During the past 3 decades, much advancement has been made in the field of transfusion medicine, particularly regarding reductions in adverse events associated with blood-product infusion. Improved donor screening and innovations such as nucleic acid testing have greatly helped to enhance safety and to reduce transfusion-associated morbidity and mortality. Nevertheless, substantial risks associated with transfusion remain.¹ The aim of this article is to provide a thorough, up-to-date reference regarding the incidence, pathogenesis, management, prevention, and reporting of transfusion reactions.

Severe Complications of Transfusion

Adverse events were selected for inclusion in this section because they have been reported to have caused transfusion-associated fatalities within the last 5 years, per U.S. Food and Drug Administration (FDA) data and/or are reactions which, historically, have been associated with adverse patient outcomes.² The signs, symptoms, laboratory findings, and management of these reactions are summarized in Table 1.

Transfusion-Related Acute Lung Injury

Overview and Incidence

Transfusion-related acute lung injury (TRALI) has gained prominence in recent years. Data regarding the incidence of TRALI is variable, with early reports suggesting rates as high as 1 per 4500 units transfused...
and more recent estimates approaching approximately 1 per 260,000 for all components. Of interest, these rates vary significantly by country; this issue derives at least partly from definitions of the condition. One confounding variable is that the incidence of TRALI is highly linked to the type of blood component being administered, with the highest rates observed for components with a high content of plasma. According to best estimates, the highest incidence occurs with transfusion of fresh frozen plasma (FFP), at roughly 1:66,000; followed by platelets (PLTs), at roughly 1:420,000; and finally, red blood cells (RBCs), at roughly 1:2,860,000. TRALI is the most frequent cause of transfusion-associated mortality in the United States for the past several years.

Pathogenesis

Transfusion related acute lung injury occurs when antibodies (often anti–human leukocyte antigen [HLA] I or II) present in transfused donor plasma interact with recipient leukocytes, resulting in leukocyte activation and adhesion to the pulmonary endothelium. This process results in the release of proteolytic enzymes and reactive oxygen species, causing endothelial injury. Several authors have suggested an additional, nonimmune mechanism that contributes to TRALI, in which certain leukocyte-priming substances, presumed to be lipids, are present in stored blood components; these components facilitate activation. Based on these data, there may be a double-hit process, in which leukocytes are first primed by nonimmune compounds and then secondarily activated by an immune mechanism. The resulting

<table>
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<tr>
<th>Diagnosis</th>
<th>Symptoms</th>
<th>Timing</th>
<th>Lab Findings</th>
<th>Management</th>
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<tbody>
<tr>
<td>TRALI</td>
<td>Dyspnea/tachypnea, Fever, Hypotension</td>
<td>During or post-transfusion (within 4-6 hrs)</td>
<td>CXR = Diffuse lung infiltrate (Non-cardiogenic), BNP/proBNP = Normal, Donor Anti-leukocyte Ab+, Abnormal leukocyte crossmatch</td>
<td>Stop transfusion if ongoing, Supportive = Oxygen (O2) Intubation, if necessary</td>
</tr>
<tr>
<td>HTR</td>
<td>Fever/chills, Chest pain, Hypotension, Severe Back or Abdominal pain *</td>
<td>Immediate up to several hours post transfusion</td>
<td>DAT+, Ab screen on repeat + 1LDH, 1Bilirubin</td>
<td>Stop transfusion, Recheck crossmatch, Recheck documentation, Supportive care, Oxygen support, Urine output &gt;100mL/hr, Monitor hematocrit</td>
</tr>
<tr>
<td>TACO</td>
<td>Dyspnea/tachypnea, Cough, Jugular vein distension</td>
<td>4-6 hours post Tx</td>
<td>1BNP/proBNP, CXR = pulmonary edema</td>
<td>Stop transfusion if ongoing, Get patient upright, Diuretics, Slow infusion or split units for future</td>
</tr>
<tr>
<td>Septic</td>
<td>Fever/chills (&gt;1-2°C rise), Hypotension/shock, Oliguria, Dyspnea</td>
<td>During transfusion or shortly after</td>
<td>Gram stain + Bag culture + Blood cultures + 1D-dimer/1 PT (if DIC)</td>
<td>Stop transfusion, Empirical antibiotics, Hemodynamic stability, Respiratory support (O2)</td>
</tr>
<tr>
<td>Anaphylactic</td>
<td>Rash/erythema, Pruritus/angioedema, Dyspnea/ chest pain, Hypotension, Vomiting/diarrhea</td>
<td>Seconds or minutes into transfusion</td>
<td>Normal CXR, Gram stain/ Blood cultures NEG</td>
<td>Stop transfusion, Supportive care (epinephrine, salmine, diphénylhydramine, airway patency)</td>
</tr>
<tr>
<td>PTP</td>
<td>Purpura, PLT-type bleeding (mucosal)</td>
<td>3-12 days post transfusion (5-10 days usual)</td>
<td>PLT count &lt;15k/µL</td>
<td>IVIg (+ random PLTs if needed)</td>
</tr>
<tr>
<td>TA-GVHD</td>
<td>Erythematous rash, Fever, Diarrhea</td>
<td>3-30 days post Tx (8-10 days usual)</td>
<td>Skin biopsy with mononuclear cell infiltrate 1LDH, 1ALT/AST, 1Bili (Hepatitis)</td>
<td>Supportive but poor prognosis</td>
</tr>
</tbody>
</table>

Ab, antibody; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Bili, total bilirubin; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; Cr, creatinine; CXR, chest x-ray; DAT, direct antiglobulin test; DIC, disseminated intravascular coagulation; HTR, hemolytic transfusion reaction; IVIg, intravenous immunoglobulin; LDH, lactate dehydrogenase; PT, prothrombin time; PTP, post-transfusion purpura; PTT, partial thromboplastin time; TACO, transfusion-associated circulatory overload; TA-GVHD, transfusion-associated graft-versus-host disease; TRALI, transfusion-related acute lung injury; TX, transfusion.
lung injury is similar to that seen in acute respiratory distress syndrome (ARDS).

