



OKLAHOMA BLOOD INSTITUTE

Transfusion Guidelines for Blood Components



These general guidelines were formed by consensus of the Transfusion Medicine physicians at the Oklahoma Blood Institute. It is recognized that the ultimate decision to transfuse a blood component is a clinical one and best left to individual physicians after assessment of the patient. These guidelines cannot substitute for good clinical judgment and were prepared to serve as an educational tool as well as a general reference.

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ADMINISTRATION OF BLOOD COMPONENTS

All blood components should be administered through a blood component administration set with an in-line filter. The filter removes small fibrin aggregates that can accumulate during storage and has an average size of between 170-260 microns (μ). Many different types of administration sets are available and the package insert should be consulted for specifics related to its proper use.

Intravenous Solutions

Generally, only isotonic saline (0.9%) may be administered with blood components. Isotonic electrolyte solutions that do not contain calcium may also be used; however, the manufacturer's directions should be consulted for compatibility with blood components. ABO compatible plasma or 5% albumin may also be used. Lactated ringers solution should not be used because it contains calcium and can form clots in the line. Five percent dextrose solution (D5W) should not be used as it can cause hemolysis of red cells. Before a blood component is administered, the line should be flushed with 0.9% normal saline to ensure that any incompatible medications and/or intravenous solutions are removed.

Blood Warmer/ Mechanical Devices

Mechanical devices can be used to increase the rate of blood transfusion. The manufacturer's instructions should be consulted to ensure proper usage. These devices must be periodically checked to document proper functioning and safety. Most hospital biomedical departments inspect and tag the equipment. Clinical situations may arise (such as massive transfusion, cold agglutinins) when blood needs to be administered using a monitored blood warming device. These devices must also be inspected to ensure proper functioning as overheating red cells ($>42^{\circ}\text{C}$) can cause hemolysis leading to an acute hemolytic transfusion reaction.

Informed Consent

Consent for transfusion of non-emergent blood products must be obtained, just as consent for any other procedure or surgery. The ordering physician is responsible for the decision to transfuse and to obtain consent. Talking with patients about the possibility of receiving a blood component involves informing the patient about the potential benefits and possible adverse outcomes that could occur. The discussion will usually be directed by what type of component the patient is likely to receive. Basic information about transfusion can be given, such as: 1) the reason for the transfusion, 2) anticipated benefit, 3) possible adverse outcomes such as transfusion reactions or infectious diseases, 4) what the likely outcome would be without transfusion, and 5) alternatives, if appropriate, such as autologous donation or drugs that may decrease the need for transfusion (Erythropoietin). It is important that supporting evidence such as physical exam findings (angina, bleeding) and laboratory data (hemoglobin/hematocrit) be well documented in the medical record, which informs why the treatment is medically necessary. Post-transfusion documentation of the benefit of transfusion is also a good idea. Allowing the patient time to process the information is very important. Patients may need additional time to think about what they have been told in order to formulate appropriate questions and weigh their options before signing a consent form. If at all possible, the consent form should not be signed immediately prior to the procedure or surgery.

Talking to the patient in language that they can understand is best and ensures everyone is on the same level. Providing the patient with written information can be helpful. The Oklahoma Blood Institute has adult and children's brochures available that may assist in providing patients with information about blood transfusion. Those patients that are transfused on an outpatient basis or those leaving the hospital shortly after transfusion (one week) must be given written information on the signs and symptoms of a delayed transfusion reaction.

Individual institutions must have specific policies and procedures regarding the administration of blood components in-house. Familiarity with your institution's policies and procedures is recommended.

IgA Deficient Patients

Patients who are IgA deficient with anti-IgA can have anaphylactic reactions when transfused. These patients require extra attention when being transfused and immediate medical treatment must be readily available. Patients that are IgA deficient and have laboratory documented anti-IgA should receive washed red cells or platelets (washed in buffered saline.) Plasma components (FFP, 24 hour plasma, cryoprecipitate) need to be from known IgA deficient donors. When a patient with IgA deficiency with antibodies is identified, anticipating their blood needs as soon as possible is needed as OBI may need to contact the Rare Donor Program to get components, which may take several days.

