

**New York State Council on Human Blood and Transfusion Services*
and
New York State Board for Nursing†**

TRANSFUSION REACTION

FACT SHEETS

*A Companion Reference To Guidelines For
Monitoring Transfusion Recipients*

**First Edition
2008**

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**NEW YORK STATE
COUNCIL ON HUMAN BLOOD AND TRANSFUSION SERVICES
AND
NEW YORK STATE
BOARD FOR NURSING**

**Appendix B
Transfusion Reaction Fact Sheets**

Table of Contents

Acute Reactions

Acute Hemolytic Reactions	6B
Sepsis/Bacterial Contamination	7B
Transfusion-Related Acute Lung Injury (TRALI)	8B
Allergic (Severe) Anaphylactic or Anaphylactoid Reactions	9B
Transfusion-Associated Circulatory Overload (TACO)	10B
Febrile Nonhemolytic Reactions	11B
Allergic (Mild) Reactions	12B

Delayed Reactions

Graft-vs-Host Disease (GVHD)	13B
Delayed Hemolytic Reactions	14B
Posttransfusion Purpura (PTP)	15B

Appendix B

Transfusion Reaction Fact Sheets

Acute Reactions

Acute Hemolytic Reactions (< 24 Hours)		
Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Fever $\geq 1^{\circ}\text{C}/2^{\circ}\text{F}$ • Rigors • Nausea • Lower back pain • Chest pain or tightness • Acute hypotension or hypertension • Tachycardia • Tachypnea, wheezing, or hypoxemia • Shock • Wine- or cola-colored urine or jaundice • Pain at infusion site or along infusion vein • Urticaria, pruritis, flushing or angioedema • Anxiety • Unexplained bleeding from mucous membranes or infusion sites • Hemoglobinuria • Renal failure • Hemoglobinemia • Direct antiglobulin test (DAT) may be positive or negative 	<p>Incompatible blood administration results in an antigen/antibody response with activation of complement and subsequent intravascular hemolysis. Acute hemolytic reactions usually involve the ABO blood system.</p> <p>Misadministration of blood often results from improper identification of transfusion recipients, either at the time of phlebotomy for the type and screen specimen or at the time of transfusion. Occasionally, acute hemolysis may occur from mixing of blood with a fluid other than normal saline or from improper warming or freezing of blood.</p>	<ul style="list-style-type: none"> • Maintain airway; provide oxygen and ventilatory support if necessary • Diuretics to promote renal perfusion • Cardiovascular support with pressor agents, as indicated (pressor agents that decrease renal blood flow are contraindicated) • Hydration to maintain urinary output • Treatment of DIC • Initiate transfusion reaction work-up; send unit and administration set with attached solutions to the laboratory, in addition to blood and first posttransfusion urine specimens • Do not initiate another transfusion without Blood Bank consultation • If patient is hemodynamically unstable, invasive monitoring of pulmonary artery occlusion pressure can guide fluid therapy • Red cell exchange may be considered in patients with a significant load of circulating incompatible red cells • Document reaction in patient's chart as per institution policy <p style="text-align: center;"><u>Prevention:</u></p> <ul style="list-style-type: none"> • ABO mistransfusions may be avoided by proper patient identification • Administer blood only with normal saline

Sepsis/Bacterial Contamination

Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Fever, often $\geq 2^{\circ}\text{C}/4^{\circ}\text{F}$ above baseline • Chills • Rigors • Hypotension • Shock • Renal failure • Unexplained bleeding from mucous membranes or infusion sites 	<p>Sepsis is the result of transfusion of bacterially contaminated blood components. The bacteria usually originate from the blood donor, either from venipuncture (e.g., <i>Staphylococcus</i>, <i>Streptococcus</i>) or from unsuspected bacteremia (e.g., <i>Yersinia</i>), but may also result from donor unit processing. Bacterial multiplication is more likely to occur in components stored at room temperature (e.g., platelets) than in components stored at refrigerator temperatures (e.g., red cells).</p>	<ul style="list-style-type: none"> • Maintain airway; provide oxygen and ventilatory support if necessary • Cardiovascular support with pressor agents, as indicated • Hydration to maintain urinary output • Treatment of DIC • Initiate transfusion reaction work-up; send unit and administration set with attached solutions to the laboratory, in addition to blood and first posttransfusion urine specimens • Do not initiate another transfusion without Blood Bank consultation • Gram stain and culture the implicated blood component; draw blood culture from patient • Prompt initiation of IV antibiotics if indicated by the Gram stain results • Document reaction in patient's chart as per institution policy <p><u>Prevention:</u></p> <ul style="list-style-type: none"> • Visual inspection of units for color changes, hemolysis, clots • Blood and components should be transfused within 4 hours after issuance • Tubing should be changed between blood units as per institutional policy

