



# A Review of Current Practice in Transfusion Therapy

Preventing and recognizing complications, including TACO, TRALI, and TRIM.

**ABSTRACT:** In the United States, roughly 4.5 million patients per year receive transfusions of various blood products. Despite the lifesaving benefits of transfusion therapy, it is an independent risk factor for infection, morbidity, and death in critically ill patients. It's important for nurses to understand the potential complications patients face when blood products are administered and to recognize that patients who have received blood products in the past remain at risk for delayed reactions, including immune compromise and infection. Here, the authors review the blood products that are commonly transfused; discuss potential complications of transfusion, as well as their associated signs and symptoms; and outline current recommendations for transfusion therapy that are widely supported in the medical and nursing literature.

**Keywords:** acute hemolytic transfusion reactions; allergic transfusion reactions; delayed hemolytic reactions; febrile nonhemolytic transfusion reactions; posttransfusion purpura; TACO, transfusion-associated circulatory overload; transfusion-associated graft versus host disease; TRALI, transfusion-related acute lung injury; TRIM, transfusion-related immunomodulation; transfusion therapy

Each year in the United States, nearly 21 million blood components are transfused to approximately 4.5 million patients.<sup>1,2</sup> Many patients will require immediate transfusion of one or more units of blood or blood products for life-threatening situations or to prevent clinical deterioration. Patients injured in motor vehicle accidents often require upward of 50 units of blood products during the initial resuscitative period, while patients sustaining acute burn injuries may require up to 20 units of platelets.<sup>2</sup> Since the supply of blood products can be rapidly depleted, all blood components must be used judiciously.

Despite the numerous benefits of transfusion, the potential for both short- and long-term adverse reactions is significant. Allogeneic transfusions (those of

human blood products) may be complicated by incompatibility of donor and recipient. Such hemolytic, or “classic,” transfusion reactions represent only one potential complication associated with transfusion therapy. Others include infection, immunosuppression, volume overload, and adverse reactions to the chemicals used in the preparation and storage of blood products.<sup>3-6</sup>

The approach to transfusion therapy has evolved over the years, based on targeted studies that examined the thresholds at which the benefits of administering whole blood or blood products outweigh the risks. When transfusion is anticipated or administered, nursing responsibilities include risk assessment and continuous monitoring for changes in patient status. Nurses need to understand current best practices



Photo © GARO / PHANIE / agefotostock

in the administration of blood products, the appropriate uses of blood products, and the potential for both immediate and delayed reactions, especially in patients who receive frequent or multiple transfusions. This article reviews the blood products that are commonly transfused, discusses the signs and symptoms associated with potential complications of transfusion, and examines current recommendations for transfusion therapy that are widely supported in the medical and nursing literature.

### WHOLE BLOOD AND BLOOD PRODUCTS

The decision to transfuse whole blood or selected blood components is based on the patient's condition and the circumstances necessitating therapy. Depending on the blood product administered, transfusion can be used to restore oxygen-carrying capacity, replenish intravascular volume, or prevent or control hemorrhage.

**Fresh whole blood** is commonly transfused in military settings and disaster or mass casualty events in which hemorrhage may be common and blood components that address trauma-related coagulopathy may be scarce. Its use in civilian care, however, fell out of favor shortly after World War II with the availability of blood components, which offer the following advantages<sup>7,8</sup>:

- safe storage for longer periods
- the ability to target specific patient needs
- a reduced risk of infection and other complications

Nevertheless, whole blood, which is collected and stored in an anticoagulant-preservative solution, is the common starting product for component isolation and modification for transfusion. After platelets are isolated from red blood cells in whole blood, the red blood cells are stored at 1°C to 6°C to extend their posttransfusion survivability.<sup>9</sup> For the purpose of transfusion therapy, there are four different components within whole blood—red blood cells, plasma, cryoprecipitate, and platelets—each of which can be modified to help achieve goal-directed outcomes while mitigating the risk of adverse effects.

