

CIRCULAR OF INFORMATION

FOR THE USE OF HUMAN BLOOD AND BLOOD COMPONENTS

This *Circular* was prepared jointly by AABB, the American Red Cross, America's Blood Centers, and the Armed Services Blood Program. The Food and Drug Administration recognizes this *Circular of Information* as an acceptable extension of container labels.

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Federal Law prohibits dispensing the blood and blood components described in this circular without a prescription.

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Notice to All Users

The *Circular of Information for the Use of Human Blood and Blood Components* (hereafter referred to as *Circular*) is an extension of container labels, as the space on those labels is limited.

Blood and blood components are biologic products and, in the form of cellular products, living human tissue intended for use in patient treatment. Professional judgment based on clinical evaluation determines the selection of components, dosage, rate of administration, and decisions in situations not covered in this general statement.

This *Circular*, as a whole or in part, cannot be considered or interpreted as an expressed or implied warranty of the safety or fitness of the described blood or blood components when used for their intended purpose. Attention to the specific indications for blood components is needed to prevent inappropriate transfusion.

Because of the risks associated with transfusion, physicians should be familiar with alternatives to allogeneic transfusion. Blood banks and transfusion services are referred to the *AABB Standards for Blood Banks and Transfusion Services* for additional information and policies, especially in the areas of recipient sample identification, compatibility testing, issue and transfusion of blood and blood components, investigation of transfusion reactions, and proper record-keeping practices. Transfusionists are referred to the *AABB Technical Manual* for applicable chapters on adult and pediatric transfusion.

The specific product manufacturer's package insert should be reviewed for instructions pertaining to use of transfusion devices (eg, filters, blood administration sets, and blood warmers).

This *Circular* is supplied to conform with applicable federal statutes and regulations of the Food and Drug Administration (FDA), United States (US) Department of Health and Human Services. The blood components in this *Circular* marked with the symbol "Ω" are blood components for which FDA currently has not received data to demonstrate that they meet prescribed requirements of safety, purity, and potency, and therefore are not licensed for distribution in interstate commerce.

General Information for Whole Blood and All Blood Components

Donors

Blood and blood components described in this *Circular* have been collected from volunteer blood donors for use in other patients (allogeneic transfusions) or from patients donating for themselves (autologous transfusions). The donors have been questioned about risk factors for transmissible infectious agents, have satisfactorily completed a health assessment that includes a questionnaire on past and present illnesses, have satisfied minimum physiologic criteria, and may have had the opportunity to confidentially exclude their donation from transfusion.

Testing of Donor Blood

Testing of a sample of donor blood is performed before units of blood or blood components are distributed for routine transfusion. The donor's ABO group and Rh type have been determined, including testing for the presence of weak D antigen.

A sample from each donation intended for allogeneic use has been tested by FDA-licensed tests and found to be nonreactive for antibodies to human immunodeficiency virus (anti-HIV-1/2), hepatitis C virus (anti-HCV), human T-cell lymphotropic virus (anti-HTLV-I/II), and hepatitis B core antigen (anti-HBc), and nonreactive for hepatitis B surface antigen (HBsAg).

Licensed nucleic acid tests (NAT) for HCV ribonucleic acid (RNA), HIV-1 RNA, and West Nile virus (WNV) RNA have been performed and found to be nonreactive. A serologic test for syphilis has been performed and found to be nonreactive.

For units labeled “FOR AUTOLOGOUS USE ONLY,” infectious disease testing requirements vary depending on whether the unit will be drawn in one facility and infused in another facility and whether the unit might be made available for allogeneic transfusion. Infectious disease testing may be omitted for autologous units drawn, stored, and infused at the same facility. Autologous units for which testing has not been performed are labeled “DONOR UNTESTED.” Autologous units with reactive test results may be used for transfusion to the donor-patient with appropriate physician authorization. A biohazard label will be applied to autologous units that are tested for evidence of infection as listed above and determined to be reactive. If the units labeled “FOR AUTOLOGOUS USE ONLY” are infused at a different facility, at a minimum the first donation from the donor-patient in each 30-day period is tested for evidence of infection as listed above. Subsequent units that are not tested will be labeled as “DONOR TESTED WITHIN THE LAST 30 DAYS.” If an establishment allows any autologous donation to be available for allogeneic transfusion, or ships autologous donations to any establishment that does, the collecting establishment must test each donation for evidence of infection as listed above. This includes units labeled “FOR AUTOLOGOUS USE ONLY.”

Tests for unexpected antibodies against red cell antigens have been performed on samples from all donors. The results of these tests are negative or have been determined to be clinically insignificant unless otherwise indicated on the label. Other tests may have been performed on donor blood as indicated by information that has been provided by the blood bank or transfusion service on an additional label or tie tag, or in a supplement to this *Circular*.

Blood and Component Labeling

All blood components identified in this *Circular* have the ISBT 128 product name listed first and other recognized component names in parentheses.

Blood and blood component labels will contain the following information:

1. The proper name, whole blood or blood component, including an indication of any qualification or modification.
2. The method by which the blood component was prepared, either by whole blood or apheresis collection.
3. The temperature range in which the blood component is to be stored.
4. The preservatives and anticoagulant used in the preparation of the blood or blood components, when appropriate.
5. The standard contents or volume is assumed unless otherwise indicated on the label or in *Circular* supplements.
6. The number of units in pooled blood components and any sedimenting agent used during cytappheresis, if applicable.
7. The name, address, registration number, and US license number (if applicable) of the collection and processing location.
8. The expiration date (and time if applicable), which varies with the method of preparation (open or closed system) and the preservatives and anticoagulant used. When the expiration time is not indicated, the product expires at midnight.
9. The donation (unit or pool) identification number.
10. The donor category (paid or volunteer, and autologous if applicable).
11. ABO group and Rh type, if applicable.
12. Special handling information, as required.
13. Statements regarding recipient identification, this *Circular*, infectious disease risk, and prescription requirement.

Instructions for Use

The following general instructions pertain to Whole Blood and all the blood components described in this *Circular*:

1. All blood and blood components must be maintained in a controlled environment and stored under appropriate conditions as described in the *AABB Standards for Blood Banks and Transfusion Services*.
2. The intended recipient and the blood container must be properly identified before the transfusion is started.
3. Aseptic technique must be employed during preparation and administration. If the container is entered in a manner that violates the integrity of the system, the component expires 4 hours after entry if maintained at room temperature (20-24 C), or 24 hours after entry if refrigerated (1-6 C).
4. All blood components must be transfused through a filter designed to remove clots and aggregates (generally a standard 170- to 260-micron filter).
5. Blood and blood components should be mixed thoroughly before use.
6. Blood and blood components must be inspected immediately before use. If, upon visual inspection, the container is not intact or the appearance is abnormal (presence of excessive hemolysis, a significant color change in the blood bag as compared with the tubing segments, floccular material, cloudy appearance, or other problems), the blood or blood component must not be used for transfusion and appropriate follow-up with the transfusion service must be performed.
7. No medications or solutions may be routinely added to or infused through the same tubing with blood or blood components with the exception of 0.9% Sodium Chloride, Injection (USP), unless 1) they have been approved for this use by the FDA or 2) there is documentation available to show that the addition is safe and does not adversely affect the blood or blood component.
8. Lactated Ringer's, Injection (USP) or other solutions containing calcium should never be added to or infused through the same tubing with blood or blood components containing citrate.
9. Blood components should be warmed if clinically indicated for situations such as exchange or massive transfusions, or for patients with cold-reactive antibodies. Warming must be accomplished using an FDA-cleared warming device so as not to cause hemolysis.
10. Some life-threatening reactions occur after the infusion of only a small volume of blood or blood components. Therefore, unless otherwise indicated by the patient's clinical condition, the rate of infusion should initially be slow.
11. Periodic observation and recording of vital signs should occur during and after the transfusion to identify suspected adverse reactions. If a transfusion reaction occurs, the transfusion must be discontinued immediately and appropriate therapy initiated. The infusion should not be restarted unless approved by transfusion service protocol.
12. Specific instructions concerning possible adverse reactions shall be provided to the patient or a responsible caregiver when direct medical observation or monitoring of the patient will not be available after transfusion.
13. Transfusion should be started before component expiration and completed within 4 hours.
14. All adverse events related to transfusion, including possible bacterial contamination of blood or a blood component or suspected disease transmission, must be reported to the transfusion service according to its local protocol.

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 pyrexia 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, severe 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 proliferation 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 (eg, *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 transfusion 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 preexisting 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; e-mail: 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>.

Components Containing Red Cells

Overview

Description

Red cells contain hemoglobin and serve as the primary agent for transport of oxygen to tissues. The primary red-cell-containing transfusion component is Red Blood Cells (RBCs). This component is prepared by centrifugation or sedimentation of Whole Blood to remove much of the plasma. RBC components can also be prepared by apheresis methods.