RED BLOOD CELLS

Red blood cells are used to improve tissue oxygenation by increasing the oxygen carrying capacity of the blood. They are not indicated for volume replacement or to increase wound healing. The same clinical indicators should be used for the transfusion of autologous blood components. The delivery of oxygen is almost always sufficient at hemoglobin levels of 7-8 g/dl in patients with normovolemic anemia without cardiac disease. Patients with significant cardiopulmonary disease may require higher hemoglobin levels. Several clinical indicators must be considered when evaluating for a red cell transfusion: 1) patient's underlying medical condition, 2) patient's symptoms (angina, dyspnea, debilitating fatigue), and 3) rate of change of hemoglobin/hematocrit. Red blood cells are collected in an anticoagulant-preservative solution which provides substrates for optimal cell viability and must be kept at 1-6°C for up to 42 days. All red blood cell transfusions must be ABO compatible; there is absolutely no medical benefit to transfusing only type specific red cells. *All red cell components supplied by the Oklahoma Blood Institute are leukoreduced.*

Dosage :

One unit will increase the hemoglobin level by 1 g/dL or the hematocrit by ~3 % in a 70 kg adult. In pediatric patients, a dose of 10-15 mL/kg should increase the hemoglobin by 2-3 g/dL. Red cells must be transfused within four hours. Generally, one unit is given over one to two hours.

Criteria for the Transfusion of Red Blood Cells (Adults)

- ❖ Acute blood loss (>15-20%) of estimated blood volume
- ❖ Hgb 7-8 g/dl or HCT < 25%. In patients with cardiovascular disease a higher threshold, 9-10 g/dl may be considered.
- ❖ Symptomatic anemia
 - Electrocardiographic signs of cardiac ischemia
 - Angina
 - SOB
- ❖ Chronic anemia (sickle cell, thalassemia)
- ❖ Complications of sickle cell disease (cerebrovascular accidents, acute chest syndrome)
- ❖ Preoperative hemoglobin < 9g/dl and getting ready to have a procedure associated with major, predictable blood loss

Criteria for the Transfusion of Red Blood Cells (Infants and Neonates)

- ❖ Hgb < 13 or HCT 39% with respiratory distress
- ❖ Acute blood loss > 10% estimated blood volume in stable infant; > 5% can be considered if respiratory support is needed
- ❖ Infants requiring supplemental O₂ and/or mechanical ventilation or other symptoms
- ❖ Hyperbilirubinemia requiring red cell exchange
- ❖ Significant apnea or bradycardia
- ❖ Significant tachycardia or tachypnea
- ❖ Low weight gain

PLATELETS

Platelets are used to control or prevent bleeding that is associated with deficiencies of platelet function or thrombocytopenia. Platelets are stored at 20-24°C (room temperature) and have a five-day shelf life. They must be constantly agitated. The agitation promotes the exchange of O₂ and CO₂ through the plastic bag which is needed to maintain the functional capacity of the platelets. *All of the platelets supplied by the Oklahoma Blood Institute are of the single-donor apheresis type and are leukoreduced.* The volume varies between 200-400 ml. ABO type compatible platelets are generally transfused; however, other types may be given. Administration of ABO incompatible platelets may cause a positive DAT and very rarely can cause some hemolysis. A blood administration set is needed. Once a platelet component is entered non-sterilely, it must be transfused within four hours.

Evaluation of Platelet Refractoriness

Patients who do not obtain the expected platelet increment after transfusion are said to be refractory to platelet transfusion. This usually occurs in patients who have been transfused multiple times. This can also occur in female multiparous patients. It is due to the development of HLA antibodies which the platelets contain.

A platelet count can be obtained between 10 minutes and one hour after platelet transfusion to evaluate for effectiveness. A suboptimal increase in the platelet count at one hour may indicate that the patient is refractory to platelet transfusions due to alloimmunization. An adequate one hour count with a low 18-24 hour count usually indicates peripheral destruction, not alloimmunization. Alloimmunization is an immune response to foreign (donor) antigens. Most cases of alloimmunization involve an antibody against class I HLA antigens. Less commonly, it can occur due to antibodies against platelet specific antigens (HPA-1a is the most common). A technique called platelet crossmatching can be done to identify compatible products. Platelet crossmatching is recommended over HLA matched products. A platelet crossmatched product can usually be obtained within two to three hours, whereas an HLA product may take days.

Peripheral destruction of platelets commonly occurs in the following clinical situations: sepsis, drug use (amphotericin), splenomegaly, or active bleeding. In these clinical situations, platelet crossmatching will not add any additional therapeutic benefit to the patient and is not recommended.

Gamma irradiation of platelets can be done to prevent graft-vs-host disease in certain patient populations (see section on recommended criteria for irradiation).