**Diagnosis**

Diagnosis of TRALI relies on a clinical presentation characterized by low-grade fever, hypotension, tachypnea, and dyspnea with diffuse lung infiltrates observed via chest X-ray, all occurring within 4 to 6 hours of transfusion. Of importance, these signs and symptoms are not secondary to volume overload; they are often described as noncardiogenic pulmonary edema. Measurement of brain natriuretic peptide (BNP) and clinical evaluation of volume status, the results of both of which should be normal, may be useful to confirm TRALI and/or to exclude other conditions. As reported by Goldman et al, several groups have developed consensus criteria for the clinical diagnosis of TRALI incorporating the findings described herein (Figure 1). Although clinical diagnosis is the mainstay, laboratory testing can serve an adjunct role. Donor plasma can be tested for antileukocyte antibodies, which are found in a high percentage of TRALI cases. If antibodies are found, leukocyte incompatibility can be tested by donor-recipient crossmatch or by recipient antigen typing. However, this is not required for diagnosis of TRALI; also, results are generally not available in time to guide management.

**Treatment and Prevention**

Treatment of TRALI is mainly supportive in nature. For mild cases, oxygen therapy is sufficient. However, for more severe cases, intubation and artificial ventilation may be required. Of importance, administration of diuretics is not recommended because the condition is not caused by volume overload and because this measure may exacerbate hypotension. No convincing data have been published, to our knowledge, regarding the efficacy of steroids in treating TRALI. Most cases of mild TRALI resolve within 48 to 72 hours; typically, no sustained lung injury is incurred. However, severe cases are not uncommon; overall mortality for TRALI is estimated at between 5% and 25%. Prevention of TRALI is of high priority, given its association with mortality. The most widespread approach thus far has been the use of male-only donor plasma. The basic premise is that male plasma is less likely to contain the antileukocyte antibodies that may cause TRALI; some evidence supports this approach. In a study conducted in the Netherlands, use of male-only plasma reduced the rate of TRALI by 33%. The United Kingdom has also demonstrated a significant reduction in TRALI incidence after implementing a male-only plasma program.

### Hemolytic Transfusion Reactions

**Overview and Incidence**

Hemolytic transfusion reactions (HTRs) involve antibody-mediated lysis of donor RBCs. The most dangerous type of hemolytic reaction involves acute, intravascular destruction of transfused RBCs. Acute hemolysis, often attributable to ABO antibodies, is estimated to occur in approximately 1 of every 30 to 70,000 RBC transfusions and has historically accounted for...
many transfusion-related fatalities. More recently, however, delayed hemolytic transfusion reactions (DHTRs), in which an evanescent antibody is redeveloped as a memory response to antigen stimulation, have become increasingly recognized as a significant cause of mortality. A report indicates the overall incidence of delayed reactions is higher than that of acute reactions, with estimates ranging from approximately 1 in 300 to 1 in 1:11,000 RBC transfusions.

**Acute Hemolytic Transfusion Reactions**

**Pathogenesis**

Acute hemolytic transfusion reactions (AHTRs) occur when donor RBCs are lysed intravascularly in the presence of preformed antibodies in the recipient. Most commonly, this involves naturally occurring ABO blood-group antibodies. In this setting, anti-A or anti-B antibodies bind to the transfused, incompatible RBCs, with ensuing activation of the complement cascade. Various compounds are released during hemolysis (eg, interleukin [IL]–1, IL-6, and tumor necrosis factor [TNF]–α) that mediate fever, hypotension, and endothelial activation. Non-ABO antibodies that repair complement, such as anti-Jka, can also drive acute, intravascular hemolysis.

**Diagnosis**

Acute hemolytic transfusion reactions tend to present immediately or within several hours after transfusion as fever, chills, chest pain, or hypotension. Less common signs and symptoms include flushing, lower back pain, dyspnea, abdominal pain, vomiting, and diarrhea. In severe cases, coagulopathy can develop and renal failure can occur. If such signs or symptoms are present, a direct antiglobulin test (DAT) should be performed immediately on a freshly drawn blood specimen. If the DAT results are positive, elution should be performed and the antibody identified. Repeat antibody screening and identification performed with a fresh blood specimen from the patient may also be warranted. A complete blood count (CBC) should be determined to establish a baseline hematocrit (HCT) value that can be followed thereafter in a serial manner. Serum lactate dehydrogenase (LDH), bilirubin, and haptoglobin levels should be monitored for evidence of hemolysis. Concurrently, repeat crossmatch and rechecking of ABO type and other documentation is necessary to ensure that a technical error has not occurred.

**Treatment and Prevention**

At the first sign of AHTR, the transfusion should be ceased and the patient treated supportively. Oxygen and fluids should be administered, as appropriate. Monitoring and maintaining urine output, at greater than 70 to 100mL/hour if possible, is important in helping maintain renal function. Further transfusion should be avoided if possible until repeated blood-bank testing has been completed and cross-matched, compatible RBCs can be obtained. If patients demonstrate evidence of coagulopathy or disseminated intravascular coagulation (DIC), use of plasma and PLT products is also warranted. For patients who have received large volumes of incompatible RBCs, consideration may be given to RBC-exchange therapy to reduce the circulating, incompatible RBC burden and to limit hemolysis.

Data indicate that most ABO-related AHTRs result from clerical errors involving patient or donor-unit identification. Therefore, much focus has been placed on proper specimen labeling. At VA Connecticut, as a safety-improvement measure, we have employed a witness-based system to verify (and to document) the identity of patients undergoing blood-bank specimen collection. Additional improvements in safety rely on ensuring patient identifiers during blood-bank testing and at the time of transfusion. Blood-banking software and technology, such as bedside barcode scanning of blood products, have been developed to address potential errors. Non-ABO AHTRs, which occur less frequently due to errors and are more often associated with undetectable antibodies, are best avoided by careful antibody screening in the blood bank. Other approaches for the prevention of HTRs due to non-ABO antibodies are discussed herein.