Depending upon the collection system used, a single whole blood donation typically contains either 450 mL ($\pm 10\%$) or 500 mL ($\pm 10\%$) of blood collected from blood donors with a minimum hematocrit of 38%, withdrawn in a sterile container that includes an anticoagulant solution licensed for this component. Occasionally, units of other volumes are collected and those volumes are stated on the label.

Red-cell-containing components can be stored for an interval (“shelf life”) determined by the properties of the anticoagulant-preservative solution (see Table 1). Whole Blood units are prepared in an aseptic manner in a ratio of 14 mL of anticoagulant-preservative solution per 100 mL of whole blood collected. Apheresis components are collected into anticoagulants as recommended by the manufacturer.

After plasma is removed, the resulting component is Red Blood Cells, which has a hematocrit of 65% to 80% and a usual volume between 225 mL and 350 mL. Additive solutions (AS) may

be mixed with the red cells remaining after removal of nearly all of the plasma (see Table 2). The typical hematocrit of AS RBCs is 55% to 65% and the volume is approximately 300 to 400 mL. AS RBCs have a shelf life of 42 days. Descriptions of specific components containing red cells are given at the end of this section.

Table 1. Contents of Anticoagulant-Preservative Solutions

Anticoagulant-Preservative	Trisodium Citrate	Citric Acid	Monobasic Sodium Phosphate	Dextrose	Adenine	Shelf Life
Anticoagulant citrate-dextrose A (ACD-A)*	22.0 g/L	8.0 g/L	0	24.5 g/L	0	21 days
Citrate-phosphate dextrose (CPD)	26.3 g/L	3.27 g/L	2.22 g/L	25.5 g/L	0	21 days
Citrate-phosphate-dextrose-dextrose (CP2D)	26.3 g/L	3.27 g/L	2.22 g/L	51.1 g/L	0	21 days
Citrate-phosphate-dextrose-adenine (CPDA-1)	26.3 g/L	3.27 g/L	2.22 g/L	31.9 g/L	0.275 g/L	35 days

*ACD is used for apheresis components.

Table 2. Content of Additive Solutions (in mg/100mL)

Additive Solution (mg/100 mL)	Dextrose	Adenine	Monobasic Sodium Phosphate	Mannitol	Sodium Chloride	Sodium Citrate	Citric Acid	Shelf Life
AS-1 (Adsol)	2200	27	0	750	900	0	0	42 days
AS-3 (Nutricel)	1100	30	276	0	410	588	42	42 days
AS-5 (Optisol)	900	30	0	525	877	0	0	42 days

Actions

All RBC components and Whole Blood increase the recipient's oxygen-carrying capacity by increasing the mass of circulating red cells. Processing and/or storage deplete the component of virtually all potential therapeutic benefit attributable to the functions of white cells and platelets; cellular elements remain in these blood components and may cause adverse immunologic or physiologic consequences. Residual plasma in the component provides the recipient with volume expansion and nonlabile plasma proteins to the extent that residual plasma is present in the preparation. Depending on the method of production, RBCs may contain approximately 20 to 100 mL of residual plasma. RBCs prepared with additive solutions are the most commonly used red cell product and have limited residual plasma.

Indications

Red-cell-containing components are indicated for treatment of symptomatic or critical deficit of oxygen-carrying capacity. They are also indicated for red cell exchange transfusion.

Contraindications

Red-cell-containing components should not be used to treat anemias that can be corrected with specific hematinic medications such as iron, vitamin B₁₂, folic acid, or erythropoietin.

RBCs or Whole Blood should not be used solely for volume expansion or to increase oncotic pressure of circulating blood.

Dosage and Administration

Each unit of RBCs or Whole Blood contains enough hemoglobin to increase the hemoglobin concentration in an average-sized adult by approximately 1 g/dL (increase hematocrit by 3%). Smaller aliquots can be made available for use with neonatal or pediatric patients, or adults with special transfusion needs.

The ABO group of all red-cell-containing components must be compatible with ABO antibodies in the recipient's plasma. Whole Blood must be ABO identical with the recipient; RBCs, which contain a reduced volume of antibody-containing plasma, need not be ABO identical.

Serologic compatibility between recipient and donor must be established before any red-cell-containing component is transfused. This may be accomplished by performing ABO/Rh typing, antibody screening, and crossmatching by serologic technique or use of a computer crossmatch. In cases when delay in transfusion will be life-threatening, uncrossmatched group O RBCs or ABO group-specific RBCs may be transfused before completion of pretransfusion compatibility testing.

The initial portion of each unit transfused should be infused cautiously and with sufficient observation to detect onset of acute reactions. Thereafter, the rate of infusion can be more rapid, as tolerated by the patient's circulatory system. It is undesirable for components that contain red cells to remain at room temperature longer than 4 hours. If the anticipated infusion rate must be so slow that the entire unit cannot be infused within 4 hours, it is appropriate to order smaller aliquots for transfusion.

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the earlier section titled Side Effects and Hazards for Whole Blood and All Blood Components. Listed below are hazards that apply specifically to components that contain red cells.

1. **Hemolytic transfusion reaction** is the immunologic destruction of transfused red cells, nearly always the result of incompatibility of antigen on the transfused cells with antibody in the recipient's circulation (see item 5 below for discussion of nonimmunologic hemolysis). The most common cause of severe, acute hemolytic reactions is transfusion of ABO-incompatible blood, resulting from identification errors occurring at some point(s) in the transfusion process. Serologic incompatibility undetected during pretransfusion testing is a much less common cause of acute hemolysis. If a transfusion reaction is suspected, the transfusion must be stopped and the transfusion service laboratory notified immediately. Information identifying the patient, the transfusion component, and associated forms and labels must be reviewed promptly to detect possible errors. A postreaction blood sample, preferably drawn from a site other than the transfusion access, must be sent to the laboratory along with the implicated unit of blood and administration set.

Acute hemolytic reactions characteristically begin with an increase in temperature and pulse rate; symptoms may include chills, dyspnea, chest or back pain, abnormal bleeding, or shock. Instability of blood pressure is frequent, the direction and magnitude of change depending upon the phase of the reaction and the magnitude of compensatory mechanisms. In anesthetized patients, hemoglobinuria, hypotension, and evidence of disseminated intravascular coagulopathy (DIC) may be the first signs of incompatibility. Laboratory

findings can include hemoglobinemia and/or hemoglobinuria, followed by elevation of serum bilirubin. The direct antiglobulin test (DAT) is usually positive, with rare exceptions (ie, complete hemolysis of incompatible red cells). Treatment includes measures to maintain or correct arterial blood pressure; correct coagulopathy, if present; and promote and maintain urine flow. Lack of symptoms does not exclude an acute hemolytic reaction.

Delayed hemolytic reactions occur in previously red-cell-alloimmunized patients in whom antigens on transfused red cells provoke anamnestic production of antibody. The anamnestic response reaches a significant circulating level while the transfused cells are still present in the circulation; the usual time frame is 2 to 14 days after transfusion. Signs may include unexplained fever, development of a positive DAT, and unexplained decrease in hemoglobin/hematocrit. Hemoglobinemia and hemoglobinuria are uncommon, but elevation of lactate dehydrogenase (LDH) or bilirubin may be noted. Most delayed hemolytic reactions have a benign course and require no treatment.

Hemolytic transfusion reactions in patients with sickle cell anemia may be particularly severe, with destruction of autologous as well as transfused red cells. In such patients, serologic investigations may not reveal the specificity of the causative antibody. Prospective matching for Rh and Kell antigens may decrease risk.

2. Antigens on transfused red cells may cause red cell **alloimmunization** of the recipient. Clinically significant antibodies to red cell antigens will usually be detected in pretransfusion antibody screening tests. For most patients, red cell antigen matching beyond ABO and Rh is unnecessary.
3. **TACO**, resulting in pulmonary edema, can accompany transfusion of any component at a rate more rapid than the recipient's cardiac output can accommodate. Whole Blood creates more of a risk than Red Blood Cells because the transfused plasma adds volume without increasing oxygen-carrying capacity. Patients with chronic anemia have increased plasma volumes and are at increased risk for circulatory overload.
4. **Iron overload** is a long-term complication of repeated RBC transfusions. Each transfusion contributes approximately 250 mg of iron. Patients requiring multiple transfusions for aplastic anemia, thalassemias, or hemoglobinopathies are at far greater risk than patients transfused for hemorrhagic indications, because blood loss is an effective means of iron excretion. Patients with predictably chronic transfusion requirements should be considered for treatment with iron-chelating agents or a program of exchange transfusion therapy, if applicable.
5. **Nonimmunologic hemolysis** occurs rarely, but can result from: 1) introduction of hypotonic fluids into the circulation, 2) effects of drugs co-administered with transfusion, 3) effects of bacterial toxins, 4) thermal injury to transfusion components, by either freezing or overheating, 5) metabolic damage to cells, as from hemoglobinopathies or enzyme deficiencies, or 6) development of physical or osmotic stresses. Examples of situations capable of causing nonimmune red cell hemolysis include: exposure to excessive heat by non-FDA-approved warming methods, mixture with hypotonic solutions, or transfusion under high pressure through small-gauge or defective needles.