**Packed red blood cells** are the most commonly transfused of all blood products.<sup>10</sup> Composed primarily of hemoglobin, packed red blood cells are used to treat acute and chronic anemias that are not caused by deficiencies in iron, vitamin B<sub>12</sub>, folic acid, or erythropoietin. Transfusion of packed red blood cells increases oxygen-carrying capacity and restores blood volume. Packed red blood cells can be prepared from whole blood through centrifugation or apheresis, in which the plasma is separated from the cellular components of blood and the unused product is

**Table 1.** Potential Complications of Blood Transfusion<sup>3, 6, 11, 18-27</sup>

Complication	Timing	Manifestations	Comments
<b>Acute transfusion reactions (within 24 hours of transfusion)</b>			
Acute hemolytic transfusion reaction	Can occur during, immediately after, or within 24 hours of transfusion	<ul style="list-style-type: none"> <li>• Increased temperature</li> <li>• Increased heart rate</li> <li>• Chills</li> <li>• Dyspnea</li> <li>• Chest or back pain</li> <li>• Abnormal bleeding or shock</li> <li>• Hemoglobinuria</li> <li>• Epistaxis</li> <li>• Oliguria or anuria</li> <li>• Disseminated intravascular coagulation</li> <li>• Pain or oozing at the IV site</li> </ul>	Follow the protocol for any acute transfusion reaction. <sup>a</sup>
Febrile nonhemolytic transfusion reaction	Usually occurs during or shortly after transfusion	Unexplained rise in temperature of 1°C (1.8°F)	A relatively common reaction following transfusion of packed red blood cells or platelets. Can be treated with antipyretics.
Allergic and anaphylactic reaction	Occurs within 4 hours of transfusion	Ranges from mild urticaria or wheezing responsive to antihistamines to severe systemic reactions, including: <ul style="list-style-type: none"> <li>• hypotension</li> <li>• tachycardia</li> <li>• nausea</li> <li>• vomiting</li> <li>• abdominal pain</li> <li>• severe dyspnea</li> <li>• pulmonary or laryngeal edema</li> <li>• bronchospasm</li> </ul>	Occurs most often with the transfusion of plasma-containing components, but can occur with the transfusion of any blood product. Treatment includes supportive care with antihistamines, epinephrine, and, if indicated, blood pressure and ventilatory support.
TACO	Typically occurs within 6 hours of blood product administration	New onset or exacerbation of at least three of the following: <ul style="list-style-type: none"> <li>• acute respiratory distress</li> <li>• elevated brain natriuretic peptide</li> <li>• elevated central venous pressure</li> <li>• positive fluid balance</li> <li>• clinical evidence of left-sided heart failure</li> <li>• radiographic evidence of pulmonary edema</li> </ul>	The deadliest and one of the two most common adverse reactions to transfusion. Requires close hemodynamic monitoring and ongoing physical assessment. May be treated with supplemental oxygen therapy, nitrates, and noninvasive positive pressure ventilation. At-risk patients should receive blood product at a slow infusion rate.
TRALI	Typically occurs within 6 hours of blood product administration	Acute onset of <ul style="list-style-type: none"> <li>• respiratory distress</li> <li>• hypoxemia</li> <li>• noncardiogenic pulmonary edema</li> </ul> May be accompanied by <ul style="list-style-type: none"> <li>• fever</li> <li>• tachycardia</li> <li>• hypothermia</li> <li>• blood pressure instability</li> </ul>	Usually self-limiting, with an overall mortality rate of 5% to 10%. Treatment includes aggressive respiratory support, mechanical ventilation, applying restrictive tidal volume and possibly diuretics, fluid restriction, and extracorporeal membrane oxygenation.
<b>Delayed transfusion reactions (days to years following transfusion)</b>			
Delayed hemolytic reaction	Can occur days to weeks after transfusion	<ul style="list-style-type: none"> <li>• Low-grade fever</li> <li>• Mild jaundice</li> <li>• Low hemoglobin levels</li> <li>• Elevated lactate dehydrogenase</li> </ul>	Direct antiglobulin testing may be positive. In the absence of brisk hemolysis, no treatment is required.