**Delayed Hemolytic Transfusion Reactions**

**Pathogenesis**

Delayed hemolytic transfusion reactions (DHTRs) may result from 2 situations. In most cases, re-emergence of a non-ABO antibody occurs in the recipient. This antibody has been developed at an earlier time through transfusion or pregnancy but has become evanescent (ie, titers have decreased to undetectable levels). Once re-exposed to the antigen in question, an anamnestic response (ie, an enhanced and quickened immune response on re-exposure) results in re-formation of the
antibody. Because re-emergence of an evanescent antibody takes 3 to 10 days on average, the resulting hemolysis is delayed. Less commonly, development of a new antibody against a non-ABO blood group antigen in donor RBCs is the underlying cause of DHTR.15

Diagnosis
Rather than presenting with acute clinical symptoms, DHTRs manifest at a delayed interval after transfusion. The reaction may be subclinical or mild; however, severe DHTRs with significant hemolysis and even death can also occur.16 Often, DHTRs are detected by laboratory studies such as repeat antibody screening rather than by clinical manifestations. Some delayed reactions are hemolytic, with a consequent decrease in HCT and haptoglobin (Hp) and an increase in LDH and bilirubin. However, others are purely serologic (ie, re-emergence of an alloantibody is detected on repeat screening); however, no clinical or laboratory evidence is observed for hemolysis.17 To confirm the presence of DHTR, it is necessary to demonstrate the emergence of an alloantibody. If a DHTR is suspected on clinical grounds, a new blood-bank sample should be obtained and subjected to repeat antibody screening, DAT, and elution studies. By these methods, the specificity of the alloantibody can be confirmed and documented, and appropriate antigen-negative RBC units can be provided for future transfusions.

Treatment and Prevention
Because most DHTRs are mild, only supportive treatment is usually necessary. However, close monitoring of the patient is recommended, including serial assessment of renal function and HCT. In the event of significant hemolysis, hydration and maintenance of sufficient urine output is needed, similar to the approach discussed herein for AHTRs. Prevention of DHTR is the main goal; this can be addressed in several ways. Most importantly, improved alloantibody data sharing between institutions would be beneficial. Use of an object that to alert health care providers to a history of alloimmunization, such as a medical bracelet or wallet card, would serve this purpose. Web-based platforms documenting alloantibody history are another option. Unfortunately, the latter mechanisms are typically unavailable or underutilized at this point. Therefore, in the absence of other modes of information sharing, data regarding previous antibody status may be obtained by a telephone call to an institution at which the patient had previously undergone blood-bank testing or transfusion (if such history is readily available for the patient).

Transfusion-associated Circulatory Overload

Overview and Incidence
Although TRALI is likely the best known (and most feared) pulmonary complication of transfusion, transfusion-associated circulatory overload (TACO) is no less clinically significant. In fact, according to recent FDA data, TACO was the second most common cause of transfusion-associated fatality in the United States from 2009 through 2010. Because of its tendency to affect critically ill patients, it is difficult to adequately ascertain the true incidence or prevalence of TACO. Nevertheless, a recent report estimates that approximately 6% of transfusions in critically ill patients may be associated with TACO. Patients at highest risk for TACO include those in intensive care settings, elderly individuals, and patients with established cardiac disease or dysfunction.18,19

Pathogenesis
Unlike other causes of transfusion reactions, which typically have complex etiologies, the onset of TACO is most often related to a patient’s underlying cardiac function and/or volume status. Those patients with a disease or condition that predisposes them to volume overload can develop TACO if too many blood products are infused in a too-brief period or if a single unit is infused at a rate more rapid than can be tolerated. When the circulatory system is overwhelmed in TACO, fluid accumulates in the air space, leading to pulmonary edema, decreased air exchange, and respiratory distress.

Diagnosis
The symptoms of TACO typically manifest as dyspnea, tachypnea, and/or cough occurring during or within a few hours of the completion of transfusion(s). Vital-sign changes may include hypertension, tachycardia, and decreased oxygen saturation. On physical examination, patients may demonstrate jugular venous distension and, if in an intensive monitored setting, evidence of increased central venous pressure. However, these signs, symptoms, and vital-sign changes are not specific for TACO; in many cases, it may be difficult to exclude TRALI based on the clinical presentation only. Hence, other clues for differentiating between these 2 diagnoses may be useful (Table 2). From a laboratory testing perspective, at least 2 studies have shown that BNP and/or N-terminal pro-BNP may be valuable
in distinguishing between the diagnoses. It is uncertain whether chest X-ray imaging may be helpful in establishing a diagnosis because, in TACO, chest imaging typically shows a picture of pulmonary edema that may not be distinguishable from TRALI. Finally, extracting a history of previous episodes of volume overload may help to support a diagnosis of TACO.

Treatment and Prevention
At the onset of any signs of respiratory distress during transfusion, cessation of the infusion is the correct first step. In some mild cases, merely ceasing the infusion and placing the patient in an upright position may be sufficient to overcome TACO. For more advanced cases, the use of diuretics can relieve patients of excess fluids and reduce respiratory symptoms. If these measures fail, more drastic steps, such as transfer to an intensive care setting or intubation, may be warranted to maintain adequate air exchange. Failure to respond to diuretics or other therapies aimed at correcting volume overload may be signs that the patient is experiencing TRALI.

By itself, the transfusion community can do little from a preventative standpoint because TACO is not a reaction caused by the blood product itself; rather, it results from excessive fluid infusion. As such, prevention of these reactions relies on a coordinated effort between the clinical services department and the blood bank. Patients recognized as being at risk for TACO should receive transfusions as slowly as possible for as long as 4 hours. If transfusion requires larger volumes or if infusions cannot be accomplished within 4 hours, blood banks may choose to split units in a sterile manner for administration. Patients with evidence of volume overload or a predisposition to TACO may also benefit from pretransfusion diuretic administration.

Septic Transfusion Reactions

Overview and Incidence
Septic transfusion reactions result from bacterial contamination of donor blood components. Due to the need for room-temperature storage, PLTs are, by far, the leading culprit in septic reactions. Before 2004, the overall incidence of septic reactions was approximately 1 per 25,000 PLT transfusions. In 2004, standards were introduced to attempt to limit sepsis associated with PLTs by formal testing for bacterial contamination using microbial detection systems. The incidence of septic reactions has been reported to be reduced since the implementation of preventive measures, with estimated ranges of 1:100,000 transfusions. Despite the implementation of these measures, septic reactions have not been completely eliminated.

Pathogenesis
Contamination of the donor unit may occur by several means. The most common mechanism involves introduction of a low concentration of skin bacteria into the component at the time of donor phlebotomy. Less commonly, asymptomatic donor bacteremia may be at fault. Finally, and least frequently, bacteria may be introduced during processing of donor components. Once inoculated, the donor unit serves as a culture medium for bacterial proliferation. Platelet units are at highest risk due to their requirement for room-temperature storage, with RBCs demonstrating lower risk due to cold-storage temperatures. The most frequently implicated bacteria in PLTs are Gram-positive organisms, most commonly skin flora such as *Streptococcus* spp. and *Staphylococcus* spp. Gram-negative contamination may also occur, the most common example being contamination of RBC components by *Yersinia enterocolitica*, a bacterium that thrives at cold temperatures.