Platelet function may be impaired in patients with liver dysfunction and may be enhanced with administration of 1-deamino-8-D-arginine vasopressin (DDAVP, desmopressin).

Dosage

One unit of apheresis platelets would be a typical dose for most patients. One unit can be expected to increase the platelet count in a 70 kg non-bleeding adult by 30,000-50,000/*ul*. In pediatric patients, a 5-10 mL/kg dose would be expected to increase the platelet count by 50,000-100,000/*ul*. Generally, a 50,000/*ul* platelet count is sufficient for hemostasis in most patients

(see Criteria.) Volume reduction of platelet concentrates is not recommended as centrifugation can activate platelets and also causes decreased recovery. Utilization of the recommended dosage should provide the desired increase.

Criteria for Platelets (Adults)

- ❖ Platelet count < 50,000- 70,000 with impending surgery or invasive procedure, or active bleeding
- ❖ Massive transfusion with microvascular bleeding
- ❖ Active brisk bleeding
- ❖ Platelet count < 10,000
- ❖ Patient undergoing CNS or eye surgery, retinal hemorrhage with platelet count less than 100,000
- ❖ Platelet function disorder (Microvascular bleeding in patients undergoing cardiopulmonary bypass)
- ❖ Tirofiban hydrochloride (Aggrastat) or Clopidogrel bisulfate (Plavix), Ticlopidine hydrochloride (Ticlid) therapy and bleeding that does not respond to discontinuation of medication and to local measures
- ❖ Aspirin ingestion with uncontrolled bleeding
- ❖ Abciximab (Reopro) use with uncontrolled bleeding
- ❖ Clinical evaluation with documented sepsis or hypothermia

Criteria for Platelets (Neonates and infants)

- ❖ Thrombocytopenia generally less than 50,000 in stable non-bleeding patient, prior to surgery or invasive procedure
- ❖ Thrombocytopenia less than 100,000 in infant at risk of intracranial bleeding or otherwise sick infant
- ❖ Qualitative platelet defect with bleeding or impending surgery or procedure

PLASMA FROZEN WITHIN 24 HOURS (FP24)

This component is made from blood that is separated and frozen at -18 C° within 24 hours of collection and is the main plasma component offered by OBI. It is comparable to FFP for almost all clinical indications and can be used interchangeably. The level of Factor VIII is less in 24 hour plasma than in FFP; however, neither FFP nor 24 hour plasma would be the products of choice for treatment of hemophilia A patients (Factor VIII deficiency.) FP24 is given to correct bleeding due to single or multiple coagulation factor abnormalities when specific factor concentrates are not available. One ml of FP24 contains approximately one unit of coagulation factor activity. FP24 should be ABO compatible with the recipient's red cells. Rh consideration is not indicated. Continued administration of FP24 to correct the PT or PTT to "normal" is usually not needed to achieve hemostasis and may not be achievable in some disease processes. When used prophylactically prior to invasive procedures it should be given as close to the procedure as possible. FP24 should not be used for volume replacement or if the patient's coagulopathy can be successfully treated with other therapies such as Vitamin K or withdrawal of medication. Once FFP or 24 hour plasma is thawed for more than 24 hours, the component must be labeled as Thawed Plasma. The component must be stored at 1-6 C° for up to four days after the initial 24 hours.

Dosage

An average dose would be 10-15 ml/kg, which would increase all coagulation factors by around 15-20% in most patients. Once thawed, it should be transfused as soon as possible. It can be stored for 24 hours at 1-6 C°.

FRESH FROZEN PLASMA

(Availability of this component is limited and released by approval of OBI physicians.)

This component is made when blood is separated and frozen within eight hours of collection. FFP is given to correct bleeding due to single or multiple coagulation factor abnormalities when specific factor concentrates are not available. FFP may be useful when a specific factor assay is less than 25%. One ml of FFP contains approximately one unit of coagulation factor activity. FFP should be ABO compatible with the recipient's red cells. Rh consideration is not indicated. Continued administration of FFP to correct the PT or PTT to "normal" is usually not needed to achieve hemostasis and may not be achievable in some disease processes. When used prophylactically prior to invasive procedures it should be given as close to the procedure as possible. FFP should not be used for volume replacement or if the patient's coagulopathy can be successfully treated with other therapies such as Vitamin K or withdrawal of medication.

