Risks of Transfusion

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Abstract: Each year, more than 4 million patients receive a blood transfusion in the United States to control symptoms associated with anemia, coagulopathy, thrombocytopenia, or some combination thereof. In each of these cases, the physician and the patient must weigh the potential benefits of the transfusion along with the associated risks. To assess accurately the risk:benefit ratio and to discuss this with the patient, the physician must be familiar with the range of adverse transfusion outcomes and the current estimates of their frequency. Most important, during the past decade the risk profile of transfusion has changed significantly. Transfusion-transmitted disease, although still a rare outcome of transfusion, is no longer an overriding concern in transfusion safety considerations; however, risks such as hemolysis, transfusion-related lung injury, and anaphylaxis continue to represent significant concerns and are relatively more common than the transmission of infectious diseases after transfusion. Against this background, the development of a national hemovigilance system, designed to evaluate more accurately transfusion adverse outcomes in the United States, will require greater precision and reliability in the assessment of adverse transfusion outcomes by clinicians if the proposed benefits of this system are to be realized.

Key Words: transfusion, transfusion reactions, transfusion-transmitted disease

Adverse outcomes of transfusion can be categorized as either transfusion-transmitted infections or noninfectious transfusion reactions. This review provides a brief survey of these potential transfusion-related adverse outcomes and a current estimate of the frequency of each adverse outcome. In addition, the various transfusion reactions listed in the National Hemovigilance Network documents are reviewed and the diagnostic features of each are provided.

The safety of transfusing blood is a concern for both physicians and patients; however, this concern is often mis-placed. For example, concern remains about the risk of transfusion-transmitted infections (TTI), even though the actual risk is now small. Conversely, the noninfectious risks of transfusion, although uncommon, often are underestimated. Nevertheless, it is incumbent upon the physician who is considering transfusion therapy for a patient to accurately understand both the benefits and potential adverse outcomes of transfusion.

A national hemovigilance system was implemented in the United States in 2010, making the accurate recognition and reporting of adverse transfusion reactions more important. This system is a joint venture between AABB (formerly the American Association of Blood Banks) and the Centers for Disease Control and Prevention and is similar to systems in a number of other countries. The intent of the program is to aggregate data on transfusion reactions in a large national database, thereby enhancing the ability to assess the risks of transfusion, identify weaknesses in the transfusion chain, and monitor the effect of new transfusion safety initiatives. The purpose of this review is twofold: it provides an overview of the risks of transfusion, including current risk estimates and reviews the diagnostic features of adverse transfusion reactions as defined by the National Hemovigilance Network.

TTI

Blood centers use a variety of techniques to minimize the risks of TTI. One technique, the blood donor interview, has two purposes. First, it serves as the primary tool to reduce the risk of TTI when no testing methodology is available. Two examples are malaria and babesiosis. Malaria is a relatively

Key Points

- The risk of transfusion-transmitted infections (TTIs) has decreased dramatically during the past 2 decades, with the current risks of HIV and hepatitis C virus transmission estimated to be approximately 1:2 million transfusions.
- The reduction in the risk of TTI has resulted largely from improved donor history screening and the development of new and more sensitive infectious disease screening tests.
- Transfusion-related acute lung injury is now the most commonly reported cause of transfusion-related death.
- Acute hemolytic transfusion reactions resulting from ABO incompatibility continue to be a significant but largely avoidable risk of adverse transfusion reaction.
Later in 1994, a test for HIV p24 antigen was added, which was in general able to detect donors infected with HIV within 15 to 16 days of infection. Finally, in 1999, nucleic acid amplification testing was introduced. This assay, as configured for blood centers, is highly sensitive and specific, with 95% detection limits of 30 to 60 viral copies per milliliter for HIV-1. The use of this technique enhanced the overall sensitivity of HIV screening by reducing the window to 12 to 13 days. The progressive reduction in the window for HIV led to a corresponding reduction in the estimated risk of transfusion-associated HIV from 1:225,000 in 1992 to 1:2.3 million in 2005. Available nucleic acid amplification testing is intended for the detection of HIV-1; HIV-2 is detected by serologic (enzyme immunoassay) HIV tests used in blood centers. Testing for both hepatitis B and C viruses has followed a generally similar pattern.