Diagnosis
The diagnosis of a septic reaction is vital because the condition must be treated quickly to avoid an adverse outcome. The most common signs and symptoms include fever and/or chills beginning during or shortly after transfusion. Because fever may be a component of several other types of reactions, a temperature elevation of greater than or equal to 2°C has been recommended as a more specific indicator of septic reaction (Table 2). Nevertheless, any temperature increase during transfusion warrants concern for a septic reaction. Other signs and symptoms of sepsis may also occur, including nausea, vomiting, hypotension, shock, oliguria, respiratory distress, or DIC. Once suspicion has been raised for a septic reaction, the diagnosis is investigated by Gram stain and culture of the patient’s blood and the component storage bag. Correlative growth of the same organism in both cultures represents strong evidence for a septic reaction. Exclusion of other bacterial sources (eg, an infected central line) is also imperative to confirm that bacteremia has resulted from transfusion.

Treatment and Prevention
Management of a septic reaction requires immediate attention to hemodynamic stability, with fluid management and respiratory support. Empiric antibiotic...
therapy should be initiated immediately; the positive results of any culture should be used to guide appropriate therapy thereafter. Many efforts have been made to prevent septic reactions. A study\(^26\) has shown that improved donor skin sterilization is a strong first step for reducing the risk for bacterial contamination. Platelet products are now also subjected to formal bacterial detection methodologies to detect possible contamination.\(^{27}\) Various methods of pathogen inactivation have also been proposed\(^28\) but none have been implemented for clinical use in the United States thus far, to our knowledge.

### Anaphylactic Transfusion Reactions

#### Overview and Incidence

Although estimates vary widely, severe anaphylactic transfusion reactions are rare. They most commonly occur with PLT transfusions; FFP is the second most common culprit. Red blood cells are rarely implicated. The overall incidence is estimated in the range of 1 in every 20,000–30,000 transfusions,\(^29\) making them approximately 10-fold less common than penicillin anaphylactic reactions.

#### Pathogenesis

Classically, severe anaphylactic transfusion reactions have been associated with anti-IgA antibodies developing in an immunoglobulin A (IgA)–deficient patient.\(^{30}\) However, it has since been recognized that other antigens are responsible for many such reactions. For example, antihaptoglobin antibodies in haptoglobin-deficient patients may form in response to transfusion and may result in anaphylaxis.\(^{31}\) Numerous potential allergens exist. In an illustrative case,\(^32\) a child with a peanut allergy developed an anaphylactic reaction to a blood product from a donor that had eaten peanuts before donation. Conversely, recipients who have consumed food products to which their blood-product donors have sensitivity have also developed anaphylactic reactions.\(^{33}\) A common end pathway is postulated to involve systemic activation of complement, mast cells, and basophils accounting for the symptomatologic manifestations described herein.

### Diagnosis

Severity and rapidity of symptom onset define a reaction as anaphylactic. The typical manifestation is a combination of skin, respiratory, cardiovascular, and gastrointestinal problems beginning within seconds or minutes of the start of a transfusion.\(^{30,33}\) In severe cases, the most common findings are generalized erythema, pruritus, urticarial eruption, and/or angioedema. Signs of upper or lower airway obstruction may accompany skin changes; they include substernal pain, wheezing, dyspnea, and cyanosis. Circulatory collapse has the potential to result in cardiac arrest. Vomiting and diarrhea are also common. A general rule of thumb is that the time to symptom onset also often corresponds to the severity of the reactions; the quickest reactions tend to be most severe. Beyond that, symptoms such as hypotension, dyspnea, and nausea are the most specific for anaphylactic reactions (Table 2). Compared with TACO, allergic cardiovascular symptoms typically occur much more quickly.

#### Table 2. Signs/Symptoms and Associated Differential Diagnoses

<table>
<thead>
<tr>
<th>Sign/ Symptom</th>
<th>Transfusion-related Differential Diagnosis</th>
<th>Non–transfusion-related</th>
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<tbody>
<tr>
<td>Fever</td>
<td>AHTR (moderate)</td>
<td>Infection/sepsis</td>
</tr>
<tr>
<td></td>
<td>Sepsis (marked, often &gt;2°C increase)</td>
<td>Post-operative fever</td>
</tr>
<tr>
<td></td>
<td>TRALI (mild)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FNHTR (mild to moderate)</td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>AHTR</td>
<td>Volume depletion</td>
</tr>
<tr>
<td></td>
<td>Sepsis</td>
<td>Vasodilation (medication/shock)</td>
</tr>
<tr>
<td></td>
<td>Severe allergic/anaphylactic reaction</td>
<td>Vasovagal response</td>
</tr>
<tr>
<td></td>
<td>Acute hypotensive reaction</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>TRALI</td>
<td>CHF</td>
</tr>
<tr>
<td></td>
<td>TACO</td>
<td>Volume overload due to other non-transfused products (eg normal saline)</td>
</tr>
<tr>
<td></td>
<td>Allergic/anaphylactic reaction</td>
<td></td>
</tr>
<tr>
<td>Rash/flushing</td>
<td>Allergic reaction</td>
<td>Medication reaction</td>
</tr>
<tr>
<td></td>
<td>AHTR</td>
<td>Allergic reaction</td>
</tr>
<tr>
<td></td>
<td>PTP</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>AHTR (ie, chest or flank pain)</td>
<td>Postoperative pain</td>
</tr>
<tr>
<td></td>
<td>Idiosyncratic pain reaction</td>
<td>Muscle cramping</td>
</tr>
<tr>
<td>Nausea</td>
<td>AHTR</td>
<td>Medication effect</td>
</tr>
<tr>
<td></td>
<td>Sepsis</td>
<td>Infection</td>
</tr>
<tr>
<td></td>
<td>Allergic/anaphylactic reaction</td>
<td></td>
</tr>
</tbody>
</table>

AHTR, acute hemolytic transfusion reactions; TRALI, transfusion-related acute lung injury; TACO, transfusion-associated circulatory overload; CHF, congestive heart failure; PTP, post-transfusion purpura.
**Treatment and Prevention**

If a patient is experiencing symptoms suggestive of an anaphylactic reaction, the most important step is cessation of the transfusion, followed by supportive care addressing the specific symptoms. This may include subcutaneous or intravenous epinephrine, volume expansion with saline for circulatory collapse, diphenhydramine for skin symptoms, and intubation to restore airway patency. Corticosteroids are not effective in the acute-care setting. Finally, despite past theories of passive transfer of donor leukocyte–derived cytokines, prestorage leukoreduction does not reduce the incidence of anaphylactic reactions.