Dosage

An average dose would be 10-15 ml/kg, which would increase all coagulation factors by around 15-20% in all patients. Once thawed, it should be transfused as soon as possible. It can be stored for 24 hours at 1-6 C°.

Criteria for Fresh Frozen Plasma/Plasma Frozen Within 24 Hours (Adults)

Bleeding or planned surgical or invasive procedure with:

- ❖ INR > 1.5, PT > 18, PTT > 45
- ❖ Documented factor deficiency with no specific factor concentrate available
- ❖ Replacement of multiple factors in patients with severe liver disease
- ❖ Reversal of warfarin in patients who need immediate surgery, are bleeding, and can't wait for drug to be stopped or vitamin K given. (Vitamin K administration should also be considered unless only transient correction is indicated.)
- ❖ Massive transfusion
- ❖ TTP/HUS
- ❖ Protein C, protein S, Antithrombin III deficiency
- ❖ Disseminated intravascular coagulopathy

Criteria for Fresh Frozen Plasma/Plasma Frozen Within 24 Hours (Infants and Neonates)

- ❖ Coagulopathy with bleeding from any etiology
- ❖ Used to reconstitute red blood cells used for exchange/intrauterine transfusion
- ❖ Any category that falls under adult indications above

CRYOPRECIPITATE

Cryoprecipitate is used in the treatment of patients with acquired or congenital fibrinogen deficiency, dysfibrinogenemia, or Factor XIII deficiency. If specific factor concentrates are not available, it can be used to treat von Willebrand's disease, and Factor VIII deficiency. It may also be utilized in patients with uremia or used to make fibrin glue.

Cryoprecipitate contains several hemostatic proteins. Cryoprecipitate made from whole blood would contain approximately 100 IU of Factor VIII:C and 150-250 mg of fibrinogen in 15 ml of plasma.. Usually ABO compatible cryoprecipitate is given, but this is only absolutely indicated in neonatal patients. Rh consideration is not indicated. A blood administration set is needed.

Dosage

One whole blood derived unit would increase the fibrinogen level by 5-10 mg/dL.

Once cryoprecipitate is thawed, it must be kept at room temperature (20-24°C) and transfused within six hours or four hours if pooled.

A more specific calculation can be used:

Calculate blood volume (BV)

Body weight x 70 ml/Kg

Calculate plasma volume (PV)

BV x (1-HCT)

Calculate mg of Fibrinogen needed

$$\frac{\text{Desired increase in Fibrinogen (\%)} - \text{Initial fibrinogen level (\%)} \times \text{PV}}{100}$$

Calculate the number of bags of cryo needed

mg of fibrinogen needed

Amount of fibrinogen per bag

Whole blood cryo = use 250 mg per bag

Example: A 70 kg male has a 40 % Hct and a fibrinogen level of 75 mg/dl. A 150 mg/dl fibrinogen level is desired.

Blood Volume 70 kg x 70 ml/Kg = 4900ml

Plasma volume 4900 x (1-.40) = 2940 ml

Fibrinogen needed $\frac{150 \text{ mg/dl} - 75 \text{ mg/dl} \times 2940 \text{ ml}}{100} = 2205 \text{ mg fibrinogen needed}$

Bags of cryo needed $\frac{2205}{250} = 8.82$ or 9 bags of cryo

Criteria for Cryoprecipitate (Adults)

- ❖ Fibrinogen deficiency < 100 mg/dl (1.0 g/L)
- ❖ Hemophilia A (if factor concentrate not available)
- ❖ Von Willebrand's disease (If Humate-P or Alphanate concentrates are not available or unsuccessful, DDAVP)
- ❖ Fibrin glue (if commercially prepared components are not available)
- ❖ Uremia if DDAVP not effective or after tachyphylaxis
- ❖ Factor XIII deficiency
- ❖ Massive transfusion
- ❖ Tissue plasminogen activator (TPA) associated bleeding

Criteria for Cryoprecipitate (Infants and Neonates)

Same indications as for adults.

GRANULOCYTES

Granulocytes can be used in patients who have neutropenia (<500/ul) or documented neutrophil dysfunction (chronic granulomatous disease). The minimum dose should be 1.0×10^{10} neutrophils per transfusion and should be administered every day for several days to provide maximal therapeutic benefit. Criteria for granulocyte transfusion would include: 1) recoverable marrow; 2) neutrophil count < 500/ul (<3000/ul for Neonates); or 3) unresponsive to appropriate antibiotics. When this type of component is needed, as much advance notice as possible is appreciated as OBI must call special donors in for collection. Granulocytes can contain a significant amount of red cells. They must be ABO compatible and must be crossmatched with the recipient. They are stored at room temperature at 20-24°C without agitation. They should be transfused as soon as possible but have a 24-hour shelf life.