Transfusion-Related Acute Lung Injury (TRALI)

Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Acute respiratory distress or failure during or within 6 hours after transfusion; often dramatic onset • Dyspnea • Cyanosis • Bilateral pulmonary infiltrates on chest x-ray • Hypoxemia (O_2 sat \leq 90% on room air or $P_aO_2 \leq$ 300 mm Hg) • No evidence of circulatory overload (pulmonary artery occlusion pressure \leq 18 mm Hg, if available) • Hypotension or, in some cases, hypertension • Fever • Tachycardia • Transient leukopenia • Most patients improve over 2-3 days • Mortality rate about 10% 	<p>TRALI most commonly results from the infusion of donor antibodies directed against recipient HLA class I or II antigens or neutrophil antigens. The antigen/antibody complex activates complement with resultant neutrophil influx into the lungs. Neutrophil activation causes capillary leakage and pulmonary damage. Infrequently, recipient antibodies against cognate donor antigens may be implicated.</p> <p>In a number of TRALI cases, no antibody is found. Biological response modifiers, such as membrane lipids, which accumulate during blood storage, may be implicated in these cases.</p> <p>TRALI may occur with any blood product, but it occurs more commonly with products containing large volumes of donor plasma. No particular patient risk factors have been identified. Donors of implicated units are usually multiparous females who have been immunized to HLA or neutrophil antigens via pregnancy.</p>	<ul style="list-style-type: none"> • Maintain airway; provide oxygen and ventilatory support if necessary • Treat hypotension • Diuretics and steroids are generally not helpful and may be contraindicated • Initiate transfusion reaction work-up; send unit and administration set with attached solutions to the laboratory, in addition to blood and first posttransfusion urine specimens • Do not initiate another transfusion without Blood Bank consultation • Document reaction in patient's chart as per institution policy <p><u>Additional Testing:</u></p> <ul style="list-style-type: none"> • Normal brain natriuretic peptide (BNP) can help distinguish from transfusion-associated circulatory overload (TACO) • Patient serum should be tested for antibodies against HLA or neutrophil-specific antigens and the patient's HLA type should be determined • The blood collection facility will test involved donors for antibodies to HLA and neutrophil-specific antigens. If found, they will be compared with the patient's phenotype <p><u>Future Transfusion:</u></p> <ul style="list-style-type: none"> • Implicated donors are deferred from further blood donation • Patients are not generally at risk for recurrence • Because HLA antibodies are more common in female donors, many centers are providing plasma from donors who are male or who have been screened.

Allergic (Severe) Anaphylactic or Anaphylactoid Reactions

Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Anxiety • Wheezing, stridor, dyspnea • Throat fullness/tightness • Cyanosis • Hypotension • Tachycardia • Urticaria • Flushing • Gastrointestinal distress • Shock • Patient is afebrile • Loss of consciousness • Cardiac arrest (rare) 	<p>The transfusion recipient has an antibody which may be an IgE directed against an antigen in donor plasma, such as an IgA-deficient patient who possesses antibodies to IgA. The cause, however, is often not identified.</p>	<ul style="list-style-type: none"> • Maintain airway; provide oxygen and ventilatory support if necessary • Treat hypotension - Trendelenberg position and fluids; dopamine if unresponsive • Epinephrine if necessary • Intubate if significant upper airway obstruction • Initiate transfusion reaction work-up; send unit and administration set with attached solutions to the laboratory, in addition to blood and first posttransfusion urine specimens • Do not initiate another transfusion without Blood Bank consultation • Document reaction in patient's chart as per institution policy <p style="margin-left: 20px;"><u>Additional Testing:</u></p> <ul style="list-style-type: none"> • Send a specimen for IgA level, if clinically indicated <p style="margin-left: 20px;"><u>Future Transfusion:</u></p> <ul style="list-style-type: none"> • Patient may be given diphenhydramine (Benadryl), steroids, and/or ephedrine prior to transfusion • IgA-deficient patients can be given washed cellular components or components from IgA-deficient donors, although such donors are rare and components may be difficult to obtain • Use washed or deglycerolized RBCs (or washed platelets) for patients experiencing severe reactions not caused by anti-IgA • Consider storing autogeneic units for future transfusions