Risk for IgA-related acute transfusion reaction occurs only when recipient IgA levels are less than 0.05 mg/dL; most assays typically have lower limits of sensitivity 100-fold higher (ie, 5 mg/dL). Hence, higher sensitivity testing must be used to identify patients truly at risk for anaphylaxis. Oddly, the presence of anti-IgA in an IgA-deficient patient does not imply that a reaction will definitely take place on exposure, for reasons that remain unclear. If anti-IgA is identified in a patient at any time, conventional wisdom dictates that special IgA-deficient blood products and derivatives, including intravenous gamma globulin (IVIg), should be provided to the patient. If such products are not readily available and immediate transfusion outweighs the risk of an anaphylactic reaction, a slow and carefully monitored infusion may be the only option. Corticosteroid or diphenhydramine administration may help reduce the severity of symptoms. For PLT and RBC transfusions, procedures for extensive washing and/or saline replacement are recommended to help minimize risk. However, while efficacious, these procedures are not a viable option for urgent needs.

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**Post-transfusion Purpura**

**Overview and Incidence**

Post-transfusion purpura (PTP) is a rare disorder with a historical incidence estimated to be between 1 in 25,000 to 100,000 transfusions. It is possible that PTP is underdiagnosed or misdiagnosed, primarily due to its similarity at presentation to heparin-induced thrombocytopenia (HIT) and its association with disorders such as DIC, which may cloud proper identification. The vast majority of PTP cases occur in women who have previously been pregnant. Post-transfusion purpura has also been reported in adults who have been previously exposed to foreign PLTs through transfusion or transplantation.

**Pathogenesis**

Alloimmunization to PLT antigens is the hallmark of PTP; however, the mechanism by which this process leads to widespread destruction of host PLTs is incompletely understood. Human PLT antigens (HPAs) are the result of polymorphisms, mainly in the surface glycoproteins (eg, GPIa, GPIb, GPIla, GPIIb, GPIIIa, and GPIIIb), that serve as receptors for collagen, von Willebrand factor, and fibrinogen. Oddly, in PTP, the alloimmune response against foreign HPAs somehow gains autoimmunity, with host PLTs ultimately becoming the target of destruction. Some evidence exists that autoantibodies develop, although this theory is not universally accepted. Human PLT antigen-1a PLT exposure in a homozygous HPA-1b (ie, PLA2) host is the most common scenario for alloimmunization; however, the prevalence of HPA-1b in the general US population is less than 2%, meaning that the probability of such a mismatch is low. Moreover, evolution into full-blown PTP is rare in cases of clear exposure. Regardless of the mechanism, in selected cases of PTP, unbridled PLT activation can result in severe thrombocytopenia and bleeding complications.

**Diagnosis**

Identification of PLT alloantibodies in the context of severe thrombocytopenia (<15,000/µL) and occasional bleeding, which occurs 3 to 12 (usually 5-10) days after blood transfusion, is the basis for diagnosis. By contrast, HIT typically results in only moderate reductions in PLT count (> 30,000/µL) and is temporally related to heparin exposure. The differential diagnosis should also include conditions such as thrombotic thrombocytopenic purpura (TTP), which can be observed with a similar precipitous decrease in PLT counts. However, TTP can be ruled out by its association with microangiopathic hemolytic anemia.

Several tests are available for detection of PLT antibodies. These include detection of antibodies on intact PLTs or on immobilized PLT antigens by immunofluorescence, flow cytometric testing, and enzyme-linked immunosorbent assay (ELISA)–based methods. These tests vary in their performance characteristics, particularly pertaining to sensitivity to different HPAs, which may be modified depending on reagent preparation. A combined testing approach is generally needed; several reference laboratories (including Mayo
Medical Laboratories and BloodCenter of Wisconsin) offer PTP workup panels aimed at maximizing sensitivity. Some of these include genotyping of PLTs, which may provide additional circumstantial evidence in certain cases.

**Treatment and Prevention**

Therapeutic options for addressing antibody-mediated PLT destruction are similar to those offered for autoimmune disorders. Plasmapheresis and IVIg have been successful, with IVIg generally considered to be the first-line therapy.\(^{39,40}\) In patients with PTP and extensive or life-threatening hemorrhage, transfusion with antigen-negative PLTs may be warranted.\(^{41}\) However, in many cases, antigen-negative PLTs may not be readily available. Thus, the provision of random-donor PLTs, although not ideal, may be effective in temporarily limiting the extent of an episode of bleeding. Some authors recommend, along with transfusions of blood products from random donors, provision of IVIg or other immunosuppressants because this practice may enhance PLT survival.\(^{42}\) Few specific preventative strategies are available for PTP. If a patient is known to lack HPA-1a and has a history of PTP, the patient should receive HPA-1a negative PLTs in future transfusions. Other blood products may contain HPA-1a positive PLTs or, theoretically, soluble HPA-1a, which could be absorbed into host PLTs (in this scenario, the risk would remain). Human PLT antigen matching of these other blood products is usually not practical.

**Transfusion-Associated Graft Versus Host Disease**

**Overview and Incidence**

The true incidence of transfusion-associated graft versus host disease (TA-GVHD) is unknown; however, it is rare and its incidence has decreased since the advent of irradiation of blood products (as discussed herein). The overall probability of developing TA-GVHD has been estimated to be less than 1 per 1,000,000 units transfused in Canada and is likely even lower at present in the United States.\(^{43}\)

**Pathogenesis**

Transfusion-associated graft versus host disease is caused by donor lymphocyte-mediated injury to recipient tissues. For TA-GVHD to occur, several initial events must take place. Viable donor lymphocytes must be delivered in sufficient quantities to foster circulation, donor lymphocytes must evade recognition by host cellular immune defenses that would otherwise destroy donor lymphocytes within a few days, engraftment must take place within host organs, lymphocytes must be activated by recipient HLA class II antigen presentation, and cytotoxic donor lymphocytes must then proliferate in sufficient numbers to cause destruction of end organs.\(^{44}\) The evasion of host defenses by donor lymphocytes is far more likely if the donor lymphocytes have an HLA class I type recognized as “self” by the host or if the host’s cellular immune defense system is immature or heavily impaired.\(^{44}\) However, a case report\(^{45}\) was published of immunocompetent host individuals who have experienced TA-GVHD.