The overall efficacy of the blood-screening measures implemented during the last 20 years is apparent in the reduced incidence of posttransfusion HIV and hepatitis B and C, as demonstrated in Table 2. It is important to note, however, that in spite of success in reducing the risk of TTI through donor screening and testing, the appearance of “emerging infections” are a small but continuing threat to transfusion safety. Recently, Stramer and colleagues reviewed and prioritized the various infectious agents that can threaten the safety of transfusion. The agents listed as being in the higher categories of concern are variant Creutzfeld-Jacob disease, dengue viruses, Babesia spp, Plasmodium spp, Chikungunya virus, St Louis encephalitis virus, and Leishmania spp.

### Table 1. Infectious disease screening: laboratory tests

<table>
<thead>
<tr>
<th>Decade</th>
<th>Date</th>
<th>Test added</th>
<th>Test type</th>
<th>Test discontinued</th>
</tr>
</thead>
<tbody>
<tr>
<td>1940</td>
<td>1947</td>
<td>Syphilis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1950</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1960</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1970</td>
<td>1971</td>
<td>HBsAg</td>
<td>RIA/EIA</td>
<td></td>
</tr>
<tr>
<td>1980</td>
<td>1985</td>
<td>Anti-HIV</td>
<td>EIA</td>
<td></td>
</tr>
<tr>
<td>1987</td>
<td></td>
<td>ALT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1988</td>
<td></td>
<td>Anti-HBcore</td>
<td>EIA</td>
<td></td>
</tr>
<tr>
<td>1989</td>
<td></td>
<td>Anti-HTLV</td>
<td>EIA</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>1990</td>
<td>Anti-HCV</td>
<td>EIA</td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>1994</td>
<td>HIV-p24</td>
<td>EIA</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>2000</td>
<td>NAT-HIV/HCV</td>
<td>NAT ALT; p24</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>2003</td>
<td>NAT-WNV</td>
<td>NAT</td>
<td></td>
</tr>
<tr>
<td>2008</td>
<td>2008</td>
<td>Chagas</td>
<td>EIA</td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>2010</td>
<td>NAT-HBV</td>
<td>NAT</td>
<td></td>
</tr>
</tbody>
</table>

ALT indicates alanine aminotransferase; EIA, enzyme immunoassay; HBcore, antibody to hepatitis B core; HBsAg, hepatitis B surface antigen; HIV, hepatitis B virus; HCV, hepatitis C virus; HTLV, human T lymphotropic virus; NAT, nucleic acid test; RIA, radioimmunoassay; WNV, West Nile virus.

**Review Article**

rare TTI, with only 17 cases reported between 1990 and 2007. The present strategy requires the temporary deferral of potential blood donors who travel to or have resided in an area endemic for malaria as defined by the Centers for Disease Control and Prevention. Babesiosis presents a somewhat different challenge. Since 1979, more than 70 cases of transfusion-transmitted babesiosis have been reported in the United States, although the actual number is presumably much higher. Because babesiosis is endemic to certain parts of the United States, the only viable approach is the deferral of potential donors with a clinical history of babesiosis.

The second role of the donor interview process is to reduce the number of donations harboring infectious agents that must then be identified by laboratory testing. This reduces the potential impact of rare false-negative test results or technical errors. Although the donor interview has obvious limitations, its efficacy is supported indirectly by observations that the prevalence of infections such as HIV and hepatitis are 5 to 10 times lower among blood donors as compared with the general population.

The laboratory tests used to screen for TTI are listed in Table 1. Coincident with the increased number of tests has been the use of progressively more sensitive tests. Because much of the estimated residual risk of TTI results from the time between infection of the donor and seroconversion, efforts have been ongoing to reduce this window. The changes in HIV testing procedures provide an example.

Before 1985, the donor interview provided the only approach to reduce the risk of HIV in donated blood products. In 1985, a specific serologic test for antibody to HIV-1 was developed, which by 1992 was reported to result in a window of approximately 45 days. Subsequent improvements in the test by 1994 resulted in a reduction of the window to approximately 22 days. Later in 1994, a test for HIV p24 antigen was added, which was in general able to detect donors infected with HIV within 15 to 16 days of infection. Finally, in 1999, nucleic acid amplification testing was introduced. This assay, as configured for blood centers, is highly sensitive and specific, with 95% detection limits of 30 to 60 viral copies per milliliter for HIV-1. The use of this technique enhanced the overall sensitivity of HIV screening by reducing the window to 12 to 13 days. The progressive reduction in the window for HIV led to a corresponding reduction in the estimated risk of transfusion-associated HIV from 1:225,000 in 1992 to 1:2.3 million in 2005. Available nucleic acid amplification testing is intended for the detection of HIV-1; HIV-2 is detected by serologic (enzyme immunoassay) HIV tests used in blood centers. Testing for both hepatitis B and C viruses has followed a generally similar pattern.