CRITERIA FOR IRRADIATION

Immunocompetent transfused lymphocytes can proliferate in severely immuno-compromised recipients such as fetuses, stem cell transplant recipients, bone marrow transplant recipients, and patients with severe deficiencies of cellular immunity (DiGeorge's, Severe Combined Immunodeficiency). The transfused lymphocytes "attack" the recipient, causing transfusion-associated graft-vs.-host disease (TA-GVHD). TA-GVHD has also been associated with receiving blood from close relatives. This occurs when the donor is homozygous for an HLA haplotype for which the recipient is haploidentical. There is no effective treatment and the focus has been on prevention. Blood components that are irradiated include any red blood cell component, platelets, and granulocytes. Gamma irradiation at 25-50 Gy should be used. The minimum central dose should be 25 Gy, and the minimum dose at any other point should be 15 Gy.

Irradiation is recommended for the following patient categories:

- ❖ All patients with Hodgkin's disease
- ❖ All directed donor units from blood relatives
- ❖ All HLA-matched blood components
- ❖ All crossmatched platelets
- ❖ All children with malignancies such as neuroblastoma and glioblastoma
- ❖ Components for peripheral stem cell/bone marrow transplant recipients (**NOTE:** peripheral stem cells or bone marrow infusions should **never** be irradiated as this will prevent engraftment)
- ❖ Patients with congenital cell-mediated immuno-deficiencies (DiGeorge's, severe combined immunodeficiency, Wiskott-Aldrich)
- ❖ Intrauterine/exchange transfusions
- ❖ All granulocyte transfusions
- ❖ Immunosuppressed lymphocytopenic patients

- ❖ All components for infants less than six months of age
- ❖ All **allogeneic** blood given to bone marrow transplant **donors** at the time of donation.
(NOTE: This is not indicated if autologous blood is given).
- ❖ All patients receiving fludarabine
- ❖ All other criteria are under the direction of a Medical Director

Criteria for CMV Safe Components

At the Oklahoma Blood Institute we feel sufficient evidence exists which supports that leukoreduction is equivalent to CMV negative serology for the transmission of CMV. One hundred percent of all cellular blood components at the Oklahoma Blood Institute are leukoreduced and considered CMV safe.

TRANSFUSION REACTIONS - SIGNS AND SYMPTOMS

Transfusion Reactions

Although significant hemolytic transfusion reactions are rare, any minor adverse outcome can be very distressing and upsetting for patients. Transfusion reactions can be classified several ways: hemolytic vs. non-hemolytic or immune vs. non-immune. Here they will be classified into acute and delayed reactions. The most common cause of an acute hemolytic transfusion reaction is clerical error, so meticulous attention must be given to proper specimen collection, as well as patient identification at the time of transfusion.

Signs and symptoms include:

- ❖ Fever, with or without chills
- ❖ Shaking chills (rigors), with or without fever
- ❖ Pain at the infusion site, or in chest, abdomen, or flanks
- ❖ Blood pressure changes, usually acute, either hypotension or hypertension
- ❖ Respiratory distress including dyspnea, tachypnea, or hypoxemia
- ❖ Urticaria (hives)
- ❖ Nausea
- ❖ Headache
- ❖ Oliguria/Anuria
- ❖ Feeling uneasy
- ❖ Flushing
- ❖ Chest Pain

Acute Transfusion Reactions

This classification contains reactions that occur during or within 24 hours of transfusion and can occur with any type of component. Acute reactions include acute hemolytic, febrile, allergic, Transfusion Related Acute Lung Injury (TRALI), volume overload, anaphylaxis, and bacterial contamination.