Transfusion-Associated Circulatory Overload (TACO)		
Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Dyspnea • Orthopnea • Cough • Rales on auscultation • Cyanosis • Headache (severe) • Tachycardia • Hypertension • Congestive heart failure • Bilateral pulmonary edema on CXR • ↑ Pulmonary artery occlusion pressure 	<p>TACO is a life-threatening condition due to rapid increases in blood volume in patients with compromised cardiac or pulmonary function and/or in patients with chronic anemia and expanded plasma volumes.</p> <p>It may also be caused by infusion of 25% albumin (oncotic pressure causes shift of fluid from extravascular to intravascular space).</p>	<ul style="list-style-type: none"> • Upright posture • Maintain airway; provide oxygen and ventilatory support if necessary • Diuretics (e.g., furosemide) • Initiate transfusion reaction work-up; send unit and administration set with attached solutions to the laboratory, in addition to blood and first posttransfusion urine specimens • Do not initiate another transfusion without Blood Bank consultation. Circulatory overload must be addressed prior to initiation of additional blood components or volume expanders • Phlebotomy (250 mL increments) to reduce blood volume • Document reaction in patient's chart as per institution policy <p><u>Additional Testing:</u></p> <ul style="list-style-type: none"> • ↑ brain natriuretic peptide (BNP) can help distinguish from TRALI <p><u>Future Transfusion:</u></p> <ul style="list-style-type: none"> • Except in conditions of ongoing rapid blood loss, blood components should be administered to at-risk patients slowly (1mL/kg/h) with attention to total fluid input and output; if extended periods of transfusion are required, request split units • Diuretics may be given prior to or during the transfusion

Febrile Nonhemolytic Reactions

Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Temperature rise of > 1°C/2°F or a temperature of ≥ 38°C during or within 4 hours of transfusion, without any other obvious cause • Chills/rigors with or without fever • Headache • Nausea/vomiting • Tachycardia, palpitations, and cough may also occur 	<p>Preformed anti-HLA antibodies in the recipient (from pregnancy or previous transfusion) react with corresponding antigens on transfused white blood cells or platelets and trigger cytokine release.</p> <p>Alternatively, preformed cytokines from white blood cell breakdown in the donor units may be directly infused.</p> <p>Most febrile nonhemolytic reactions are benign, although some may cause significant discomfort and hemodynamic or respiratory changes.</p>	<ul style="list-style-type: none"> • Non-salicylate antipyretic (acetaminophen) • Meperidine (injection) may be useful in patients with rigors • Initiate transfusion reaction work-up; send unit and administration set with attached solutions to the laboratory, in addition to blood and first posttransfusion urine specimens • Do not initiate another transfusion without Blood Bank consultation • Document reaction in patient's chart as per institution policy <p><u>Future Transfusion:</u></p> <ul style="list-style-type: none"> • Leukocyte-reduced (pre-storage) blood components may be indicated in patients with a history of febrile non-hemolytic transfusion reaction or who are chronically transfused • Platelets that are not leukocyte-reduced should be ≤ 3 days old to reduce cytokine-mediated reactions • Plasma removal may decrease frequency of febrile reactions • Premedication with acetaminophen has not been shown to be of benefit when leukocyte-reduced components are given

Allergic (Mild) Reactions

Clinical Presentation	Pathophysiology	Treatment/Prevention
<p>Skin</p> <ul style="list-style-type: none"> • Urticaria • Itching • Flushing • Erythema • Localized angioedema <p>Respiratory tract</p> <ul style="list-style-type: none"> • Cough • Hoarseness • Stridor • Wheezing • Chest tightness or pain • Dyspnea <p>Gastrointestinal tract</p> <ul style="list-style-type: none"> • Cramps • Nausea • Vomiting • Diarrhea <p>Cardiovascular system</p> <ul style="list-style-type: none"> • Tachycardia • Other arrhythmias • Cardiac arrest 	<p>The transfusion recipient usually has an IgE antibody on mast cells directed against an antigen in donor plasma resulting in activation and release of histamine.</p>	<ul style="list-style-type: none"> • Diphenhydramine (Benadryl) if urticaria is only symptom • In the case of mild reactions, the transfusion may be restarted after treatment, provided unit can be completed within 4 hours of issuance • Do not restart unit if urticaria severe or patient develops significant local swelling, respiratory or gastrointestinal symptoms, or hypotension • Monitor closely for any other signs or symptoms • Document reaction in patient's chart as per institution policy <p style="text-align: center;"><u>Future Transfusion:</u></p> <ul style="list-style-type: none"> • Patient may be given antihistamine (diphenhydramine) prior to transfusion • If antihistamine is insufficient, hydrocortisone one hour prior to transfusion may be helpful • In cases of recurrent or severe reactions, washed or deglycerolized frozen red cells may be useful