The overall efficacy of the blood-screening measures implemented during the last 20 years is apparent in the reduced incidence of posttransfusion HIV and hepatitis B and C, as demonstrated in Table 2. It is important to note, however, that in spite of success in reducing the risk of TTI through donor screening and testing, the appearance of “emerging infections” are a small but continuing threat to transfusion safety. Recently, Stramer and colleagues reviewed and prioritized the various infectious agents that can threaten the safety of transfusion. The agents listed as being in the higher categories of concern are variant Creutzfeld-Jacob disease, dengue viruses, Babesia spp, Plasmodium spp, Chikungunya virus, St Louis encephalitis virus, and Leishmania spp.

### Bacterial Contamination of Blood Products

Blood components can become contaminated by bacteria in 3 ways: donor bacteremia (even transient), contamination of blood collection bags at the time of manufacture (rare), and contamination of the venipuncture site (most common). Approximately 56% of the cases in which red cell components are contaminated bacterially are caused by Yersinia enterocolitica, with Serratia spp and Pseudomonas spp also occasionally

### Table 2. Comparative risks of TTI (1992–2007)

<table>
<thead>
<tr>
<th>Infectious agent</th>
<th>1992 (Dodd10)</th>
<th>2007 (Bihl et al11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1,225,000</td>
<td>1,213,000</td>
</tr>
<tr>
<td>HCV</td>
<td>1,330,000</td>
<td>1,193,000</td>
</tr>
<tr>
<td>HBV</td>
<td>1,200,000</td>
<td>1,277,000</td>
</tr>
<tr>
<td>HTLV</td>
<td>1,500,000</td>
<td>1,299,000</td>
</tr>
<tr>
<td>WNV</td>
<td>N/D</td>
<td>1,550,000</td>
</tr>
</tbody>
</table>

TTI indicates transfusion-transmitted infection; all other abbreviations, see Table 1.
identified. Platelet product contamination is caused most commonly by normal skin flora, with *Staphylococcus aureus* being the most frequent; other identified organisms include coagulase-negative *Staphylococci*, Gram-positive and Gram-negative diphtheroids, and *Streptococci*. Bacterial contamination of red cells has been reported to occur in approximately 1:38,000 units, whereas for platelets the rate has been estimated to be as high as 1:2000 to 1:3000. Septic reactions arising from the transfusion of these products is much less frequent, occurring in approximately 1:250,000 red cells transfused and 1:25,000 platelets transfused. Several factors undoubtedly account for this discrepancy, such as the bacterial load of the product at the time of transfusion, the virulence of the organism, and the clinical condition of the patient. The more common association of platelet products with both bacterial contamination and septic reactions led to the requirement for some type of bacterial screening procedure for platelet products. In 2007, Eder and coworkers reported the impact of implementation of a bacterial screening test for apheresis (single donor) platelet products. They noted that in screening 1,004,206 apheresis platelets, 186 had confirmed positive bacterial culture results (1:5399). All but one of these products was interdicted before transfusion. Nevertheless, during the same period, 20 septic transfusion reactions in which bacterially screened platelet products were transfused were reported. In comparison with previous time periods, when no bacterial screening test was in place, the authors suggested that bacterial testing reduced the risk of septic reaction by approximately 50%.  

**Noninfectious Complications**  

Noninfectious complications continue to represent uncommon but often serious risks of transfusion. In fact, with the dramatically decreasing risks of TTI, noninfectious risks, which have changed little in incidence during the last 2 to 3 decades, are now much more frequently associated with adverse patient outcomes.

**Acute Transfusion Reactions**  

**Allergic**

Simple allergic transfusion reactions are, in general, the result of type 1 hypersensitivity reactions, in which preformed immunoglobulin E (IgE) antibody reacts with an allergen (most often a plasma protein in the transfused product) causing the activation of mast cells. The signs and symptoms of these reactions (Table 3) have their onset typically after only a few milliliters of product have been infused. These patients often respond to the administration of antihistamines.