Acute Hemolytic Transfusion Reactions (Intravascular)

These reactions are life threatening and are rate and dose dependent. They occur because the recipient has pre-formed antibodies against an antigen on the red cell surface which causes rapid complement activation and intravascular lysis of red cells. They are most commonly due to ABO incompatibility, but can occur with other red blood cell antigen systems. HTR can occur with the infusion of plasma containing components, although this is less common. The donor will develop symptoms immediately and can include hypotension, fever, chills, or back pain. Complications can include shock, DIC, acute renal failure, and death. Immediate treatment is needed, which would include stopping the transfusion and maintaining adequate volume and blood pressure. Evaluation for gross hemoglobinemia by spinning down a blood sample is a quick way to evaluate for hemolysis. Monitoring coagulation parameters is usually warranted. A direct coombs can be done to look for in-vivo antibody binding; however, a negative DAT does not absolutely rule out hemolysis. Measurement of unconjugated bilirubin may be helpful, but

depends on the amount of hemolysis and liver function. Lactate dehydrogenase levels will be elevated.

Febrile Nonhemolytic Transfusion Reactions

This type of reaction is defined by a rise in temperature of greater than 1°C during or after transfusion with or without chills. Fever is a presenting symptom of many types of transfusion reactions and other causes must be excluded before making this diagnosis. These reactions are usually seen in patients who have antibodies against HLA antigens present on donor leukocytes. The rise in temperature is caused by the release of cytokines from leukocytes which stimulate the release of endogenous pyrogens. Laboratory evaluation does not show serological incompatibility. Acetaminophen is the antipyretic of choice. Routine use of prophylactic antipyretics is not recommended due to the possibility it could mask symptoms of hemolysis. Most patients will not experience another nonhemolytic transfusion reaction as it is usually donor specific. Most of these reactions have been eliminated by 100% leukoreduction of blood components; however, cytokine accumulation prior to leukoreduction can still occur.

Allergic Transfusion Reactions

These reactions occur due to an allergen, usually a protein, that is present in the plasma of the blood component to which the patient was previously sensitized. The antibody-antigen reaction causes the release of histamine from mast cells and basophils, which leads to hives and itching. Symptoms usually occur within 20-30 minutes of starting the infusion and consist of hives, generalized pruritus, wheals, and anxiety. More severe symptoms of laryngeal edema, bronchial asthma, and hypotension may be observed in anaphylactoid reactions. For mild allergic reactions, the transfusion should be stopped and 25-50 mg IM diphenhydramine given. If the symptoms resolve, the transfusion can be started again slowly.

Anaphylactic Reactions

One in 700 individuals is IgA deficient and has the potential to make anti-IgA. Symptoms are immediate after the infusion of only a small amount of blood and can include bronchospasm, respiratory distress, and loss of consciousness, nausea, vomiting, and diarrhea. Death can occur from airway obstruction or from circulatory collapse. Fever is not usually seen with this type of reaction. Treatment includes stopping the transfusion, fluid administration, oxygen if hypoxia develops, and possibly endotracheal intubation. 0.2-0.5 ml of 1:1000 epinephrine can be given SQ, and it may be repeated as necessary. The patient should have continuous monitoring of vital signs until stable. Once a patient has been identified as IgA deficient, arrangements can be made to obtain components from IgA deficient donors if available. Alternatively, washed red cells or platelets may be used.

Transfusion Related Acute Lung Injury (TRALI)

TRALI is a non-infectious complication of blood transfusion which presents as acute hypoxemia due to non-cardiogenic pulmonary edema. Clinically, the symptoms are indistinguishable from ARDS.

In most cases, the symptoms start within two hours after transfusion but can be up to six hours. The clinical severity can be mild or fatal.

This type of reaction can be caused with any component, but usually occurs in components containing large amounts of plasma, i.e., FFP, 24 hour plasma, or platelets. Radiologic features include patchy infiltrates in dependent areas of the lungs at first with progression to widespread interstitial and alveolar infiltrates.

In contrast to circulatory overload, patients have a normal jugular venous pressure and a low or normal pulmonary wedge pressure. The hypotension does not respond to fluids. The etiology is still being investigated; however, it is thought to have three possible mechanisms: 1) the donor has HLA antibodies directed against the recipient's leukocytes, which causes activation leading to alveolar capillary endothelial damage; 2) the recipient has antibodies that bind to the infused donor's leukocytes causing activation and capillary damage; and 3) biologically active lipids that are generated in patients with some type of systemic illness. Currently OBI is investigating ways to try and prevent this type of reaction.

Transfusion Related Circulatory (Volume) Overload (TACO)

Symptoms can include dyspnea, hypertension, dry cough, and headache and usually occur within two hours of transfusion. Circulatory overload occurs because the transfusion occurs at a rate faster than the patient's cardiovascular status can tolerate. Symptoms include shortness of breath, systolic hypertension, pulmonary edema, and a non-productive cough. They can usually be prevented by slowing down the rate of transfusion. Treatment includes sitting the patient up and administering oxygen and/or diuretics.