Components Available

1. **RED BLOOD CELLS (RED BLOOD CELLS)** are prepared from blood collected into any of the anticoagulant-preservative solutions approved by the FDA, and separated from the plasma by centrifugation or sedimentation. Separation may be done at any time during the allowable storage interval ("shelf life"). Red Blood Cells may contain from 160 to 275 mL of red cells (50-80 g of hemoglobin) suspended in varying quantities of residual plasma.

2. **RED BLOOD CELLS ADENINE SALINE ADDED (RED BLOOD CELLS ADENINE SALINE ADDED)** are prepared by centrifuging whole blood to remove as much plasma as possible, and replacing the plasma with usually 100 to 110 mL of an additive solution that contains some combination of dextrose, adenine, sodium chloride, and either monobasic sodium phosphate (AS-3) or mannitol (AS-1 and AS-5); the hematocrit is usually between 55% and 65%. Red Blood Cells in an additive solution have lower viscosity than Red Blood Cells, and flow through administration systems in a manner more comparable to that of Whole Blood. Red Blood Cells stored with an additive solution have an extended shelf life.
3. **RED BLOOD CELLS LEUKOCYTES REDUCED (RED BLOOD CELLS LEUKOCYTES REDUCED)** are prepared from a unit of Whole Blood (collected in anticoagulant-preservative solution as noted above) containing ≥ 1 to 10×10^9 white cells. In general, leukocyte reduction is achieved by filtration: 1) soon after collection (prestorage) or 2) after varying periods of storage in the laboratory. Leukocyte reduction will decrease the cellular content and volume of blood according to characteristics of the filter system used. RBCs Leukocytes Reduced must have a residual content of leukocytes $< 5.0 \times 10^6$. Leukocyte reduction filters variably remove other cellular elements in addition to white cells. The leukocyte-reduced component contains at least 85% of the original red cell content.
4. **APHERESIS RED BLOOD CELLS (RED BLOOD CELLS PHERESIS)** are red cells collected by apheresis. This component must be collected in an approved anticoagulant. The red cell volume collected and the anticoagulant used are noted on the label. Aside from the automated collection method used, the component is comparable to whole-blood-derived RBCs in all aspects. The dosage can be calculated, as for RBCs, from the red cell content of the product. Apheresis RBCs contain on average 60 g of hemoglobin per unit.
5. **APHERESIS RED BLOOD CELLS LEUKOCYTES REDUCED (RED BLOOD CELLS PHERESIS LEUKOCYTES REDUCED)** are collected by apheresis methods. Leukocyte reduction is achieved in the manufacturing process resulting in a final product containing $< 5.0 \times 10^6$ leukocytes and at least 85% of the target red cell content.
6. **RED BLOOD CELLS, LOW VOLUME (RED BLOOD CELLS, LOW VOLUME)** are products prepared when 300 to 404 mL of whole blood is collected into an anticoagulant volume calculated for 450 mL \pm 45 mL or when 333 to 449 mL of whole blood is collected into an anticoagulant volume calculated for 500 mL \pm 50 mL. These products reflect a collection with an altered ratio of anticoagulant to red cells and may not be an indication of a lower dose of hemoglobin. Plasma and platelet components should not be prepared from low-volume collections.
7. **WHOLE BLOOD (WHOLE BLOOD)** is rarely used for transfusion. In situations where Whole Blood is indicated but RBCs are used, a suitable plasma volume expander should be administered. See also General Information for Whole Blood and All Blood Components, Instructions for Use. All whole blood transfusions must be ABO identical.
8. **FROZEN RED BLOOD CELLS (RED BLOOD CELLS FROZEN)** and **FROZEN REJUVENATED RED BLOOD CELLS (RED BLOOD CELLS REJUVENATED FROZEN)** are prepared by adding glycerol to red cells as a cryoprotective agent before freezing. The glycerol must be removed from the thawed component before it is infused. Frozen RBCs may be stored for up to 10 years, and for longer intervals if there is particular need for specific units. Ω Frozen storage is especially suitable for red cells with unusual antigenic phenotypes.
9. **DEGLYCEROLIZED RED BLOOD CELLS (RED BLOOD CELLS DEGLYCEROLIZED)** is the form in which cryopreserved red cells (Frozen Red Blood Cells) are made available for infusion. Glycerol is added to red cells as a cryoprotective agent before freezing, and must be removed from the thawed component before it is infused.

Deglycerolized RBCs contain 80% or more of the red cells present in the original unit of blood, and have approximately the same expected posttransfusion survival as RBCs. Glycerol is removed by washing the cells with successively lower concentrations of Sodium Chloride, Injection (USP); the final suspension is in 0.9% Sodium Chloride, Injection (USP), with or without small amounts of dextrose. Small amounts of residual-free hemoglobin may cause the supernatant fluid to be pink-tinged.

Deglycerolized RBCs provide the same physiologic benefits as RBCs, but their use is usually restricted to situations in which standard transfusion components are inappropriate or unavailable. Deglycerolized RBCs may be useful for transfusions to patients with previous severe allergic transfusion reactions, because the process efficiently removes plasma constituents.

In addition to the side effects and hazards of RBC transfusion, Deglycerolized RBCs carry a risk of intravascular hemolysis if deglycerolization has been inadequate.

Deglycerolized RBCs must be transfused within 24 hours after thawing if prepared in an open system. If prepared in a closed system, they can be infused within a 2-week interval after thawing.

10. **REJUVENATED RED BLOOD CELLS (RED BLOOD CELLS REJUVENATED)** may be prepared from red cells stored in CPD, CPDA-1, and AS-1 storage solutions up to 3 days after expiration. Addition of an FDA-approved solution containing inosine, phosphate, and adenine restores 2,3-diphosphoglycerate and adenosine triphosphate to levels approximating those of freshly drawn cells. These products must be washed before infusion to remove the inosine, which may be toxic. Rejuvenated RBCs may be prepared and transfused within 24 hours or frozen for long-term storage.
11. **DEGLYCEROLIZED REJUVENATED RED BLOOD CELLS (RED BLOOD CELLS REJUVENATED DEGLYCEROLIZED)** is the form in which rejuvenated, cryopreserved red cells (Frozen Rejuvenated Red Blood Cells) are made available for infusion. For additional information, see sections on Rejuvenated RBCs and Deglycerolized RBCs above.
12. **Autologous Whole Blood and RBCs** are drawn from patients who anticipate requiring blood transfusions. Donor-safety screening criteria and testing procedures applicable to collection from allogeneic donors do not always apply to these components. Each unit must be labeled "FOR AUTOLOGOUS USE ONLY." A biohazard label is required if these units have a reactive test result. In addition, if these units are untested, they must be labeled as "DONOR UNTESTED." Autologous Whole Blood or RBCs can be modified into any of the components described above. If a facility allows for autologous units to be crossed over for inclusion in the general blood inventory, the donors and units must be subjected to the same donor eligibility requirements and test requirements as allogeneic donors and units.
13. See section on Further Processing for irradiated products.

Plasma Components

Overview

Plasma is the aqueous part of blood and can be derived from the separation of a whole-blood collection or by apheresis collection. Important elements in plasma include albumin, coagulation factors, fibrinolytic proteins, immunoglobulin, and other proteins. Once plasma is collected, it can be stored frozen and subsequently thawed and kept in a liquid state. If Fresh Frozen Plasma (FFP) is thawed at 1 to 6 C, and the insoluble cryoprecipitate (see Cryoprecipitated Components) is removed by centrifugation, the supernatant plasma can be refrozen and labeled as Plasma Cryoprecipitate Reduced. Labile coagulation factor levels vary based upon ABO group, storage conditions, and/or further processing (see Table 3).