Anaphylactic transfusion reactions occur most often in patients with severe IgA deficiency (<0.05 mg/dL) who develop an IgG anti-IgA antibody. Occasionally, IgG antibodies can be formed against specific allotypes of IgA, causing severe anaphylactic reactions in patients with normal total IgA levels. Even more rarely, deficiencies of other plasma constituents such as haptoglobin have been associated with anaphylactic reactions. Anaphylactic reactions are differentiated from simple allergic reactions by their more systemic and severe manifestation (Table 3). Patients who develop anaphylactic reactions during a blood transfusion should be screened for the presence of anti-IgA; however, it should be noted that the majority of anaphylactic transfusion reactions has no detectable cause. Patients who have documented anaphylactic reactions caused by IgA deficiency should receive saline-washed red cells (plasma removed) or plasma/platelets collected from IgA-deficient blood donors.

**Hemolytic**

Acute hemolytic transfusion reactions are caused most frequently by the inadvertent transfusion of red cells that are incompatible with antibodies present in a patient. A review of transfusion-related fatalities reported to the Food and Drug Administration between 1976 and 1985 showed that approximately 43% resulted from errors at the time of phlebotomy or blood administration, which led to the administration of ABO-incompatible blood. A more recent report of transfusion errors in New York State indicated that 1:19,000 red cell transfusions were erroneously administered and 51% of those errors occurred outside the blood bank. The characteristic symptoms of an acute hemolytic transfusion reaction are described in Table 3; however, it should be noted that symptoms can vary significantly from case to case. Linden et al reported that 47% of patients receiving incompatible red cells experienced no ill effects even after receiving a full unit of incompatible red cells, 41% experienced many of the typical symptoms described in Table 3, and approximately 2% died as a result of transfusion. This variability is dependent upon a number of factors such as the volume of incompatible blood transfused, the rate of transfusion, and the nature of the antibody involved and whether it can efficiently activate complement and cause intravascular hemolysis.
# Table 3. Acute transfusion reactions identified by the National Hemovigilance Network

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Allergic: Simple allergic: type I hypersensitivity to plasma allergen</th>
<th>Anaphylactic: usually IgG anti-IgA in IgA-deficient patient</th>
<th>Hemolytic: Red cell antigens incompatible with patient plasma antibodies</th>
<th>Hypotensive: Multifactorial; mediated through bradykinin</th>
<th>Hypotensive: Red cell antigens incompatible with patient plasma antibodies</th>
<th>Febrile: Pysogenic cytokines or other inflammatory mediators</th>
<th>TRALI: Leukocyte antibodies in donor that activate patient neutrophils causing endothelial damage</th>
<th>TACO: Rapid infusion of excess volume precipitating congestive failure</th>
<th>TXF-associated dyspnea: Uncertain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Simple allergic: 1:100–1:300</td>
<td>Anaphylactic: 1:20,000–1:50,000</td>
<td>ABO: 1:6000–1:20,000</td>
<td>Dependent on clinical situation</td>
<td>1:100–1:1000</td>
<td>1:5000–1:190,000</td>
<td>&lt;1:100</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Signs/Symptoms</td>
<td>Maculopapular rash</td>
<td>Urticaria</td>
<td>Fever</td>
<td>Hypotension</td>
<td>Hypotension</td>
<td>Occurs within 4 h of TXF and either Fever ≥C from pre-TXF or chill/rigor are present</td>
<td>Occurs within 4 h of TXF and either Fever ≥C from pre-TXF or chill/rigor are present</td>
<td>New onset or exacerbation of ≥C of the following within 6 h of TXF Acute respiratory distress Evidence of positive fluid balance ↑BNP X-ray evidence of pulmonary edema Evidence of left ventricular heart failure ↑CVP Acute respiratory distress within 24 h of TXF and TRALI TACO and anaphylaxis ruled out</td>
<td></td>
</tr>
<tr>
<td>Laboratory</td>
<td>Simple allergic: none IgA; quantitative</td>
<td>Anaphylactic: screen patient for anti-IgA</td>
<td>Clerical check</td>
<td>Rule out hemolysis</td>
<td>Rule out hemolysis</td>
<td>Rule out hemolysis (DAT; visual inspection for hemoglobin)</td>
<td>Rule out hemolysis (DAT; visual inspection for hemoglobin)</td>
<td>Chest x-ray</td>
<td></td>
</tr>
</tbody>
</table>

*Signs and symptoms listed for each reaction are those included in the hemovigilance documents. BP indicates blood pressure; CVP, central venous pressure; DAT, direct antiglobulin test (Coombs test); DIC, disseminated intravascular coagulation; Ig, immunoglobulin; TACO, transfusion-associated circulatory overload; TRALI, transfusion-related acute lung injury; TXF, transfusion.*
enzyme inhibitors in the patient, and genetic predisposition such as defects in the metabolism of BK in recipients.23,24