Bacterial Contamination

Currently, all apheresis platelet components are cultured utilizing the Bac-T Alert 3D Microbial Detection System. Although rare, this type of reaction is life threatening, and immediate medical attention is needed. This occurs due to the infusion of blood components that contain bacteria. Most commonly, the components involved are platelets or red blood cells, although rare reported cases involving fresh frozen plasma or cryoprecipitate have occurred. Platelets, which are kept at room temperature, are most commonly contaminated by *Staphylococcus epidermidis* (a gram positive cocci); red cells are most commonly contaminated by *Yersinia enterocolitica* (a gram negative rod), due to its ability to grow at cold temperatures (1-6⁰). Depending on the bacterium, many of the symptoms may be due to the endotoxin produced by the bacteria. Clinically, a wide variety of symptoms including fever, hypotension, rigors, nausea, and vomiting can occur. Disseminated intravascular coagulation and septic shock can also develop. Symptoms are usually immediate, but can occur a short time after transfusion. The clinical outcome is dependent on the patient's underlying medical condition and the dose and type of bacterium. Treatment would include stopping the transfusion, giving a broad spectrum antibiotic and implementing other supportive care. Investigation by the blood bank would include a gram stain and culturing of the suspected component. Although a gram stain is insensitive, it may be able to provide useful information to help guide antibiotic therapy. Reporting this type of suspected transfusion to the blood bank is important because other components from the same donor need to be placed in quarantine.

Delayed Transfusion Reactions

These reactions occur greater than 24 hours after transfusion and include delayed hemolysis and graft vs. host disease. Infectious disease transmission can be included as a type of delayed reactions. It will not be discussed further here.

Delayed Hemolytic Transfusion Reaction (Extravascular)

Delayed hemolytic reactions typically occur when a patient has been previously transfused and developed an antibody, but the antibody level has decreased and is not detected by the antibody screen prior to transfusion. Kidd and Duffy antibodies are good examples. The antibody very commonly decreases below detection levels. When the patient is transfused with antigen positive red cells, an anamnestic response occurs with a rapid increase in the antibody titer within days. The hemolysis generally occurs extravascular in the spleen due to the red cells being coated with IgG antibody, which does not usually fix complement. Symptoms may include mild jaundice, weakness, and fatigue. Many times treatment is not needed. This can also occur due to primary immunization. In this instance, the antibody would not develop for two to three weeks. The recently transfused red cells are cleared from circulation. Clinically, a decrease in hemoglobin and hematocrit is seen. Recognition of these types of reactions are important to the patient for future transfusion therapy.

Transfusion-Associated Graft vs. Host Disease (TA-GVHD)

Immunocompetent transfused lymphocytes can proliferate in severely immunocompromised recipients such as fetuses, stem cell transplant recipients, bone marrow transplant recipients, and patients with severe deficiencies of cellular immunity (DiGeorge's, Severe Combined Immunodeficiency). The transfused lymphocytes "attack" the recipient, causing transfusion-associated graft-vs-host disease (TA-GVHD). TA-GVHD has also been associated with receiving blood from close relatives. This occurs when the donor is homozygous for an HLA haplotype for which the recipient is haploidentical. **There is no effective treatment, and the focus is on prevention.** Blood components that are irradiated include any red blood cell component, platelets, and granulocytes. Gamma irradiation at 25-50 Gy should be used. The minimum central dose should be 25 Gy, and the minimum dose at any other point should be 15 Gy. TA-GVHD would occur 12-14 days after transfusion. The initial symptom is usually a rash followed by fever, diarrhea, liver dysfunction and marrow aplasia. Death usually occurs within 30 days (see the section on Criteria for Irradiation.)

Post-Transfusion Purpura (PTP)

The patient makes an antibody to a platelet-specific antigen and when re-exposed to the antigen, the antibody titer rises with destruction of both autologous and allogeneic platelets. PTP is analogous to delayed hemolytic transfusion reaction seen with red cells. The mechanism for this destruction is not completely understood and is beyond the scope of this publication. Patients present with thrombocytopenia 7- 14 days after transfusion and can be seen with red cell or platelet transfusions. Clinically, petechiae and/or bleeding may be seen. Thrombocytopenia is usually self-limited with platelet recovery occurring 9-46 days post-transfusion. The most commonly involved platelet antigen is Human Platelet Antigen 1 (HPA-1). Interestingly, transfused platelets that lack the HPA-1 antigen are still destroyed. Therefore, platelet transfusions should be reserved for patients with life threatening bleeding. IVIG has been

effective in some patients. Prednisone may also be used and usually is effective in about one week.