Table 3. Coagulation Factor Activity of Thawed Plasma Derived from FFP*

Coagulation Factor	Level [†]					Mean Change from Day 1 to Day 5 (%)	p Values
	Day 1	Day 2	Day 3	Day 4	Day 5		
Factor VIII (%)							
Blood group A	107 ± 26	76 ± 19	66 ± 18	65 ± 17	63 ± 16	41	<0.004 [‡]
Blood group B	103 ± 44	74 ± 37	71 ± 35	67 ± 36	67 ± 33	35	<0.02 [‡]
Blood group O	70 ± 16	51 ± 10	43 ± 10	43 ± 7	41 ± 8	41	<0.001 [‡]
Factor II (%)	81 ± 9	81 ± 9	81 ± 9	80 ± 10	80 ± 10	1	NS
Factor V (%)	79 ± 7	75 ± 8	71 ± 9	68 ± 9	66 ± 9	16	NS
Factor VII (%)	90 ± 18	81 ± 15	76 ± 15	72 ± 14	72 ± 15	20	NS
Factor X	85 ± 13	84 ± 13	84 ± 15	82 ± 11	80 ± 11	6	NS
Fibrinogen (mg/dL)	225 ± 12	224 ± 13	224 ± 13	224 ± 17	225 ± 12	0	NS

*Reported with permission from Downes KA, Wilson E, Yomtovian R, Sarode R. Serial measurement of clotting factors in thawed plasma for 5 days (letter). *Transfusion* 2001;41:570.

[†]Mean ± SD.

[‡]Comparison of Factor VIII activity at Day 1 and that at Day 3 was statistically significant.

Fresh Frozen Plasma

Description

FRESH FROZEN PLASMA (FRESH FROZEN PLASMA) is prepared from a whole blood or apheresis collection and frozen at -18 C or colder within the time frame as specified in the directions for use for the blood collection, processing, and storage system. The anticoagulant solution used and the component volume are indicated on the label. On average, units contain 200 to 250 mL, but apheresis-derived units may contain as much as 400 to 600 mL. FFP contains plasma proteins including all coagulation factors. FFP contains high levels of the labile coagulation Factors V and VIII.

FFP should be infused immediately after thawing or stored at 1 to 6 C for up to 24 hours. If stored longer than 24 hours, the component must be relabeled (see Thawed Plasma) or discarded depending on the method of collection.

Action

FFP serves as a source of plasma proteins for patients who are deficient in or have defective plasma proteins.

Indications

FFP is indicated in the following conditions:

1. Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors (eg, liver disease, DIC).
2. Patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
3. Patients taking warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect or who need only transient reversal of warfarin effect.
4. For transfusion or plasma exchange in patients with thrombotic thrombocytopenic purpura (TTP).

5. Management of patients with selected coagulation factor deficiencies, congenital or acquired, for which no specific coagulation concentrates are available.
6. Management of patients with rare specific plasma protein deficiencies, such as C1 inhibitor, when recombinant products are unavailable.

Contraindications

Do not use this product when coagulopathy can be corrected more effectively with specific therapy, such as vitamin K, Cryoprecipitated AHF (Antihemophilic Factor), or specific coagulation factor concentrates.

Do not use this product when blood volume can be safely and adequately replaced with other volume expanders.

Dosage and Administration

Compatibility tests before transfusion are not necessary. Plasma must be ABO compatible with the recipient's red cells. The volume transfused depends on the clinical situation and patient size, and may be guided by laboratory assays of coagulation function.

Do not use FFP if there is evidence of container breakage or of thawing during storage. FFP must be thawed in a waterbath at 30 to 37 C or in an FDA-cleared device. If a waterbath is used, thaw the component in a protective plastic overwrap using gentle agitation.

Side Effects and Hazards

Hazards that pertain to all transfusion components, including FFP, are described in the earlier section on Side Effects and Hazards for Whole Blood and All Blood Components.

Plasma Frozen Within 24 Hours After Phlebotomy

Description

PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY (PLASMA FROZEN WITHIN 24 HOURS AFTER PHLEBOTOMY) is prepared from a whole blood collection and must be separated and placed at -18 C or below within 24 hours from whole blood collection. The anticoagulant solution used and the component volume are indicated on the label. On average, units contain 200 to 250 mL. This plasma component is a source of nonlabile plasma proteins. Levels of Factor VIII are significantly reduced and levels of Factor V and other labile plasma proteins are variable compared with FFP.

Plasma Frozen Within 24 Hours After Phlebotomy should be infused immediately after thawing or stored at 1 to 6 C for up to 24 hours. If stored longer than 24 hours, the component must be relabeled (see Thawed Plasma) or discarded.

Action

This plasma component serves as a source of plasma proteins for patients who are deficient in or have defective plasma proteins. Coagulation factor levels might be lower than those of FFP, especially labile coagulation Factors VIII and V.

Indications

See Fresh Frozen Plasma.

Contraindications

See Fresh Frozen Plasma. In addition, this product is not indicated for treatment of deficiencies of labile coagulation factors including Factors VIII and V.

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

Plasma Cryoprecipitate Reduced*Description*

PLASMA CRYOPRECIPITATE REDUCED (PLASMA, CRYOPRECIPITATE REDUCED) is prepared from FFP after thawing and centrifugation and removal of the cryoprecipitate. The remaining product is plasma that is deficient in fibrinogen, Factor VIII, Factor XIII, von Willebrand factor (vWF), cryoglobulin, and fibronectin. This supernatant plasma must be refrozen within 24 hours. Proteins such as albumin; ADAMTS13; and Factors II, V, VII, IX, X, and XI remain in almost the same levels as in FFP [the high-molecular-weight forms of vWF (multimers) are more thoroughly removed by this process than smaller multimers].

Action

This component serves as a source for plasma proteins except for fibrinogen, Factor VIII, Factor XIII, and vWF.

Indications

Plasma Cryoprecipitate Reduced is used for transfusion or plasma exchange in patients with TTP. It may be used to provide clotting factors except fibrinogen, Factor VIII, Factor XIII, and vWF.

Contraindications

This component should not be used as a substitute for FFP, Plasma Frozen Within 24 Hours After Phlebotomy, or Thawed Plasma.

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

Liquid Plasma Components*Description*

Other plasma components may be made from whole blood collected in all approved anticoagulants. Levels and activation state of coagulation proteins in these products are variable. The volume is indicated on the label.

THAWED PLASMA Ω (THAWED PLASMA) is derived from FFP or Plasma Frozen Within 24 Hours After Phlebotomy, prepared using aseptic techniques (closed system), thawed at 30 to 37 C, and maintained at 1 to 6 C for up to 4 days after the initial 24-hour post-thaw period has elapsed. The volume is indicated on the label. Thawed Plasma contains stable coagulation factors such as Factor II and fibrinogen in concentrations similar to those of FFP, but variably reduced amounts of other factors (see Table 3).

Action

This component serves as a source of plasma proteins. Levels and activation state of coagulation proteins in thawed plasma are variable and change over time.

Indications

1. Management of preoperative or bleeding patients who require replacement of multiple plasma coagulation factors except for patients with a consumptive coagulopathy.
2. Initial treatment of patients undergoing massive transfusion who have clinically significant coagulation deficiencies.
3. Patients taking warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect or who need only transient reversal of warfarin effect.

This component should not be used to treat isolated coagulation factor deficiencies where other products are available with higher concentrations of the specific factor(s).

Contraindications

See Fresh Frozen Plasma. Do not use liquid plasma components as the treatment for isolated coagulation factor deficiencies where other products are available with higher concentrations of the specific factor(s).

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

LIQUID PLASMA (LIQUID PLASMA) is separated no later than 5 days after the expiration date of the Whole Blood and is stored at 1 to 6 C. The profile of plasma proteins in Liquid Plasma is poorly characterized. Levels and activation state of coagulation proteins in Liquid Plasma are dependent upon and change with time in contact with cells, as well as the conditions and duration of storage.

Action

This component serves as a source of plasma proteins. Levels and activation state of coagulation proteins are variable and change over time.

Indications

Initial treatment of patients who are undergoing massive transfusion because of life-threatening trauma/hemorrhages and who have clinically significant coagulation deficiencies.

Contraindications

See Fresh Frozen Plasma. Do not use liquid plasma components as the treatment for isolated coagulation factor deficiencies where other products are available with higher concentrations of the specific factor(s).

Dosage and Administration

See Fresh Frozen Plasma.

Side Effects and Hazards

See Fresh Frozen Plasma.

Cryoprecipitated Components

Overview

Description

Cryoprecipitated Antihemophilic Factor (AHF) is prepared by thawing whole-blood-derived FFP between 1 and 6 C and recovering the precipitate. The cold-insoluble precipitate is refrozen within 1 hour. Cryoprecipitated AHF contains fibrinogen, Factor VIII, Factor XIII, vWF, and fibronectin. Each unit of Cryoprecipitated AHF should contain ≥ 80 IU Factor VIII units and ≥ 150 mg of fibrinogen in approximately 5 to 20 mL of plasma.