**Diagnosis**

Symptoms related to TA-GVHD include fever, skin rash, diarrhea, and hepatitis, all of which are directly related to the pathogenesis of the disorder. Fever, a universal finding, is usually the first symptom to appear, resulting from the cytokine release related to indiscriminate, systemic donor T-cell activation. An erythematous skin rash, arising from activated, cytokine-releasing engrafted donor lymphocytes within the epidermis, often follows shortly thereafter. Characteristic skin biopsy findings include basal cell vacuolation, mononuclear cell infiltrate throughout the epidermis, degeneration of the basal cell layer, formation of bullae, and skin ulceration.\(^{44}\) Enteric or colonic invasion by donor lymphocytes will often result in diarrhea. Hepatic disease is often also noted at later stages with increases in levels of LDH, transaminases, and bilirubin. Over time, pancytopenia ensues as a prelude to death. Cytotoxic donor lymphocytes take time to engraft and to become stimulated; hence, the onset of symptoms occurs between 3 and 30 days after transfusion (8-10 days is typical).\(^{44}\) Thus, TA-GVHD is typically a delayed-onset reaction.

**Treatment and Prevention**

Mortality rates from TA-GVHD have been observed to be between 90% and 100%, with death usually expected 3 to 4 weeks after transfusion for adults (and after 1-2 months for newborns).\(^{44}\) Therefore, prevention is the most effective mode of management. Appropriate use of irradiation can help eliminate the likelihood of TA-GVHD.\(^{48}\) Subgroups identified as being at particular risk (Table 3) should receive irradiated cellular blood products, namely, RBCs, PLTs, and granulocytes. Of note, TA-GVHD is not associated with human immunodeficiency virus (HIV) infection.\(^{45}\)
or AIDS. Irradiation is also not necessary for patients with solid tumors or for those with other hematologic deficiencies.\textsuperscript{46} Finally, two reports have indicated that leukocyte reduction and pathogen inactivation technologies may help lower the risk for TA-GVHD; however, it remains unclear whether these treatments completely incapacitate donor lymphocytes. Thus, at present, irradiation should be considered the only reliable means to prevent TA-GVHD.

Table 3. Indications for Irradiation of Cellular Blood Products

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>When to Irradiate</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Directed donor transfusions from blood relatives</td>
<td>Always</td>
<td>Can evade host cellular immune defense</td>
</tr>
<tr>
<td>HLA-matched transfusion\textsuperscript{a}</td>
<td>Always</td>
<td>Can evade host cellular immune defense</td>
</tr>
<tr>
<td>Granulocyte transfusions</td>
<td>Always</td>
<td>Immunocompromise and high lymphocyte dose\textsuperscript{a}</td>
</tr>
<tr>
<td>Intrauterine transfusions</td>
<td>Always</td>
<td>Host defenses low</td>
</tr>
<tr>
<td>Exchange transfusions in newborns</td>
<td>Always</td>
<td>Host defenses low and large lymphocyte load</td>
</tr>
<tr>
<td>Congenital cellular immunodeficiency\textsuperscript{b}</td>
<td>Always</td>
<td>Immune defect</td>
</tr>
<tr>
<td>Bone marrow and stem cell transplant patients</td>
<td>Per clinical decision made from 14 d before to 3-6 mo or an indefinite period after</td>
<td>Persistent immune defect</td>
</tr>
<tr>
<td>Hodgkin disease</td>
<td>Always</td>
<td>Some immune defect but lower risk than in Hodgkin disease</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>Per clinical decision, usually yes</td>
<td>Host defenses low</td>
</tr>
<tr>
<td>Purine analog medication recipient</td>
<td>During therapy</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Eg, for idiopathic thrombocytopenia purpura.  
\textsuperscript{b}No irradiation is necessary for HIV, solid tumors, or other heme deficiencies.  
\textsuperscript{c}Eg, severe combined immune deficiency, Wiskott-Aldrich syndrome, DiGeorge syndrome, and ataxia-telangiectasia.

### Mild-to-Moderate Complications of Transfusion

Mild-to-moderate transfusion reactions are those with short-lived symptoms not typically associated with mortality. These clinically benign reactions are commonly encountered. Hence, detailed knowledge of the pathogenesis, diagnosis, and treatment of these reac-

Table 4. Summary of Diagnostic Findings and Management Strategy for Mild Transfusion Reactions

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Symptoms</th>
<th>Timing</th>
<th>Laboratory Findings</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>FNHTR</td>
<td>Fever (ie, &gt;1°C rise)\textsuperscript{a}</td>
<td>DTx</td>
<td>DAT results: NEG</td>
<td>Cease Tx if ongoing Antipyretics</td>
</tr>
<tr>
<td></td>
<td>Rigor/chills</td>
<td>As long as 1-2 h ATx</td>
<td>If necessary (results):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild dyspnea</td>
<td></td>
<td>*Gram stain: NEG</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*Culture: NEG</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>*CBC: unchanged</td>
<td></td>
</tr>
<tr>
<td>Mild allergic reaction</td>
<td>Urticaria</td>
<td>DTx</td>
<td>DAT results: NEG</td>
<td>Cease Tx if ongoing Antihistamines</td>
</tr>
<tr>
<td>(or DMSO toxicity for HPC infusion)</td>
<td>Pruritus</td>
<td>As long as 2 h ATx</td>
<td>If necessary (results):</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flushing</td>
<td></td>
<td>*Corticosteroids</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mild wheezing</td>
<td></td>
<td>*Wash units\textsuperscript{c}</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Usually none needed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute hypotension</td>
<td>Isolated decrease in blood pressure</td>
<td>DTx</td>
<td>Usually none needed</td>
<td>Cease Tx if ongoing D/C ACE inhibitors for future transfusions</td>
</tr>
</tbody>
</table>

\textsuperscript{a}FNHTR, febrile nonhemolytic transfusion reaction; DTx, during transfusion; ATx, after transfusion; DAT, direct antiglobulin test; NEG, negative; CBC, complete blood count; DMSO, dimethylsulfoxide; HPC, hematopoietic progenitor cells; D/C, discontinue; ACE, angiotensin-converting enzyme.  
\textsuperscript{b}Fever may be absent.  
\textsuperscript{c}For severe rigor.  
\textsuperscript{d}As a last resort.
tions is an important aspect of the routine practice of transfusion medicine. The signs, symptoms, laboratory findings, and management of these reactions are summarized in Table 4.