Febrile, Nonhemolytic

Febrile, nonhemolytic transfusion reactions (FNHTR) are believed to be caused by either infused leukocyte antigens25 that stimulate in vivo generation of cytokines or the infusion of pyrogenic cytokines or other inflammatory response mediators26 that accumulate in stored cellular blood products.27 Because fever is an early manifestation of a number of serious transfusion reactions (hemolytic reactions, TRALI, and bacterial contamination), an FNHTR requires a thorough investigation and elimination of other causes of fever. Several studies have demonstrated that leukoreduction of cellular blood products results in a significant reduction in FNHTR. Yazer and coworkers reported that before the institution of prestorage leukoreduction, FNHTR occurred in 0.33% of red cell transfusions and 0.45% of platelet transfusions. After leukoreduction, the incidence of FNHTR was reduced to 0.19% after red cell transfusions and 0.11% after platelet transfusions.28

TRALI

In 2004, an international consensus conference developed a case definition that attempted to make the recognition of TRALI more reliable and consistent.29 The 5 elements of that definition include acute onset of respiratory distress during or within 6 hours of transfusion, severe hypoxemia with O2 saturations <90% on room air, chest x-ray showing bilateral pulmonary infiltrates, exclusion of circulatory overload, and no preexisting acute lung injury (eg, acute respiratory distress syndrome). There are two hypotheses concerning the etiology of TRALI.30 The first suggests that pulmonary endothelial damage is caused by the transfusion of donor-derived human leukocyte antigen (HLA) class I or class II antibodies (or granulocyte-specific antibodies). These antibodies activate a patient’s antigen-positive neutrophils in the pulmonary capillaries, ultimately resulting in endothelial damage. Because antibodies cannot be demonstrated in many cases of TRALI,31 however, a second hypothesis, often referred to as the “two-hit model,” has been suggested. This model suggests that certain clinical events such as surgery, trauma, or severe infection result in the activation of the pulmonary endothelium, causing the release of cytokines and an increase in endothelial membrane surface adhesion molecules. The second hit would occur with the transfusion of biologically active lipids and cytokines in the transfused component, again resulting in endothelial damage. TRALI is the most common cause of transfusion-related fatality reported to the Food and Drug Administration, with 127 fatalities reported between 2005 and 2009 (48% of all reported fatalities).32 Strategies to minimize the risk of TRALI have focused on reducing exposure of transfusion recipients to plasma products that are likely to carry HLA or granulocyte antibodies. Because women who have been pregnant are more likely to carry these antibodies,33 many blood centers collect plasma for transfusion exclusively from male donors. Evidence from both the United Kingdom and the American Red Cross suggests that this approach has resulted in a decrease in the number of patients experiencing symptoms that can be attributed to TRALI.34,35

Transfusion-Associated Circulatory Overload

For more than 60 years, transfusion-associated circulatory overload (TACO) has been recognized as a risk of transfusion.36 Although patients with TRALI and TACO present with pulmonary edema and respiratory distress, these entities can be distinguished in general on the basis of a number of symptoms (Table 4). Recently, a cardiac marker, B-natriuretic peptide, has been suggested as a tool in differentiating these 2 entities.37 In cases of congestive failure (TACO), B-natriuretic peptide levels are elevated with a posttransfusion-to-pretransfusion ratio ≥1.5; however, more recent studies38 have emphasized the limited diagnostic value of this test because of the large overlap between values seen in patients with TACO and patients with TRALI.

Patients occasionally experience respiratory distress in association with transfusion that cannot be attributed to either TRALI or TACO. Bux and Sachs have suggested that these ill-defined reactions be assigned to a category known as transfusion-associated dyspnea.39

Delayed Transfusion Reactions

Delayed hemolytic. Approximately 2.6% of the general population carry antibodies to red cell antigens other than...
anti-A or anti-B, with rates as high as 5% to 47% in patients who receive transfusions frequently. These antibodies, which are stimulated most commonly by previous transfusion or pregnancy, often are undetectable at the time of pretransfusion testing. When a red cell unit that carries an antigen specific for a previously stimulated antibody is transfused, the antibody may redevelop quickly (anamnestic response), which can lead to hemolysis of the transfused red cells. The clinical manifestations of these reactions (Table 5) have their onset in general 7 to 21 days after the transfusion. Diagnosis of a delayed hemolytic transfusion reaction requires the identification of a red cell antibody that was not identifiable before transfusion. These antibodies are usually IgG, with anti-Kidd and anti-Duffy being the most commonly identified. Included within this general category are patients in whom there is no clinical evidence of hemolysis but in whom a red cell antibody is identified that was not detectable at the time of pretransfusion testing. These cases are referred to as delayed serologic transfusion reactions.