If the label indicates “Pooled Cryoprecipitated AHF,” several units of Cryoprecipitated AHF have been pooled. The volume of the pool is indicated on the label and, if used, the volume of 0.9% Sodium Chloride, Injection (USP) added may be separately listed. To determine the minimum potency of this component, assume 80 IU of Factor VIII and 150 mg of fibrinogen for each unit of Cryoprecipitated AHF indicated on the label.

Action

Cryoprecipitate serves as a source of fibrinogen, Factor VIII, Factor XIII, vWF, and fibronectin.

Indications

This component is used in the control of bleeding associated with fibrinogen deficiency and to treat Factor XIII deficiency. It is also indicated as second-line therapy for von Willebrand disease and hemophilia A (Factor VIII deficiency). Coagulation factor preparations other than cryoprecipitate are preferred when blood component therapy is needed for management of von Willebrand disease and Factor VIII deficiency. Use of this component may be considered for control of uremic bleeding after other modalities have failed. Indications for use as a source of fibronectin are not clear.

Contraindications

Do not use this component unless results of laboratory studies indicate a specific hemostatic defect for which this product is indicated. Cryoprecipitate should not be used if virus-inactivated Factor VIII concentrates or recombinant factor preparations are available for management of patients with von Willebrand disease or hemophilia A.

Dosage and Administration

Compatibility testing is unnecessary. ABO-compatible material is preferred. Rh type need not be considered when using this component.

The frozen component is thawed in a protective plastic overwrap in a waterbath at 30 to 37 C up to 15 minutes (thawing time may need to be extended if product is pooled before freezing). This component should not be given if there is evidence of container breakage or of thawing during storage. Do not refreeze after thawing. Thawed Cryoprecipitated AHF should be kept at room temperature and transfused as soon as possible after thawing, within 6 hours if it is a single unit (from individual donor, or pooled before freezing or administration using an FDA-cleared sterile connecting device), and within 4 hours after entering the container (eg, to attach an administration set or to pool) without using an FDA-cleared sterile connecting device.

Cryoprecipitated AHF may be transfused as individual units or pooled. For pooling, the precipitate in one or more concentrates should be mixed well with 10 to 15 mL of diluent to ensure complete removal of all material from the container. The preferred diluent is 0.9%

Sodium Chloride, Injection (USP). Serial use of each bag's contents to resuspend the precipitate into subsequent bags may be used to efficiently pool cryoprecipitate into a single bag.

The recovery of transfused fibrinogen is 50% to 60%. When used to correct hypofibrinogenemia, Cryoprecipitated AHF may be dosed according to the following formula to raise plasma fibrinogen by approximately 50 to 100 mg/dL: Number of bags = $0.2 \times$ body weight in kg. Thrombosis alters fibrinogen kinetics; therefore, patients receiving cryoprecipitate as fibrinogen replacement in conditions associated with increased fibrinogen turnover should be monitored with fibrinogen assays.

For treatment of bleeding in patients with hemophilia A when Factor VIII concentrates are not available, rapid infusion of a loading dose expected to produce the desired level of Factor VIII is usually followed by a smaller maintenance dose every 8 to 12 hours. To maintain hemostasis after surgery, a regimen of therapy for 10 days or longer may be required. If circulating antibodies to Factor VIII are present, the use of larger doses, activated concentrates, porcine-derived concentrates, or other special measures may be indicated. To calculate cryoprecipitate dosage as a source of Factor VIII, the following formula is helpful: Number of bags = (Desired increase in Factor VIII level in % \times 40 \times body weight in kg) / average units of Factor VIII per bag, minimum 80. Good patient management requires that the Cryoprecipitated AHF treatment responses of Factor VIII-deficient recipients be monitored with periodic plasma Factor VIII assays.

For treatment of von Willebrand disease, smaller amounts of Cryoprecipitated AHF will correct the bleeding time. Because the vWF content of Cryoprecipitated AHF is not usually known, an empiric dose of 1 bag per 10 kg of body weight has been recommended. These patients should be monitored by appropriate laboratory studies to determine the frequency of Cryoprecipitated AHF administration.

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the earlier section on Side Effects and Hazards for Whole Blood and All Blood Components.

If a large volume of ABO-incompatible cryoprecipitate is used, the recipient may develop a positive DAT and, very rarely, mild hemolysis.

Components Available

1. **CRYOPRECIPITATED AHF (CRYOPRECIPITATED AHF)**
2. **POOLED CRYOPRECIPITATED AHF (CRYOPRECIPITATED AHF, POOLED)**

Platelet Components

Overview

Description

Platelet therapy may be achieved by infusion of either Apheresis Platelets or Platelets (whole-blood-derived platelet concentrates). In either component, platelets are suspended in an appropriate volume of the original plasma, which contains near-normal levels of stable coagulation factors that are stored at room temperature. One unit of Platelets derived from a whole blood collection usually contains no fewer than 5.5×10^{10} platelets suspended in 40 to 70 mL of plasma. Platelets may be provided either singly or as a pool. One unit of Apheresis Platelets usually contains $\geq 3.0 \times 10^{11}$ platelets and is a therapeutic equivalent to 4 to 6 units of

Platelets. Platelet components may contain a varying number of leukocytes depending upon the technique used in preparation. Some units may contain more than the trace amounts of red cells usually present and will appear pink to salmon in color.

Actions

Platelets are essential for normal hemostasis. Complex reactions occur between platelets, vWF, collagen in the walls of disturbed vasculature, phospholipids, and soluble coagulation factors, including thrombin. These changes induce platelet adherence to vessel walls and platelet activation, which leads to platelet aggregation and formation of a primary hemostatic plug. The therapeutic goal of platelet transfusion is to provide adequate numbers of normally functioning platelets for the prevention or cessation of bleeding.

Indications

Platelet transfusions may be given to patients with thrombocytopenia, dysfunctional platelet disorders, active platelet-related bleeding, or serious risk of bleeding (ie, prophylactic use). Patients with the following medical conditions may require platelet transfusion: leukemia, myelodysplasia, aplastic anemia, solid tumors, congenital or acquired platelet dysfunction, central nervous system trauma. Patients undergoing extracorporeal membrane oxygenation or cardiopulmonary bypass may also need platelet transfusion. Thrombocytopenia is unlikely to be the cause of bleeding in patients with platelet counts of at least 50,000/ μ L. Higher transfusion thresholds may be appropriate for patients with platelet dysfunction. For the clinically stable patient with an intact vascular system and normal platelet function, prophylactic platelet transfusions may be appropriate at 5000 to 10,000/ μ L.

Prophylactic platelet transfusion may not be of therapeutic benefit when thrombocytopenia is related to destruction of circulating platelets secondary to autoimmune disorders [eg, immune thrombocytopenic purpura (ITP)]; however, when these patients bleed, platelet therapy is often useful.

Platelets Leukocytes Reduced or Apheresis Platelets Leukocytes Reduced are indicated to decrease the frequency of recurrent febrile, nonhemolytic transfusion reaction, HLA alloimmunization, and transfusion-transmitted CMV infection (see section on Further Processing).

Contraindications

Do not use this component if bleeding is unrelated to decreased numbers of, or abnormally functioning, platelets. If platelet function is normal, platelets should not be transfused when the platelet count is greater than 100,000/ μ L. Prophylactic transfusion is generally not indicated when platelet dysfunction is extrinsic to the platelet, such as in uremia, certain types of von Willebrand disease, and hyperglobulinemia. Patients with congenital surface glycoprotein(s) defects should be transfused conservatively to reduce the possibility for alloimmunization to the missing protein(s).

Do not use in patients with activation or autoimmune destruction of endogenous platelets, such as in heparin-induced thrombocytopenia (HIT), TTP, or ITP, unless the patient has a life-threatening hemorrhage.

Dosage and Administration

Compatibility testing is not necessary in routine platelet transfusion. Except in unusual circumstances, the donor plasma should be ABO compatible with the recipient's red cells when this component is to be transfused to infants or when large volumes are to be transfused. The number of platelet units to be administered depends on the clinical situation of each patient. One unit of Platelets would be expected to increase the platelet count of a 70-kg adult by 5000 to

10,000/ μL and increase the count of an 18-kg child by 20,000/ μL . The therapeutic adult dose is 1 unit of Apheresis Platelets or 4 to 6 units of whole-blood-derived platelets, either of which usually contain $\geq 3.0 \times 10^{11}$ platelets. For prophylaxis, this dose may need to be repeated in 1 to 3 days because of the short lifespan of transfused platelets (3-4 days). Platelet components must be examined before administration. Units with excessive aggregates should not be administered. Transfusion may proceed as quickly as tolerated, but must take less than 4 hours. Do not refrigerate platelets.