**Table 1.** Continued

TA-GVHD	Occurs within 2 weeks of transfusion	Characterized by <ul style="list-style-type: none"> <li>• fever</li> <li>• rash</li> <li>• diarrhea</li> </ul> May also present as <ul style="list-style-type: none"> <li>• hepatitis</li> <li>• marrow aplasia</li> </ul>	Seen primarily in immunocompromised patients receiving allogenic stem cell transplants. Often fatal. May be prevented by irradiating donor lymphocytes prior to transfusion.
Posttransfusion purpura	May occur 1–3 weeks after transfusion	Thrombocytopenia	Often resolves spontaneously. Patients at risk for bleeding are treated with iv immunoglobulins, plasmapheresis, or platelet transfusion.
TRIM		Characterized by immunosuppression	The CDC does not classify TRIM by specific criteria as an adverse reaction to transfusion.

CDC = Centers for Disease Control and Prevention; TACO = transfusion-associated circulatory overload; TA-GVHD = transfusion-associated graft versus host disease; TRALI = transfusion-related acute lung injury; TRIM = transfusion-related immunomodulation.

<sup>a</sup>In response to any acute transfusion reaction:

- Stop the transfusion immediately.
- Notify the ordering provider.
- Send the remaining blood component to the blood bank for analysis.
- Maintain a patent iv line with normal saline for potential emergency intervention.
- Reassess the patient every five to 15 minutes, observing for signs of coagulopathy and renal failure.

returned to the donor.<sup>11</sup> The cells are packed with additive solutions containing varying concentrations of dextrose, adenine, sodium phosphate, mannitol, sodium bicarbonate, sodium chloride, sodium citrate, or citric acid and can be prepared in ways that limit the risk of transfusion reactions.<sup>11</sup>

**Leukoreduction**, or the reduction of white blood cells contained in a unit of packed red blood cells to a threshold below  $5 \times 10^6$  in accordance with the standards of the AABB (formerly known as the American Association of Blood Banks),<sup>11</sup> is commonly used to reduce such risks as viral transmission, febrile nonhemolytic transfusion reaction, human leukocyte antigen (HLA) alloimmunization, and platelet refractoriness, especially in patients who are immunosuppressed or who require multiple transfusions.<sup>12</sup> Further investigation is required to determine the effectiveness of this strategy in reducing such adverse transfusion reactions.<sup>13</sup>

**Low-volume packed red blood cells** may be used to treat patients who have low cardiac output, such as those with heart failure. Such patients need hemoglobin but cannot tolerate excessive volume. The definition of “low-volume” transfusion varies across studies<sup>14-17</sup>; we define low volume as the reduction of total blood product volume administered.

**Fresh frozen plasma** contains albumin, multiple coagulation factors, fibrinolytic proteins, and immunoglobulin. Fresh frozen plasma contributes to volume expansion because the proteins it contains can

pull fluid from the extracellular space back into the vessels through an oncotic pressure gradient. However, it should not be transfused primarily for this purpose; rather, it is used to treat coagulation deficiencies.<sup>11</sup> Plasma contains all the coagulation factors, which is an important consideration for certain subpopulations requiring emergency care, such as patients with trauma-associated coagulopathy, massive hemorrhage, or complications from anticoagulant therapy. Plasma is frozen at a temperature of  $-18^{\circ}\text{C}$  or colder within 24 hours of collection.<sup>11</sup> It normally requires 40 minutes for thawing and pooling in the blood bank before it can be issued. Once plasma has been thawed, it must be transfused within 24 hours of preparation or discarded.

**Cryoprecipitate** is prepared from fresh frozen plasma thawed to  $1^{\circ}\text{C}$  to  $6^{\circ}\text{C}$ ; the cold-insoluble precipitate is recovered after centrifugation.<sup>11</sup> This product, which contains concentrates of factor VIII, fibrinogen, factor XIII, von Willebrand factor, and fibronectin, is used to treat fibrinogen deficiency and to control bleeding in hemophilia or other coagulation deficiencies. Cryoprecipitate is seldom used in emergency care, but may be considered for patients presenting with bleeding secondary to these deficits. Cryoprecipitate normally requires 40 minutes for thawing and pooling in the blood bank before issue and must be infused within four hours of pooling.

