Transfusion Reactions

William J. Savage, MD, PhD

KEYWORDS

• Transfusion • Reaction • Adverse event • Red blood cell • Platelet • Plasma

KEY POINTS

- Transfusion reactions may be defined by case type, timing, severity, and imputability.
- The differential diagnosis of any untoward clinical event should always consider adverse sequelae of transfusion.
- Fever, dyspnea, hypotension, and urticaria are common manifestations of transfusion reactions.

Transfusion reactions are common occurrences, and clinicians who order or transfuse blood components need to be able to recognize adverse sequelae of transfusion. The differential diagnosis of any untoward clinical event should always consider adverse sequelae of transfusion, even when transfusion occurred weeks earlier. There is no pathognomonic sign or symptom that differentiates a transfusion reaction from other potential medical problems, so vigilance is required during and after transfusion when a patient presents with a change in clinical status. Although transfusion reactions are common, they are uncommonly fatal. The Food and Drug Administration (FDA) receives reports of approximately 40 fatalities attributable to transfusion every year.

Transfusion reactions may be defined by case type, timing, severity, and imputability (the causal relationship of a reaction to transfusion) (**Table 1**). Other classification schemes differentiate reactions by mechanism; for example, immunologic/nonimmunologic, or by type of blood component. This review covers the presentation, mechanisms, and management of transfusion reactions that are commonly encountered, as well as transfusion reactions that can be life-threatening. Approximate risks of selected transfusion reactions are shown in **Fig. 1**.

HEMOLYTIC TRANSFUSION REACTIONS

Hemolytic transfusion reactions are caused by the immune-mediated clearance of transfused red blood cells (RBCs). Immune-mediated hemolysis can be acute or delayed. Hemolytic transfusion reactions are classically thought of as immune-mediated

Disclosure Statement: The author has nothing to disclose.
Transfusion Medicine, Brigham and Women's Hospital, Harvard Medical School, 75 Francis Street, Amory 260, Boston, MA 02115, USA
E-mail address: wjsavage@partners.org

Hematol Oncol Clin N Am 30 (2016) 619–634
http://dx.doi.org/10.1016/j.hoc.2016.01.012 **hemonc.theclinics.com**
0889-8588/16/$ – see front matter

Table 1
Timing and manifestations of transfusion reactions

Reaction Type	Typical Timing in Relation to Transfusion (Range)	Presenting Signs and Symptoms
Acute hemolytic	During (up to 24 h after)	Fever, chills, dyspnea, hypotension, tachycardia, infusion site pain, back pain, hemoglobinuria, hemoglobinemia, indirect hyperbilirubinemia, renal failure, disseminated intravascular coagulation
Febrile nonhemolytic	During (up to 4 h after)	Fever, chills, rigors
Allergic	During (up to 4 h after)	Urticaria, pruritus, flushing, angioedema, dyspnea, bronchospasm, hypotension, tachycardia, abdominal cramping
Transfusion-associated circulatory overload	Within 2 h (up to 6 h)	Dyspnea, tachycardia, hypertension, headache, jugular venous distention
Septic	During (may be subclinical)	Fever, chills, hypotension, tachycardia, vomiting (may be delayed several hours after transfusion)
Hypotensive	During	Isolated hypotension
Transfusion-related acute lung injury	Within 2 h (up to 6 h)	Dyspnea, hypoxemia, fever, hypotension
Transfusion-associated graft-versus-host disease	8–10 d after (up to 6 wk)	Fever, erythroderma, bloody diarrhea, pancytopenia, liver function abnormalities
Posttransfusion purpura	5–12 d after	Purpura, hemorrhage

Modified from Savage WJ. Transfusion reactions to blood and cell therapy products. In: Hoffman R, Benz E, Silberstein L, et al, editors. Hematology. 7th edition. Philadelphia: Elsevier; in press.

reactions caused by donor RBC antigen incompatibility, but thermal, osmotic, infectious, and mechanical derangements are causes of transfusion-associated hemolysis. Mechanical valves, blood warmers, infusion catheters, and infusion pumps can cause non–alloimmune-mediated hemolytic transfusion reactions. Additionally, free hemoglobin that has leaked into RBC unit supernatant during storage can be passively transfused and can cause hemoglobinuria and hyperbilirubinemia that is not related to acute in vivo hemolysis.[1]

Acute, immune-mediated hemolytic transfusion reactions are those that occur during or immediately after incompatible RBCs are transfused into a patient who already possesses the corresponding antibody. ABO-incompatible RBC transfusion is the prototypical example of an acute hemolytic transfusion reaction. ABO antibodies are spontaneously occurring immunoglobulin (Ig)M and IgG antibodies to A and/or B blood group antigens that are nonself. IgM antibodies efficiently fix complement after binding to ABO-incompatible blood and are responsible for initiating the hemolytic and inflammatory cascades that cause a clinically apparent acute intravascular hemolytic transfusion reaction. Such a reaction could occur, for example, after transfusion of A-type RBCs into an O recipient, who has anti-A. Transfusing as little as 30 mL of incompatible blood can be fatal, and there is a direct relationship between increasing volumes of incompatible blood transfused and mortality.[2]