Febrile Nonhemolytic Transfusion Reactions

Overview and Incidence

According to several reports, febrile nonhemolytic transfusion reactions (FNHTRs) are among the most common adverse events reported to blood banks. An estimated 0.2% to 1.0% of all RBC transfusions may be associated with an FNHTR, with even higher rates observed for PLT transfusions. It should be noted that many earlier studies on rates of FNHTR were performed at times when universal leukoreduction was uncommon. As discussed herein, leukoreduction decreases the frequency of FNHTRs. With growing usage of leukoreduced blood products, it is likely that rates for FNHTRs should decrease in turn. The main importance of establishing a firm diagnosis of FNHTR is to rule out more significant reactions associated with fever (Table 2).

Pathogenesis

Despite years of observational studies and in vitro experiments, the definitive mechanisms underlying FNHTRs remain elusive. Current evidence suggests that FNHTRs are likely mediated by antileukocyte antibodies present in recipient plasma and/or biologic response modifiers (BRMs) that accumulate in blood products during storage. In the first model, antileukocyte antibodies in recipients interact with residual donor white blood cells (WBCs) to induce activation and release of mediators of fever and inflammation, such as TNF-α, IL-1β, and IL-6. Some authors have argued that anti-WBC antibodies are the mechanism most likely underlying FNHTRs associated with RBC transfusion. However, FNHTRs due to PLTs have been more definitively linked with the second mechanistic model, namely, the accumulation of BRMs over time during storage. In this model, PLTs and WBCs in the component release cytokines, chemokines, and byproducts of the complement cascade during storage. On infusion, these BRMs induce a self-limited febrile response.

Diagnosis

Febrile nonhemolytic transfusion reactions are frequently defined as a 1°C (or approximately 2°F) increase in temperature above baseline during or within 1 to 2 hours of completion of a transfusion. Most FNHTRs are typically accompanied by rigor and chills; in some cases, they may be associated with mild dyspnea or tachypnea. Of interest, Heddle reports cases of atypical febrile reactions (or nonebrile reactions) in which patients experience rigor or chills without an increase in temperature. In these cases, patients may be unable to generate an adequate temperature response due to underlying conditions or pretransfusion administration of antipyretics. For pure FNHTRs, patients generally display no additional signs or symptoms.

Laboratory testing (eg, DAT, CBC) should reveal no changes compared with pretransfusion levels. Because other, more serious transfusion reactions are associated with fever (Table 2), FNHTR should be a diagnosis of exclusion. Also, because many patients undergoing transfusion are immunosuppressed or have comorbid conditions, health care professionals should also consider the possibility that the temperature increase is unrelated to transfusion and may rather be the result of an underlying or emerging infectious process.

Treatment and Prevention

As with nearly every reaction, the first step in dealing with an FNHTR is to discontinue the infusion. Although there has been some controversy regarding whether this is necessary for FNHTRs, in our opinion, complete cessation of infusion is the safest approach when confronted with a fever during transfusion. Fever is a common and nonspecific finding; because mild fevers can be observed with severe reactions such as TRALI (Table 2), continuing transfusion may be considerably risky. For many FNHTRs, increases in temperature and associated symptoms will resolve without specific treatment. However, although FNHTRs are mostly benign reactions, patients may experience uncomfortable adverse effects, including high temperatures or severe rigor. Patients experiencing such symptoms often benefit from a one-time dose of an antipyretic such as acetaminophen. Also, meperidine can be useful to counteract severe rigor and chills associated with an FNHTR.

Because the mechanistic models of FNHTRs are based on the activation of infused WBCs or the accumulation of WBC-derived BRMs, many investigators have examined the role of leukoreduction in preventing FNHTRs. Certain studies have found that prestorage leukoreduction yields a significant reduction in FNHTRs. There is some debate regarding the usefulness of pretransfusion medication with antipyretics. This practice,

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although showing no proven benefit for the prevention of FNHTRs, may be of limited use for patients with repeated reactions. Removal of the supernatant plasma of RBC and PLT products by washing or saline replacement is another option. However, due to the labor-intensive and potentially deleterious nature of these actions, washing or saline replacement should be reserved only for patients with repeated, severe reactions.

Mild Allergic Reactions

Overview and Incidence

Along with FNHTRs, mild allergic reactions are arguably the most common adverse event associated with transfusion. Although it can be difficult to define mild versus severe allergic reactions, for the purposes of this review, we use the term “mild” to refer to those adverse events associated only with pruritis, flushing, and/or urticaria. Severe allergic reactions, best characterized as those with evidence of anaphylaxis, are discussed in detail in an earlier section herein.

According to a recent large-scale study, mild allergic symptoms were reported in approximately 0.05% of total transfusion events at the investigators’ facility. Similar to FNHTRs, mild allergic reactions typically result only in fleeting discomfort to the transfusion recipient and are not usually associated with long-term morbidity.

Pathogenesis

Similar to other adverse events resulting from transfusion, there are multiple mechanisms underlying mild allergic transfusion reactions. One of the most commonly theorized models involves preformed IgE or IgG class antibodies in the recipient reacting against proteins present in the donor product. As a result of this interaction, the recipient develops a hypersensitivity response. Proteins, drugs, and even food are among the various allergens reported in association with allergic reactions. Of interest, a recipient need not form an endogenous IgG or IgE antibody to have an allergic reaction. A report was published regarding the passive transfer of such antibodies via donor plasma, which then mediate allergic responses in the recipient.

Alternatively, donor units may contain mediators of hypersensitivity reactions (e.g., histamine and bradykinins) which can directly induce a hypersensitivity response in the recipient in the absence of preformed IgE or IgG class antibodies. Based on a report in the literature, the transfer of mediators such as histamine more likely appears to be associated with a mild allergic reaction, whereas the involvement of preformed or transferred antibodies correlates with more severe reactions. Further research in this area may better elucidate whether the mechanism of an allergic reaction can better help predict its severity.