**Platelets** are used to replenish low platelet counts or to treat platelet dysfunction. The goal of platelet transfusion is to provide enough normally functioning



platelets to facilitate platelet aggregation and clot formation. Platelets are either derived from whole blood or prepared by apheresis and suspended in plasma. Of note, the method of preparation affects the concentration of platelets. Whereas a unit derived from whole blood contains at least  $5.5 \times 10^{10}$  platelets, a unit prepared by apheresis contains at least  $3 \times 10^{11}$ . For this reason, the therapeutic adult dose of at least  $3 \times 10^{11}$  is ordered as either one unit of apheresis platelets derived from a single donor or four to six units of pooled platelets derived from the whole blood of multiple donors (commonly called a “four pack” or a “six pack”).<sup>11</sup> Since apheresis platelets are obtained from a single donor, their use reduces the recipient’s risk of alloimmunity.

### TYPING AND COMPATIBILITY

Two classification systems are commonly used to determine compatibility between donor blood products and transfusion recipients: ABO and D antigen typing. ABO typing identifies the antigen that resides on a person’s red blood cell membranes; circulating antibodies to the opposing blood type are found in this person’s plasma. In other words, people with type A antigens on their red blood cell membranes will have type B antibodies in their plasma, which will react to a transfusion of type B red blood cells; those with type B antigens on their red blood cell membranes will have type A antibodies in their plasma, which will react to a transfusion of type A red blood cells. People with type O blood express neither A antigens nor B antigens on their red blood cells. Conversely, people with type AB blood have both A and B antigens on their red blood cell membranes but no A or B antibodies in their plasma.

The D antigen, or Rh, classification system, initially named for an erroneous association with the Rhesus monkey species, identifies an antibody response to the D antigen, which is also located on the red blood cell membrane. The D antigen triggers an aggressive immunologic response, such as the fatal hemolytic reaction that can occur in the pregnancies of an Rh-negative (D antigen–negative) mother previously exposed to a D antigen–positive fetus. Unless steps are taken to prevent Rh (D antigen) alloimmunization, such as the timely administration of Rho(D) immune globulin, D antigen–positive fetuses in subsequent pregnancies would be vulnerable to attack by maternal D antibodies.

Patients who may require transfusion therapy should have their serum typed and screened to determine ABO and D antigen classification, as well as the presence of other infectious or allergenic antibodies. The final phase of donor–recipient compatibility testing is a crossmatch in which a portion of the donor blood product is combined with a sample of the recipient’s blood. If agglutination occurs, it indicates incompatibility.

### COMPLICATIONS OF TRANSFUSION THERAPY

As with any therapy, transfusion is associated with a risk of complications (see Table 1<sup>3, 6, 11, 18-27</sup>). There are two broad categories of complications: acute and delayed. Acute transfusion reactions are defined in the Serious Hazards of Transfusion (SHOT) reporting categories as allergic or febrile transfusion reactions occurring within 24 hours of blood component transfusion.<sup>28</sup> These include acute hemolytic transfusion reactions, febrile nonhemolytic transfusion reactions, allergic and anaphylactic reactions, transfusion-associated circulatory overload (TACO), and transfusion-related acute lung injury (TRALI). Delayed transfusion reactions of varying severity may occur days to years after transfusion. These include delayed hemolytic reactions, transfusion-associated graft versus host disease (TA-GVHD), posttransfusion purpura, and transfusion-related immunomodulation (TRIM).<sup>19, 29, 30</sup> Nurses need to be able to identify patients at risk for acute as well as delayed complications, thereby improving surveillance along the entire trajectory of care.

### ACUTE TRANSFUSION REACTIONS

**Acute hemolytic transfusion reactions** are caused by incompatibility of antigens on transfused red blood cells and antibodies in the recipient’s plasma.<sup>11</sup> The identification errors responsible for such reactions may occur during crossmatching or during pretransfusion identification of the patient and the product. The reaction may be signaled by a rise in temperature and heart rate, chills, dyspnea, chest or back pain, and abnormal bleeding or shock.<sup>11</sup>

In response to any acute transfusion reaction, nurses need to take the following immediate actions:

- Stop the transfusion.
- Notify the ordering provider.
- Send the remaining blood component to the blood bank for analysis.
- Maintain a patent IV line with normal saline for potential emergency intervention.
- Reassess the patient every five to 15 minutes, observing for signs of coagulopathy and renal failure.

