</tr>
<tr>
<td>CMV</td>
<td>cytomegalovirus</td>
</tr>
<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>CPD</td>
<td>citrate-phosphate-dextrose</td>
</tr>
<tr>
<td>CP2D</td>
<td>citrate-phosphate-dextrose-dextrose</td>
</tr>
<tr>
<td>CPDA</td>
<td>citrate-phosphate-dextrose-adenine</td>
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<tr>
<td>DIC</td>
<td>disseminated intravascular coagulation</td>
</tr>
<tr>
<td>EBV</td>
<td>Epstein-Barr virus</td>
</tr>
<tr>
<td>ELISA</td>
<td>enzyme-linked immunosorbent assay</td>
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<tr>
<td>FFP</td>
<td>fresh frozen plasma</td>
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<tr>
<td>FNHR</td>
<td>febrile nonhemolytic reaction</td>
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<tr>
<td>FP24</td>
<td>plasma frozen within 24 hours of phlebotomy</td>
</tr>
<tr>
<td>Gy</td>
<td>Gray</td>
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<tr>
<td>HBc</td>
<td>hepatitis B core</td>
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<tr>
<td>HbS</td>
<td>hemoglobin S</td>
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<td>HBsAg</td>
<td>hepatitis B surface antigen</td>
</tr>
<tr>
<td>HBV</td>
<td>hepatitis B virus</td>
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<tr>
<td>Hct</td>
<td>hematocrit</td>
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<td>HCV</td>
<td>hepatitis C virus</td>
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<td>HDFN</td>
<td>hemolytic disease of the fetus and newborn</td>
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<tr>
<td>Hgb</td>
<td>hemoglobin</td>
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<td>HITT</td>
<td>heparin-induced thrombocytopenia and thrombosis</td>
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<td>HIV</td>
<td>human immunodeficiency virus</td>
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<td>HLA</td>
<td>human leukocyte antigen</td>
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<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>HPA</td>
<td>human platelet antigen</td>
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<td>HPC</td>
<td>hematopoietic progenitor cell</td>
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<td>HTLV</td>
<td>human T-cell lymphotropic virus</td>
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<td>INR</td>
<td>international normalized ratio</td>
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<td>IVIG</td>
<td>intravenous immune globulin</td>
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<tr>
<td>LR</td>
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<td>NAIT</td>
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<tr>
<td>PCR</td>
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<td>PT</td>
<td>prothrombin time</td>
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<td>RBC</td>
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<td>RIBA</td>
<td>recombinant immunoblot assay</td>
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<td>TACO</td>
<td>transfusion-associated circulatory overload</td>
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<td>TA-</td>
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<td>graft-vs-host disease</td>
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<td>TEG</td>
<td>thromboelastography</td>
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<td>TMA</td>
<td>transcription mediated amplification</td>
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<td>TRALI</td>
<td>transfusion-related acute lung injury</td>
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<td>TTP</td>
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<td>vCJD</td>
<td>variant Creutzfeld-Jakob disease</td>
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<tr>
<td>vWD</td>
<td>von Willebrand disease</td>
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<tr>
<td>WBD</td>
<td>whole blood-derived</td>
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CRYOPRECIPITATED AHF | UTILIZATION GUIDELINES
Acquired Fibrinogen Deficiency and Bleeding
Fibrin Sealant
Massive Transfusion
Uremic Bleeding
Disseminated Intravascular Coagulation (DIC)
Fibronectin Replacement
Congenital Factor Deficiencies

Blood Component Modifications
1. Leukocyte-Reduced Components
2. Cytomegalovirus (CMV)-Reduced-Risk Components
3. Irradiated Components
4. Washed Cellular Components

The Hospital Transfusion Committee

Appendix 1: Side Effects and Hazards for Whole Blood and All Blood Components
Immunologic Complications, Immediate
Immunologic Complications, Delayed
Nonimmunologic Complications
Fatal Transfusion Reactions

Appendix 2: Published Estimates of Transfusion Risks

Appendix 3: Brief History of Infectious Disease Testing in the United States

Appendix 4: Current Test Methods, Infectious Disease, American Red Cross (2010)

Appendix 5: Prevalence of Infectious Markers among Blood Donors and Residual Risk of Transfusion-Transmitted Infections