Diagnosis

Mild allergic reactions are associated with the development of urticaria, pruritus, flushing, and occasional mild wheezing during the 1 to 2 hours after transfusion. Patients may demonstrate patches of itchy, flushed skin with occasional hives. Despite these sometimes worrisome and widespread manifestations, mild allergic reactions are not associated with fever, hypotension, or cardiovascular compromise. A mild allergic reaction does not require imaging studies and is not typically associated with any abnormalities in the results of basic laboratory studies.

Treatment and Prevention

On demonstration of signs or symptoms consistent with a mild allergic reaction, blood-product infusion should be discontinued. In some cases, the cessation of a transfusion is the only treatment indicated. However, for patients with uncomfortable itching, flushing, or hives, the use of an antihistamine agent, such as diphenhydramine, may be indicated. Due to the relatively mild nature of simple allergic reactions, some facilities allow a reinitiation of transfusion with the same unit that was implicated in the reaction. Although this is acceptable, such a practice should be performed with caution; a report indicates that allergic reactions can become more severe over time.

Randomized, placebo-controlled trials have shown no reduction in allergic reactions when diphenhydramine is provided to transfusion recipients. However, patients who repeatedly demonstrate allergic symptoms and who require chronic transfusion therapy may benefit from preinfusion dosage of antihistamines. Of note, concomitant use of H2 blockers (e.g., ranitidine) may be useful in such settings to promote a more complete blockade of the histamine receptor; however, this practice has not been confirmed by clinical trials. At our institution, patients with recurrent mild-to-moderate allergic reactions are occasionally premedicated with corticosteroids. However, due to the potential side effects of corticosteroids, we recommend that this practice be restricted to patients whose conditions are refractory to
other forms of premedication therapy. Another option for prevention of allergic symptoms is the removal of the supernatant plasma of RBCs and PLTs. However, washing or saline replacement are recommended only for patients with repeated reactions whose conditions do not respond to premedication therapy.

Acute Hypotensive Reactions

Overview and Incidence
A decrease in blood pressure during transfusion is a relatively uncommon occurrence. Although hypotension may be understood as a component of sepsis, anaphylaxis, and TRALI (Table 2), the occurrence of isolated decreases in blood pressure during transfusion with a virtual absence of other signs and symptoms is best characterized as an acute hypotensive reaction (AHR).56 Overall, these reactions are relatively rare, with no compelling/clear data available on their true incidence, to our knowledge.

Pathogenesis
Much research on AHRs has focused on the possible role of bradykinins and their metabolites.57,58 These peptides have the potential to induce vasodilation and smooth muscle relaxation in vivo, with a resultant decrease in blood pressure. Studies57,58 have shown that blood products often contain coagulation factor XII and prekallikreins; on infusion to recipients, these products can lead to the increased synthesis of bradykinins. In vulnerable patients, this increased synthesis can cause acute hypotension. Moreover, the effects of bradykinin generation may be exacerbated in patients taking angiotensin-converting enzyme (ACE) inhibitor antihypertensives because ACE is a key enzyme in the degradation of bradykinin. Likewise, reports59,60 have been published of AHRs occurring in patients taking ACE inhibitors.

Diagnosis
Acute hypotensive reactions typically occur with significant, isolated decreases in systolic and diastolic blood pressure.56,59,60 Certain reported cases59,60 have also included associated flushing and mild dyspnea. Otherwise, patients are expected to lack symptoms such as fever, chest pain, flank pain, and nausea. The results of laboratory and imaging studies are typically the same as the baseline values. Currently, no helpful acute-care tests are available to aid in the diagnosis of AHRs; as a result, AHR remains a diagnosis of exclusion. Therefore, it is critical to rule out other, more serious adverse events of transfusion also associated with hypotension (Table 2).

Treatment and Prevention
Most AHRs will resolve quickly after cessation of transfusion without the need for any specific treatment.60 In some cases of severe or sustained decreases of blood pressure, fluid boluses of normal saline may be required. The use of pressors is highly unusual in the setting of hypotensive reactions but may be necessary for those patients whose conditions are refractory to other forms of intervention. From a preventative standpoint, because of the well-established association between ACE inhibitors and hypotensive reactions,59,60 patients taking these medications who demonstrate episodes of hypotension during transfusion may benefit from a switch to another antihypertensive agent, particularly if they are expected to require ongoing transfusion support.

Reporting of Transfusion Reactions
The evaluation of a transfusion reaction represents an excellent opportunity for a clinical consultation, from the laboratory medicine or blood-bank standpoint. Establishing a viable and useful means of consultation regarding transfusion reactions raises the visibility of the blood bank as a source of clinical service and, ultimately, can improve transfusion safety. Moreover, few physicians or health care providers have extensive experience in the evaluation or management of transfusion reactions. The input of a physician experienced in transfusion medicine can make a meaningful difference in the treatment and prevention of acute reactions.

At our facility, we have adopted a consultative approach to the evaluation of transfusion reactions. On notification of a reaction, blood-bank staff contacts laboratory residents and/or fellows covering the service, who are trained to immediately perform an investigation into the circumstances of the reaction. Their procedures include interviewing the patient, notating vital signs, collecting other data, and presenting the case to an on-call attending physician. After this initial investigation, the clinical team is informed of the findings; treatment and management recommendations are made.

Subsequently, a formal Transfusion Reaction Evaluation note is placed in the electronic medical record within 24
hours of the initial call. This note is typically written by the trainee using data collected from his or her investigation; it is edited by the attending physician.

The presence of a formal note in the patient’s medical record can serve many purposes. First and foremost, it can provide detailed guidance on the management of a reported reaction. Often, information provided via telephone may not be effectively communicated, nor is it always passed down accurately among shifts. Hence, important details regarding patient management after a reaction could be lost without appropriate documentation. Also, a Transfusion Reaction Evaluation note is available for review in the future. This feature, particularly for electronic records, brings the history of reactions to the attention of any other health care providers and may allow more readily for preventative measures to be performed before the onset of a reaction.

Summary

Transfusion reactions remain a significant risk associated with blood-product administration. From severe, life-threatening reactions to benign side effects, patients are exposed to a number of hazards when receiving blood products. However, with knowledge of these reactions, blood banks and transfusion services are uniquely positioned to provide guidance regarding their diagnosis, treatment, and prevention. LM

Acknowledgements

This material results from investigation supported with resources and the use of facilities at the VA Connecticut Healthcare System, West Haven, Connecticut. Also, the writing and publication were made possible in part by Clinical and Translational Science Awards grant UL1 RR024139 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the NCRR or the NIH.

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