Although hemolytic reactions can be devastating, uncrossmatched blood, including Rh-positive (D antigen–positive) blood, may be required in the setting of uncontrolled hemorrhage, when resources are depleted. In 2008, Murthi and colleagues examined the outcomes of patients treated in their trauma receiving unit with transfusions of uncrossmatched group O red cells for uncontrolled hemorrhage.<sup>31</sup> The authors found that the benefits of transfusion often outweighed the risks of Rh incompatibility.

**Febrile nonhemolytic transfusion reactions** are among the more common reactions to the transfusion of packed red blood cells or platelets,<sup>23, 24</sup> and manifest as an unexplained 1°C (1.8°F) rise in temperature

during or shortly after transfusion.<sup>25</sup> These generally mild reactions are thought to be caused by a cytokine response to antibodies directed against white blood cells in the product<sup>19</sup> or through the actions of cytokines present in the product.<sup>25</sup> Antipyretics can be used to treat symptoms of febrile nonhemolytic reactions.<sup>19</sup> It is important for nursing assessments to reflect any findings that suggest the patient's response is caused by an infection.

**Allergic and anaphylactic reactions** range from mild urticaria or wheezing that responds to antihistamines to severe systemic reactions characterized by hypotension, tachycardia, nausea, vomiting, abdominal pain, severe dyspnea, pulmonary or laryngeal edema, or bronchospasm.<sup>11</sup> Severe systemic reactions occur most often with the transfusion of plasma-containing components, but can occur with the transfusion of any blood product, as even packed red blood cells contain small amounts of plasma.<sup>11</sup> Treatment includes supportive care with antihistamines, epinephrine, and, if indicated, blood pressure and ventilatory support.

In 2011, Murthi and colleagues published an update on transfusion safety in the setting of traumatic injury that addressed the practice of reconstituting blood products (packed red blood cells, plasma, and platelets) to create a "modified whole blood" that supplies the needed individual component while limiting exposure to bloodborne infectious agents.<sup>32</sup> As the science of transfusion medicine evolves, the approach to managing massive hemorrhage will remain a topic of research, and guidelines will be revised accordingly.

**TACO**, the most deadly and one of the two most common adverse reactions associated with transfusion, typically occurs within six hours of blood product administration.<sup>18,26,27</sup> Depending on patient characteristics, as well as the rate and volume of transfusion required, reported incidence ranges from less than 1% to 11%.<sup>3,26,27,33</sup> (See *Diagnostic Criteria for TACO*.<sup>20</sup>)

TACO prevention requires nurses to obtain a thorough patient history and to assess fluid volume status prior to transfusion. Patients over age 70 or under age three, those with a history of cardiogenic pulmonary edema (as indicated by an ejection fraction of less than 60% on echocardiogram or the need for daily diuretic therapy), and those with renal dysfunction should be considered at high risk. Further research is required to identify more precisely the populations at elevated risk for TACO.<sup>26</sup> Patients who require transfusion therapy and have been determined to be at risk for TACO should receive the blood product at a slower infusion rate; if possible, only one unit of blood product should be ordered at a time and diuretic therapy should be administered.<sup>3</sup> In addition to close hemodynamic monitoring and ongoing physical assessment, supplemental oxygen therapy and nitrates may be used to treat TACO; patients with

## Diagnostic Criteria for TACO<sup>20</sup>

According to the Centers for Disease Control and Prevention, diagnostic criteria for transfusion-associated circulatory overload (TACO) include new onset or exacerbation of three or more of the following findings within six hours of transfusion completion:

- acute respiratory distress
- elevated brain natriuretic peptide
- elevated central venous pressure
- positive fluid balance
- clinical evidence of left-sided heart failure (for example, crackles on chest auscultation, presence of jugular venous distension, hypotension, or decrease in ejection fraction on echocardiogram)
- radiographic evidence of pulmonary edema

respiratory fatigue may benefit from a trial of noninvasive positive pressure ventilation.<sup>6</sup> Clear communication between caregivers, especially regarding the rate at which blood products are administered and appropriate diuresis, is essential when patients are at risk for TACO. Protocols and pretransfusion checklists can reduce the risk of TACO. A protocol developed by Tseng and colleagues resulted in no cases of transfusion-associated overload, and no cases of severe hypokalemia associated with the preemptive use of loop diuretics.<sup>18</sup> TACO surveillance and early identification, combined with aggressive treatment of pulmonary edema, may prevent patient decompensation and respiratory failure. Transfusing low-volume blood products and minimizing colloid use in patients at risk is also beneficial.<sup>34</sup>

**TRALI** presents as an acute onset of respiratory distress, hypoxemia, and noncardiogenic pulmonary edema within six hours of transfusion.<sup>24</sup> (See *Diagnostic Criteria for TRALI*.<sup>20</sup>) It typically occurs when white blood cell antibodies, proinflammatory molecules, and cytokines in blood products trigger an inflammatory cascade of granulocyte activation and degranulation, causing injury to the alveolar capillary membrane.<sup>22</sup> Margination, or alignment of neutrophils against the endothelial walls of the capillaries, and the subsequent production of cytokines along the pulmonary endothelium are thought to be a major reason for increased capillary permeability, leading to acute lung injury.<sup>22,35</sup> Activation of an immune response is often caused by transfusion of donor HLA antibodies and activation of alveolar neutrophils, which elicit signs that may be confused with infection.<sup>22</sup>

Inflammatory and immune mediators may produce fever, tachycardia, hypothermia, or blood pressure instability.<sup>22</sup> As with TACO, the diagnosis of TRALI is complicated by the underlying conditions generally seen in patients requiring transfusion, many of

which may cause acute lung injury. For this reason, it's important to note trends in patient decompensation relative to the timing of the transfusion.

TRALI is usually a self-limiting process with an overall mortality rate of 5% to 10%.<sup>22</sup> Treatment for TRALI requires aggressive respiratory support, including mechanical ventilation, applying restrictive tidal volume and possibly diuretics, fluid restriction, and extracorporeal membrane oxygenation. If the patient has a history of TRALI, the following strategies may be used to prevent subsequent incidents<sup>22</sup>:

- adopting a restrictive transfusion approach
- selecting blood components based on patient risk factors and history
- transfusing fresh blood or transfusing components to reduce antibody transmission
- washing stored cellular components to remove antibodies

### DELAYED TRANSFUSION REACTIONS

**Delayed hemolytic reactions** can occur days to weeks after transfusion. Like acute hemolytic reactions, they are caused by incompatibility of antigens on transfused red blood cells and the antibodies in the recipient's plasma. Patients with such reactions may develop a low-grade fever and mild jaundice. Direct antiglobulin testing may be positive. Blood tests may reveal low hemoglobin levels and elevated lactate dehydrogenase. In the absence of brisk hemolysis, no treatment is required.<sup>19</sup>

**TA-GVHD** is seen primarily in immunocompromised patients receiving allogenic stem cell transplants. Often fatal, TA-GVHD is characterized by fever, rash, and diarrhea occurring within two weeks of transfusion, but may also present as hepatitis or marrow dysfunction. TA-GVHD may be prevented by irradiating donor lymphocytes prior to transfusion.<sup>19</sup>

**Posttransfusion purpura**, an immune response to platelet antigens that produces thrombocytopenia,

may occur one to three weeks after transfusion. In many patients, the condition resolves spontaneously. Patients at risk for bleeding are treated with iv immunoglobulins, plasmapheresis, or platelet transfusion.<sup>19</sup>

**TRIM** is a response that may develop in patients receiving multiple transfusions. At this time, TRIM is not classified by specific criteria as an adverse reaction to transfusion.<sup>20</sup> The leukocytes, soluble mediators derived from white blood cells, and HLA molecules commonly found in blood products are thought to contribute to the immunosuppression often seen following transfusion.<sup>36</sup> Given the immunomodulating effects of critical illness, it is difficult to pinpoint the direct effects of TRIM and the timeline over which it may develop. Nurses, however, need to bear in mind that transfusion therapy is an independent risk factor for infection, morbidity, and death in critically ill patients.<sup>4</sup> Accordingly, they need to carefully consider potential complications in anticipation of transfusion, during blood product administration, and when caring for patients who have received blood products in the past, understanding that such patients remain at risk for immune compromise and infection.