The corrected count increment (CCI) is a calculated measure of patient response to platelet transfusion that adjusts for the number of platelets infused and the size of the recipient, based upon body surface area (BSA)

$$\text{CCI} = (\text{post-count} - \text{pre-count}) \times \text{BSA} / \text{platelets transfused}$$

where post-count and pre-count are platelet counts (μL) after and before transfusion, respectively; BSA is the patient body surface area (meter^2); and platelets transfused is the number of administered platelets ($\times 10^{11}$). The CCI is usually determined 10 to 60 minutes after transfusion. For example:

A patient with acute myelogenous leukemia with a nomogram-derived BSA of 1.40 meter^2 is transfused with a unit of Apheresis Platelets (a platelet dose of 4.5×10^{11}). The pretransfusion platelet count is 2000/ μL . The patient's platelet count from a sample of blood collected 15 minutes after platelet transfusion is 29,000/ μL . The CCI is calculated as $(29,000 - 2000) \times 1.4 / 4.5 = 8,400/\mu\text{L}$ per 10^{11} per m^2 .

In the clinically stable patient, the CCI is typically greater than 7500 at 10 minutes to 1 hour after transfusion and remains above 4500 at 24 hours. Both immune and nonimmune mechanisms may contribute to reduced platelet recovery and survival. Along with supportive serologic test results, a CCI of less than 5000 at 10 minutes to 1 hour after transfusion may indicate an immune-mediated refractory state to platelet therapy. With nonimmune mechanisms, platelet recovery within 1 hour may be adequate, although survival at 24 hours is reduced (refer to Platelet Alloimmunization).

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the section on Side Effects and Hazards for Whole Blood and All Blood Components. Listed below are hazards that apply specifically to components that contain platelets.

1. **Bacterial Contamination:** Although methods to limit and detect bacterial contamination have been implemented for most platelet components, they remain the most likely blood components to be contaminated with bacteria. Gram-positive skin flora are the most commonly recovered bacteria. Symptoms may include high fever (≥ 2.0 C or ≥ 3.5 F increase in temperature), severe chills, hypotension, or circulatory collapse during or immediately after transfusion. In some instances, symptoms, especially when associated with contamination by gram-positive organisms, may be delayed for several hours following transfusion. Prompt management should include broad-spectrum antibiotic therapy along with cultures from the patient, suspected blood component(s), and administration set. A Gram's stain of suspected contaminated unit(s) should be performed whenever possible. Apheresis Platelets are usually tested for bacterial contamination before issue.
2. **Platelet Alloimmunization:** Platelets bear a variety of antigens, including HLA and platelet-specific antigens. Patients transfused with platelets often develop HLA antibodies. The patient may become refractory to incompatible platelets. When platelets are transfused to a patient with an antibody specific for an expressed antigen, the survival time of the transfused

platelets may be markedly shortened. Nonimmune events may also contribute to reduced platelet survival. It is possible to distinguish between immune and nonimmune platelet refractoriness by assessing platelet recovery soon after infusion (ie, a 10- to 60-minute postinfusion platelet increment). In immune refractory states secondary to serologic incompatibility, there is poor recovery in the early postinfusion interval. In nonimmune mechanisms (ie, splenomegaly, sepsis, fever, intravascular devices, and DIC) platelet recovery within 1 hour of infusion may be adequate while longer-term survival (ie, 24-hour survival) is reduced. Serologic tests may confirm the presence of alloimmunization. Serologic tests (HLA typing or a platelet crossmatch) may also be helpful in selecting platelets with acceptable survival.

3. **Red Blood Cell Alloimmunization:** Immunization to red cell antigens may occur because of the presence of residual red cells in Platelets. Red cell compatibility testing is necessary only if the component is prepared by a method that allows the component to contain 2 mL or more of red cells, making the unit appear pink to salmon in color. When platelet components from Rh-positive donors must be given to Rh-negative females of childbearing potential because of lack of availability of Rh-negative platelets, prevention of D immunization by use of Rh Immune Globulin should be considered.
4. **Hemolysis:** Platelet transfusions that are not ABO identical may contain incompatible plasma and may cause a positive DAT and possibly, hemolysis. Platelet transfusions from group O donors with high-titer isohemagglutinins (anti-A or anti-B) may cause acute hemolytic reactions in susceptible patients.

Components Available

1. **PLATELETS (PLATELETS)** are a concentrate of platelets separated from a single unit of Whole Blood. One unit of Platelets should contain no fewer than 5.5×10^{10} platelets suspended in 40 to 70 mL of plasma. This component is usually provided as a pool. See below.
2. **POOLED PLATELETS (PLATELETS POOLED)** are composed of individual platelet units combined by aseptic technique and have an allowable shelf life as specified in the directions for use for the blood collection, processing, and storage system. The number of units of Platelets in the pool will be indicated on the label. To determine the minimum potency of this component, assume 5.5×10^{10} platelets per unit of Platelets indicated on the label. See the label for the approximate volume.
3. **PLATELETS LEUKOCYTES REDUCED (PLATELETS LEUKOCYTES REDUCED)** may be prepared using an open or closed system. One unit of Platelets Leukocytes Reduced should contain 5.5×10^{10} platelets and $<8.3 \times 10^5$ leukocytes. Components prepared using an open system will expire 4 hours after preparation. Components prepared using a closed system will have a shelf life as specified in the directions for use for the blood collection, processing, and storage system. This component is usually provided as a pool. See below.
4. **POOLED PLATELETS LEUKOCYTES REDUCED (PLATELETS LEUKOCYTES REDUCED, POOLED)** may be prepared by pooling and filtering Platelets or pooling Platelets Leukocytes Reduced in an open system that will have a 4-hour shelf life. The number of units in the pool will be indicated on the label. To determine the minimum potency of this component, assume 5.5×10^{10} platelets per unit of Platelets Leukocytes Reduced indicated on the label and $<5 \times 10^6$ leukocytes in the pool. See the label for the approximate volume. This component can also be prepared and pooled using an FDA-cleared system to provide a product with a 5-day shelf life. Components prepared using this system provide a therapeutic adult dose of platelets and $<5.0 \times 10^6$ leukocytes.

5. **APHERESIS PLATELETS (PLATELETS PHERESIS)** are an effective way to harvest a therapeutic adult dose of platelets from a single donor. Apheresis Platelets should contain $\geq 3.0 \times 10^{11}$ platelets. One unit of Apheresis Platelets may replace 4 to 6 units of Platelets. The volume of plasma is indicated on the label and varies between 100 and 500 mL. The number of leukocytes contained in this component varies depending upon the blood cell separator and protocol used for collection. Apheresis Platelets are supplied in one bag or in two connected bags to improve platelet viability during storage by providing more surface area for gas exchange. ACD-A is the anticoagulant solution currently used for the collection and preservation of Apheresis Platelets.
6. **APHERESIS PLATELETS LEUKOCYTES REDUCED (PLATELETS PHERESIS LEUKOCYTES REDUCED)** can be leukocyte reduced during the collection process or may be prepared by further processing using leukocyte reduction filters. Apheresis Platelets Leukocytes Reduced should contain $\geq 3.0 \times 10^{11}$ platelets and $< 5.0 \times 10^6$ leukocytes. When Apheresis Platelets Leukocytes Reduced are prepared by further processing, these may be labeled Apheresis Platelets Leukocytes Reduced provided the requirement for residual leukocyte count is met and the platelet recovery is at least 85% of the prefiltration content. The volume, anticoagulant-preservative, and storage conditions for Apheresis Platelets Leukocytes Reduced are the same as those for Apheresis Platelets. Apheresis Platelets Leukocytes Reduced have a shelf life of 5 days, unless the facility is participating in a post-marketing program, which allows a 7-day expiration date.

Granulocyte Components

Description

APHERESIS GRANULOCYTES Ω (GRANULOCYTES PHERESIS) contain numerous leukocytes and platelets as well as 20 to 50 mL of red cells. The number of granulocytes in each concentrate is usually $> 1.0 \times 10^{10}$. Various modalities may be used to improve granulocyte harvest, including donor administration of granulocyte colony-stimulating factor and/or corticosteroids. The final volume of the product is 200 to 300 mL including anticoagulant and plasma as indicated on the label.

Red cell sedimenting agents approved by the FDA, such as hydroxyethyl starch (HES), are typically used in the collection of granulocytes. Residual agents will be present in the final component and are described on the label. Apheresis Granulocytes should be administered as soon after collection as possible because of well-documented deterioration of granulocyte function during short-term storage. If stored, maintain at 20 to 24 C without agitation for no more than 24 hours.

Actions

Granulocytes migrate toward, phagocytize, and kill bacteria and fungi. A quantitative relationship exists between the level of circulating granulocytes and the prevalence of bacterial and fungal infection in neutropenic patients. The ultimate goal is to provide the patient with the ability to fight infection. The infusion of a granulocyte component may not be associated with a significant increase in the patient's granulocyte count and is dependent on multiple factors, including the patient's clinical condition.