Posttransfusion purpura. Posttransfusion purpura is an uncommon but potentially serious complication of blood transfusion that is characterized by severe, self-limited thrombocytopenia (≤10,000/µL) developing 5 to 10 days after the transfusion of red cells, plasma, or platelets. Posttransfusion purpura is seen only in adults who have received previous transfusions or have been pregnant. It is caused by the development of an antibody to platelet-specific antigens (usually human platelet antigen-1a). The mechanism by which autologous platelets also are destroyed is unclear, but it may result from the formation of immune complexes of platelet-specific antigen and anti-platelet antibody. Thrombocytopenia is generally unresponsive to antigen-positive or antigen-negative platelet transfusions, but in general, it resolves in 2 to 4 weeks even in untreated patients.

**Transfusion-associated graft-versus-host disease.** Transfusion-associated graft-versus-host disease (TAGVHD) occurs when immunocompetent lymphocytes are infused to immunocompromised patients who are unable to destroy transfused T lymphocytes. These transfused T cells can proliferate and subsequently induce an immune response that “rejects” the host tissues. The symptoms of TAGVHD (Table 5) have their onset within 8 to 10 days of a transfusion. The time course for TAGVHD is rapid, with death occurring within 1 to 3 weeks after the initial symptoms. Because the usual therapies for GVHD mostly are ineffective, prevention of TAGVHD by gamma-irradiation of cellular blood products is critical. Most of the patients considered to be at risk for GVHD who require irradiated cellular blood products are immunocompromised. In relatively rare circumstances, however, TAGVHD can occur in immunocompetent patients. The majority of these patients have received transfusions from family members. This probably occurs in situations in which the donor is HLA homozygous and shares one haplotype with the recipient. Here, the HLA-homozygous cells would not be recognized as foreign and hence would not be destroyed by the recipient’s immune system. The transfused lymphocytes would recognize

| Delayed transfusion reactions identified by the National Hemovigilance Network |
|-----------------------------|---------------------|----------------|--------------------|
| **Etiology**                | **Delayed hemolytic** | **Delayed serologic** | **PTP**               | **TAGVHD**             |
| Antigen antibody response to red cell antigens | Antibody production to foreign antigens on transfused red cells | Patient platelet-specific antibodies (often anti-HPA-1a) | Donor lymphocytes engraft and react against host |
| Frequency                   | 1:2500-1:11,000     | 1:100            | Rare                | Rare                  |
| Signs and symptoms          | Patient may be asymptomatic or have mild symptoms including Chills/rigors, Fever, Jaundice, Hemoglobinuria, Hypotension | No clinical or laboratory evidence of hemolysis | Thrombocytopenia (<20% of pretransfusion count) that occurs 5–12 d posttransfusion | Fever Characteristic rash Hepatomegaly Diarrhea |
| Laboratory                  | + DAT               | + DAT            | + DAT               | Elevated liver Function tests (ALT, AST) Pancreatitis Skin biopsy characteristic of GVHD |
|                            | + Antibody screen  | + Antibody screen with new antibody | + Platelet antibody screen |                      |
| Bilirubinemia               |                     |                   |                     |                      |

**Table 5.** Delayed transfusion reactions identified by the National Hemovigilance Network

*Signs and symptoms listed for each reaction type are those included in the hemovigilance documents. ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; PTP, posttransfusion purpura; TAGVHD, transfusion-associated graft-versus-host disease.*
the host as foreign and induce an immune response that would cause TAGVHD.48

This review provides a survey of the most significant adverse transfusion outcomes. Clearly, transfusion still carries a slight risk of HIV, hepatitis B virus, and hepatitis C virus, and newly emerging infections will continue to be a concern. Some of the most serious reactions such as acute hemolytic transfusion reactions (especially those related to ABO incompatibility) are within the control of a healthcare facility, however. This point is made most obvious from the data of a mature hemovigilance system such as the Serious Hazards of Transfusion program in the United Kingdom, in which nearly 70% of the reported transfusion “incidents” fall into the category “Incorrect Blood Component Transfused.”49

References


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