Neonatal Transfusions: Special Notes

Metabolic complications are more commonly seen in this patient population.

Hyperkalemia

The amount of extracellular K⁺ increases with older red blood cells as K⁺ leaks out of the RBC's. Irradiation does increase the rate of leakage. It is routine to provide less than seven-day old components to neonates undergoing cardiac bypass or extracorporeal membrane oxygenation (ECMO), and exchange transfusion studies have shown that small volume transfusions (10-20 ml/ks) over two to three hours do not elevate K levels.

Calcium Levels

Hypocalcemia can occur when components are infused rapidly. This more commonly occurs in components containing large amounts of citrate such as platelets or fresh frozen plasma.

Metabolic alkalosis can also occur.

Hyperglycemia and Hypoglycemia

Glucose is present in blood components and can alter glucose measurements during an RBC transfusion, which can result in a paradoxical hypoglycemia due to endogenous insulin release.

Hyperthermia

This is more of a problem in neonatal patients. It can be prevented by the use of a properly maintained blood warmer by trained personnel. Blood should not be warmed by other methods such as immersion in hot water as this can cause hemolysis.

HOSPITAL/CONSIGNEE NOTIFICATIONS

The following information is provided to clarify the different types of notifications that the Oklahoma Blood Institute sends out to member hospitals or other consignees of blood products.

Recalls are conducted when OBI discovers that an error occurred in the manufacturing process which could impact the quality of the blood component, but the component was collected and distributed. For example, a donor is allowed to donate six months after travel to a malaria endemic area instead of the required 12-month deferral period. For questions, contact Event Management at (405) 297-5766 or (800) 749-0670, extension 5766.

Hospital (Consignee) Responsibilities: Consult internal procedures and policies. Your blood bank medical director will determine if patient and/or physician must be notified.

Market Withdrawals are conducted when blood components are collected and distributed appropriately by OBI (no error in the manufacturing process occurred), but after distribution information provided by the donor or other reliable source is received that indicates that the quality of the component may be impacted. For example, a donor calls back to report they became ill with a cold the day after donating. For questions, contact Event Management at (405) 297-5766 or (800) 749-0670, extension 5766.

Hospital (Consignee) Responsibilities: Consult internal procedures. Your blood bank medical director will determine if patient and/or physician must be notified.

Quarantines are conducted for recalls and market withdrawals (companion components that have not been released). In addition, quarantines are conducted when OBI identifies a donor with repeat reactive results and prior products are still in-date and may be available for transfusion in the hospital inventory. The consignee is notified to quarantine, return or destroy the product. If confirmatory testing is positive, OBI will notify consignee that a lookback (patient notification) is required. If confirmatory testing is negative, the quarantined product may be released for transfusion. For questions, contact Notification and Counseling Services at (405) 297-5667 or (800) 749-0670, extension 5667.

Hospital (Consignee) Responsibilities: Quarantine, return or destroy product. Notify OBI of product disposition (transfused, destroyed, returned, expired, etc.).

Lookbacks are conducted when OBI identifies that a donor who has previous donations (all testing was negative at that time) currently confirms positive for a viral infection (HIV, HCV, HBV, WNV). The recipient(s) of the donor's prior donations are notified of the need for testing in order to reduce secondary transmission and provide the recipient(s) with opportunities for treatment if infected. For questions, contact Notification and Counseling Services at (405) 297-5667 or (800) 749-0670, extension 5667.

Hospital (Consignee) Responsibilities: Consult internal procedures. Notification will be under the direction of your medical director. OBI will perform this testing at no charge to the patient(s). For questions, contact Notification & Counseling Services to arrange testing (405) 297-5667 or (800) 749-0670.

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COMPATIBLE BLOOD PRODUCTS

Recipient's Blood Type	DONOR'S BLOOD TYPE		
	Red Blood Cells - 1 st Choice	Red Blood Cells - Other Compatible Types	Plasma (FFP) - Compatible Types
O	O	NONE	O,A,B,AB
A	A	O	A, AB
B	B	O	B, AB
AB	AB	A,B,O	AB



Oklahoma Blood Institute
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