Indications

Granulocyte transfusion therapy is controversial. Apheresis Granulocytes are typically used in the treatment of patients with documented infections (especially gram-negative bacteria and

fungi) unresponsive to antimicrobial therapy in the setting of neutropenia [absolute granulocyte count $<0.5 \times 10^9/L$ (500/ μ L)] with expected eventual marrow recovery, or neonatal sepsis. A trial of broad-spectrum antimicrobial agents should be used before granulocyte transfusion therapy is initiated. If the intended recipient is CMV-seronegative and severely immunosuppressed (eg, a marrow transplant recipient), serious consideration should be given before administration of CMV-seropositive granulocytes. In addition to neutropenic patients, patients with hereditary neutrophil function defects (such as chronic granulomatous disease) may be candidates for granulocyte transfusion therapy.

Contraindications

Prophylactic use of granulocytes in noninfected patients is not routinely recommended.

Dosage and Administration

Transfuse as soon as possible. A standard blood infusion set is to be used for the administration of Apheresis Granulocytes. Do not administer using leukocyte reduction filters. Depth-type microaggregate filters and leukocyte reduction filters remove granulocytes.

The red cells in Apheresis Granulocytes must be ABO compatible. Once granulocyte transfusion therapy is initiated, support should continue at least daily until infection is cured, defervescence occurs, the absolute granulocyte count returns to at least $0.5 \times 10^9/L$ (500/ μ L), or the physician in charge decides to halt the therapy.

Because most patients receiving these products are severely immunosuppressed, Apheresis Granulocytes are usually irradiated to prevent TA-GVHD (see section on Further Processing).

Side Effects and Hazards

Hazards that pertain to all transfusion components are described in the section on Side Effects and Hazards for Whole Blood and All Blood Components. Listed below are hazards that apply specifically to Apheresis Granulocytes.

1. **Febrile Nonhemolytic Reactions:** These reactions are frequently noted in patients receiving granulocyte transfusions. Fever and chills in patients receiving granulocyte components may be avoided or mitigated by slow administration and recipient premedication.
2. **Allergic Reactions:** Allergic reactions to HES and other red cell sedimenting solutions may occur during granulocyte transfusion.
3. **Pulmonary Reactions:** Granulocyte transfusion can cause worsening of pulmonary function in patients with pneumonia, and rarely severe pulmonary reactions, especially in patients receiving concomitant amphotericin B.
4. **Alloimmunization:** Immunization to HLA antigens frequently occurs with granulocyte transfusion and can cause refractoriness to platelet transfusion.

Further Processing

This section addresses further processing of previously described blood components. The processes described in this section are: Leukocyte reduction, identification of CMV-seronegative components, irradiation, and washing. A component may undergo one or more of these processes.

Leukocyte Reduction

Description

A unit of whole blood generally contains ≥ 1 to 10×10^9 white cells. Leukocyte reduction may be achieved by in-process collection or filtration: 1) soon after collection (prestorage), 2) after varying periods of storage in the laboratory, or 3) at the bedside. The method used in the laboratory for leukocyte reduction is subject to quality control testing; leukocyte-reduced components prepared at the bedside are not routinely subjected to quality control testing. Leukocyte reduction will decrease the cellular content and volume of blood according to characteristics of the filter system used. Red Blood Cells Leukocytes Reduced, Apheresis Red Blood Cells Leukocytes Reduced, and Apheresis Platelets Leukocytes Reduced must have a residual content of leukocytes $< 5.0 \times 10^6$ and Platelets Leukocytes Reduced must have $< 8.3 \times 10^5$ residual leukocytes. Leukocyte reduction filters variably remove other cellular elements in addition to white cells. Washing is not a substitute for leukocyte reduction. Leukocyte reduction is not a substitute for irradiation.

Indications

Leukocyte-reduced components are indicated to decrease the frequency of recurrent febrile nonhemolytic transfusion reactions. They have also been shown to reduce the risk of transfusion-transmitted CMV and to reduce the incidence of HLA alloimmunization.

Contraindications

Leukocyte-reduced components do not prevent TA-GVHD. Leukocyte reduction filters are not to be used in the administration of Apheresis Granulocytes or Apheresis Granulocytes/Platelets.

Side Effects and Hazards

The use of blood components that are leukocyte reduced at the bedside may cause unexpected severe hypotension in some recipients, particularly those taking angiotensin converting enzyme inhibitor medication.

Specific Leukocyte-Reduced Components

RED BLOOD CELLS LEUKOCYTES REDUCED (RED BLOOD CELLS LEUKOCYTES REDUCED)

APHERESIS RED BLOOD CELLS LEUKOCYTES REDUCED (RED BLOOD CELLS PHERESIS LEUKOCYTES REDUCED)

PLATELETS LEUKOCYTES REDUCED (PLATELETS LEUKOCYTES REDUCED)

APHERESIS PLATELETS LEUKOCYTES REDUCED (PLATELETS PHERESIS LEUKOCYTES REDUCED)

Further Testing to Identify CMV-Seronegative Blood

Description

CMV-seronegative blood is selected by performing testing for antibodies to CMV. Transmission of CMV disease is associated with cellular blood components. Plasma, cryoprecipitate, and other plasma-derived blood components do not transmit CMV; therefore, CMV testing is not required for these components.

Indications

Transfusion of CMV-negative blood is indicated in CMV-seronegative recipients who are at risk for severe CMV infections. These at-risk groups include pregnant women and their fetuses, low

birthweight infants, hematopoietic progenitor cell transplant recipients, solid-organ transplant recipients, severely immunosuppressed recipients, and HIV-infected patients. Leukocyte-reduced components may be an alternative to CMV-seronegative transfusion in some clinical conditions.

Irradiation

Description

Blood components that contain viable lymphocytes may be irradiated to prevent proliferation of T lymphocytes, which is the immediate cause of TA-GVHD. Irradiated blood is prepared by exposing the component to a radiation source. The standard dose of gamma irradiation is 2500 cGy targeted to the central portion of the container with a minimum dose of 1500 cGy delivered to any part of the component.

Indications

Irradiated cellular components are indicated for use in patient groups that are at risk for TA-GVHD from transfusion. At-risk groups include: fetal and neonatal recipients of intrauterine transfusions, selected immunocompromised recipients, recipients of cellular components known to be from a blood relative, recipients who have undergone marrow or peripheral blood progenitor cell transplantation, and recipients of cellular components whose donor is selected for HLA compatibility.

Side Effects and Hazards

Irradiation induces erythrocyte membrane damage. Irradiated red cells have been shown to have higher supernatant potassium levels than nonirradiated red cells. Removal of residual supernatant plasma before transfusion may reduce the risks associated with elevated plasma potassium. The expiration date of irradiated red cells is changed to 28 days after irradiation if remaining shelf life exceeds 28 days. There are no known adverse effects following irradiation of platelets; the expiration date is unchanged.

Washing

Description

Washed components are typically prepared using 0.9% Sodium Chloride, Injection (USP) with or without small amounts of dextrose. Washing removes unwanted plasma proteins, including antibodies and glycerol from previously frozen units. There will also be some loss of red cells and platelets, as well as a loss of platelet function through platelet activation. The shelf life of washed components is no more than 24 hours at 1 to 6 C or 4 hours at 20 to 24 C. Washing is not a substitute for leukocyte reduction.

Indications

Washing of blood components is indicated to remove unwanted plasma when it contains constituents that predispose patients to significant transfusion reactions (eg, the removal of IgA-containing plasma in providing transfusion support for an IgA-deficient recipient or in rare recipients experiencing anaphylactoid reactions to plasma components).

*Specific Washed Components***WASHED RED BLOOD CELLS (RED BLOOD CELLS WASHED)****WASHED APHERESIS RED BLOOD CELLS (RED BLOOD CELLS PHERESIS WASHED)****WASHED PLATELETS (PLATELETS WASHED)****WASHED APHERESIS PLATELETS (PLATELETS PHERESIS WASHED)****Volume Reduction***Description*

Volume reduction is a special manipulation of cellular blood products using centrifugation. The process involves the aseptic removal of a portion of the supernatant, containing plasma and storage medium. Volume reduction removes excess plasma, thereby reducing unwanted plasma proteins, including antibodies. It is more commonly used in pediatric and in-utero transfusions. There will be some loss of platelet function through platelet activation as a result of volume reduction. The shelf life of volume-reduced components is no more than 24 hours at 1 to 6 C or 4 hours at 20 to 24 C.