Delayed Reactions

Graft-vs-Host Disease (GVHD)		
Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Fever • Watery diarrhea (profuse) • Vomiting • Rash (maculopapular) • Hepatitis (elevated liver function tests) • Refractory pancytopenia with bleeding and infectious complications • Symptoms typically appear 8-10 days following transfusion (range 3-30 days) • Rapid progression with virtually 100% mortality 	<p>GVHD can occur when, following successful engraftment of donor T-lymphocytes, the transfused foreign lymphocytes, if HLA-incompatible with the transfusion recipient, mount an attack against the recipient's tissues, causing enterocolitis, rash, and pancytopenia. Because of resultant marrow aplasia, patients succumb, primarily from sepsis.</p> <p>GVHD is rare in U.S. transfusion recipients and is observed almost exclusively in immunocompromised patients.</p> <p>The diagnosis is proven by demonstration of donor-derived lymphocytes in recipient's peripheral blood or tissues (by HLA typing).</p>	<ul style="list-style-type: none"> • Immunosuppressive agents (corticosteroids, cytotoxic agents, intravenous immune globulin) • Treatment is usually not successful • Only stem cell transplant is curative <p><u>Prevention:</u></p> <ul style="list-style-type: none"> • Patients at increased risk should receive irradiated cellular components (see <i>Guidelines for Irradiation of Blood and Blood Components</i>) • Directed blood donations (cellular components) from blood relatives and cellular components from donors selected for HLA compatibility should be irradiated

Delayed Hemolytic Reactions (> 24 Hours)

Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Fall in hemoglobin and hematocrit • Fever • Jaundice • ↑ Lactate dehydrogenase (LDH) • Leukocytosis may occur • Reaction typically occurs 3-7 days after transfusion, but may occur 14 days after transfusion or later • Patient may be asymptomatic • Direct antiglobulin test (DAT) may be positive and an antibody, not detected prior to the transfusion, may be identified 	<p>A patient has made an antibody against a red cell antigen in the remote past. Over time, the titer of this antibody has decreased to below detectable levels, so the antibody screen performed prior to the current transfusion does not detect the antibody. Administration of antigen-positive blood presents a second challenge to the immune system and provokes a subsequent anamnestic response. Hemolysis is usually extravascular; however, it may be intravascular.</p>	<ul style="list-style-type: none"> • Send a new blood specimen for antibody screen, antibody identification and DAT • Monitor renal function • Document reaction in patient's chart as per institution policy <p><u>Future Transfusion:</u></p> <ul style="list-style-type: none"> • Transfuse with antigen-negative blood, as indicated

Posttransfusion Purpura (PTP)

Clinical Presentation	Pathophysiology	Treatment/Prevention
<ul style="list-style-type: none"> • Thrombocytopenia, which may be severe, occurring with abrupt onset 1-2 weeks after a transfusion • Melena • Hematuria • Vaginal bleeding • Occurs most commonly in multiparous women • Usually self-limited (≤ 2 weeks), but bleeding may be severe and can be fatal (e.g., intracranial bleeding) 	<p>Thrombocytopenia occurs in a patient who has made an antibody against a foreign platelet antigen as a result of pregnancy or a previous transfusion. After a transfusion of red cells or platelets, antibodies attach to surface antigen sites on platelets, resulting in their destruction by splenic and liver macrophages. Most commonly the implicated antibody is against the HPA-1a (PL^{A1}) antigen (60% of cases). Through a mechanism not clearly elucidated, likely auto-immune, the patient's own antigen-negative platelets are also destroyed.</p>	<ul style="list-style-type: none"> • Intravenous immune globulin (IVIg) • Plasmapheresis with FFP replacement, if refractory to IVIG • Steroids, although their benefit has not been documented • Send blood specimen to laboratory for platelet antibody work-up • Document reaction in patient's chart as per institution policy • Transfusion of antigen-negative platelets is generally ineffective <p><u>Future Transfusion:</u></p> <ul style="list-style-type: none"> • Repeat reactions are rare, but patients with a documented history of PTP should receive antigen-negative blood components, if available • Platelet typing of family members may help identify potential antigen-negative donors