Indications

Reducing the plasma volume of cellular components is indicated in cases where the volume status of a patient is being aggressively managed, such as in infants with compromised cardiac function. Volume reduction may be used to reduce exposure to plasma proteins or additives (such as mannitol), to achieve a specific component concentration, or to reduce exposure to antibodies targeting known recipient antigens (especially in an Apheresis Platelet unit containing ABO-incompatible plasma collected from a mother for the treatment of neonatal alloimmune thrombocytopenia).

Contraindications

Volume reduction is not a substitute for washing or for dosing with small aliquots.

Volume reduction of platelets may result in adverse consequences associated with overtransfusion of platelets.

*Specific Volume-Reduced Components***RED BLOOD CELLS VOLUME REDUCED (VOLUME REDUCED RED BLOOD CELLS)****APHERESIS RED BLOOD CELLS VOLUME REDUCED (VOLUME REDUCED RED BLOOD CELLS PHERESIS)****PLATELETS VOLUME REDUCED (VOLUME REDUCED PLATELETS)****APHERESIS PLATELETS VOLUME REDUCED (VOLUME REDUCED PLATELETS PHERESIS)****References**

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Table 4. Summary Chart of Blood Components

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Red Blood Cells; Red Blood Cells, Low Volume; Apheresis Red Blood Cells	Symptomatic anemia.	Increases oxygen-carrying capacity.	Pharmacologically treatable anemia. Coagulation deficiency. Volume expansion.	Must be ABO compatible.	Infectious diseases. Hemolytic, septic/toxic, allergic, febrile reactions. TACO. TRALI. TA-GVHD.	As fast as patient can tolerate but less than 4 hours.
Deglycerolized Red Blood Cells	See Red Blood Cells. IgA deficiency with anaphylactoid reaction.	See Red Blood Cells. Deglycerolization removes plasma proteins. Risk of allergic and febrile reactions reduced.	See Red Blood Cells.	See Red Blood Cells.	See Red Blood Cells. Hemolysis due to incomplete deglycerolization can occur.	See Red Blood Cells.
Red Blood Cells Leukocytes Reduced; Apheresis Red Blood Cells Leukocytes Reduced	See Red Blood Cells. Reduction of febrile reactions.	See Red Blood Cells. Reduction of leukocytes reduces risk of febrile reactions, HLA alloimmunization and CMV infection.	See Red Blood Cells. Leukocyte reduction should not be used to prevent TA-GVHD.	See Red Blood Cells.	See Red Blood Cells. Hypotensive reaction may occur if bedside leukocyte reduction filter is used.	See Red Blood Cells.
Washed Red Blood Cells	See Red Blood Cells. IgA deficiency with anaphylatoid reaction. Recurrent severe allergic reactions to unwashed red cell products.	See Red Blood Cells. Washing reduces plasma proteins. Risk of allergic reactions may be reduced.	See Red Blood Cells.	See Red Blood Cells.	See Red Blood Cells.	See Red Blood Cells.

(Continued)

Table 4. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Whole Blood	Symptomatic anemia with large volume deficit.	Increases oxygen-carrying capacity. Increases blood volume.	Condition responsive to specific component. Treatment of coagulopathy.	Must be ABO identical.	See Red Blood Cells.	As fast as patient can tolerate but less than 4 hours.
Fresh Frozen Plasma (FFP)	Clinically significant plasma protein deficiencies when no specific coagulation factors are available. TTP.	Source of plasma proteins, including all coagulation factors.	Volume expansion. Coagulopathy that can be more effectively treated with specific therapy.	Must be ABO compatible.	Infectious diseases. Allergic reactions. TACO. TRALI.	Less than 4 hours.
Plasma Frozen Within 24 Hours After Phlebotomy (PF24)	Clinically significant deficiency of stable coagulation factors.	Source of nonlabile plasma proteins. Levels of Factor VIII are significantly reduced and levels of Factor V and other labile plasma proteins are variable compared with FFP.	Volume expansion. Deficiencies of labile coagulation factors including Factors VIII and V.	Must be ABO compatible.	See FFP.	Less than 4 hours.
Plasma Cryoprecipitate Reduced	TTP.	Plasma protein replacement for plasma exchange in TTP. Deficient in fibrinogen, Factor VIII, vWF, and Factor XIII. Deficient in high-molecular-weight vWF multimers as compared to FFP.	Volume expansion. Deficiency of coagulation factors known to be depleted in this product, fibrinogen, Factors VIII, vWF, and XIII.	Must be ABO compatible.	See FFP.	Less than 4 hours.

(Continued)

Table 4. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Thawed Plasma Ω	Bleeding patients except consumptive coagulopathy.	Source of plasma proteins.	Not indicated as treatment for isolated coagulation factor deficiencies.	Must be ABO compatible.	See FFP.	Less than 4 hours.
	Reversal of warfarin effect.	Levels and activation state of coagulation proteins in thawed plasma are variable and change over time.	Levels and activation state of coagulation proteins in thawed plasma are variable and change over time.			
Liquid Plasma	Initial treatment of patients undergoing massive transfusion.	Coagulation support for life-threatening trauma/hemorrhages. The profile of plasma proteins in Liquid Plasma is poorly characterized. Levels and activation state of coagulation proteins are dependent upon and change with time in contact with cells, as well as the conditions and duration of storage.	Not indicated as treatment for isolated coagulation factor deficiencies. The profile of plasma proteins in Liquid Plasma is poorly characterized. Levels and activation state of coagulation proteins are dependent upon and change with time in contact with cells, as well as the conditions and duration of storage.	Must be ABO compatible.	See FFP.	Less than 4 hours.

(Continued)

Table 4. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Cryoprecipitated AHF; Pooled Cryoprecipitated AHF	Hypofibrinogenemia. Factor XIII deficiency. von Willebrand disease. Hemophilia A.	Provides fibrinogen, vWF, Factor XIII, and Factor VIII.	Deficiency of any plasma protein other than those enriched in Cryoprecipitated AHF.		Infectious diseases. Allergic reactions.	Less than 4 hours.
Platelets; Pooled Platelets	Bleeding due to thrombocytopenia or platelet function abnormality. Prevention of bleeding from marrow hypoplasia.	Improves hemostasis.	Plasma coagulation deficits. Some conditions with rapid platelet destruction (eg, ITP, TTP) unless life-threatening hemorrhage.	Should not use some filters (check manufacturer's instructions).	Infectious diseases. Septic/toxic, allergic, febrile reactions. TACO. TRALI. TA-GVHD.	Less than 4 hours.
Apheresis Platelets	See Platelets.	See Platelets. May be HLA (or other antigen) selected.	See Platelets.	See Platelets.	See Platelets.	See Platelets.
Platelets Leukocytes Reduced; Pooled Platelets Leukocytes Reduced; Apheresis Platelets Leukocytes Reduced	See Platelets. Reduction of febrile reactions. Reduction of HLA alloimmunization.	See Platelets. Reduction of leukocytes reduces risk of febrile reactions, HLA alloimmunization, and CMV infection.	See Platelets. Leukocyte reduction should not be used to prevent TA-GVHD.	See Platelets.	See Platelets.	See Platelets.
Apheresis Granulocytes Ω ; Apheresis Granulocytes/ Platelets Ω	See Platelets. Neutropenia with infection, unresponsive to appropriate antibiotics.	Provides granulocytes with or without platelets.	Infection responsive to antibiotics, eventual marrow recovery not expected.	Must be ABO compatible. Should not use some filters (check manufacturer's instructions).	Infectious diseases. Hemolytic, allergic, febrile reactions. TACO. TRALI. TA-GVHD.	One unit over 2-4 hours. Closely observe for reactions.

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Table 4. Summary Chart of Blood Components (Continued)

Category	Major Indications	Action/Recipient Benefit	Not Indicated for	Special Precautions	Hazards*	Rate of Infusion
Further Processing:						
Irradiated Components	See component. Increased risk for TA-GVHD (eg, congenital immunodeficiencies, HLA-matched platelets or transfusions from blood relatives).	Donor lymphocytes are inactivated reducing risk of TA-GVHD.	See component.	See component.	See component.	See component.

*For all cellular components there is a risk the recipient may become alloimmunized and experience rapid destruction of certain types of blood products. Red-cell-containing components and thawed plasma (thawed FFP, thawed PF24, or Thawed Plasma) should be stored at 1-6 C. Platelets, Granulocytes, and thawed Cryoprecipitate should be stored at 20-24 C. Disclaimer: Please check the corresponding section of the *Circular* for more detailed information.

TACO = transfusion-associated circulatory overload; TRALI = transfusion-related acute lung injury; TA-GVHD = transfusion-associated graft-vs-host disease; CMV = cytomegalovirus; TTP = thrombotic thrombocytopenic purpura; AHF = antihemophilic factor; ITP = immune thrombocytopenic purpura; vWF = von Willebrand factor.

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