### COMPLICATIONS RELATED TO PRODUCT STORAGE

Metabolic derangements may occur following transfusion but are most often associated with large-volume or massive transfusion, particularly in patients with underlying liver or kidney dysfunction.<sup>26,37</sup> Several of the additive solutions used to preserve and store blood products, as well as the anticoagulant solutions used for component manufacturing, contain citrate, sodium phosphate, sodium bicarbonate, mannitol, and other constituents that can contribute to metabolic alkalosis or acidosis, hypocalcemia, hypokalemia, or hyperkalemia. When patients require transfusions, nurses must provide baseline and ongoing assessments while monitoring any transfusion reactions. When patients are transferred following transfusion, communication to the receiving team should include risk factors for acute or delayed complications.

### TRANSFUSION CONSIDERATIONS IN TRAUMA CARE

Traumatic injury is the leading cause of death among people ages five through 49.<sup>38</sup> Trauma can cause rapid blood loss, reducing both oxygen-carrying capacity and cardiac output as intravascular volume decreases. In addition to the direct loss of blood through uncontrolled hemorrhage, trauma can cause patients to develop severe coagulopathy, especially in the presence of acidosis and hypothermia.<sup>39</sup>

Traditionally, hemorrhagic shock with refractory hypotension or active bleeding was treated with a two-liter infusion of a crystalloid solution, followed by a transfusion of packed red blood cells.<sup>31</sup> The approach to transfusion therapy after traumatic injury has changed dramatically. Efforts to limit morbidity

### Diagnostic Criteria for TRALI<sup>20</sup>

The Centers for Disease Control and Prevention defines diagnostic criteria for transfusion-related acute lung injury (TRALI) as follows:

- no evidence of acute lung injury prior to transfusion
- onset of respiratory symptoms within six hours of transfusion completion
- hypoxemia as determined by one of the following findings:
  - o a ratio of partial pressure of arterial oxygen to fractional inspired oxygen of  $\leq 300$  mmHg
  - o oxygen saturation levels  $< 90\%$  on room air
  - o clinical evidence of acute lung injury
- bilateral infiltrates on chest X-ray
- no evidence of circulatory overload

## Restrictive Transfusion Strategies: The TRICC Trial

In 1999, Hébert and colleagues published the large, randomized controlled Transfusion Requirements in Critical Care (TRICC) trial.<sup>44</sup> The investigators had enrolled 838 critically ill patients whose hemoglobin levels had dropped below 9 g/dL within 72 hours of ICU admission. They randomly assigned 418 of the patients to a restrictive transfusion strategy in which hemoglobin values were maintained at concentrations of 7 to 9 g/dL, with 7 g/dL the threshold for red blood cell transfusion, and 420 of the patients to a liberal transfusion strategy in which hemoglobin values were maintained at concentrations of 10 to 12 g/dL, with 10 g/dL the threshold for red blood cell transfusion. There was no significant difference in the primary outcome of 30-day mortality rate, or in the secondary outcomes of organ failure and dysfunction scores, between patients assigned to the restrictive and liberal transfusion strategies.

The TRICC trial generated discussions on the use of a more uniform and restrictive transfusion strategy to reduce transfusion risks and to allocate transfusion resources more appropriately. Over time, several other studies that examined the use of restrictive transfusion strategies supported this approach.<sup>6,23,45</sup>

The TRICC study examined outcomes in euvoletic, hemodynamically stable patients without active hemorrhage in the critical care setting. The specificity of this study sample is in contrast to many of the patients seen in the ED who would be considered for transfusion therapy. Additional research has focused on the question of whether restrictive transfusion practices are generalizable to other patient populations, including patients with traumatic injury<sup>45-49</sup> and patients in the resuscitative phase of septic shock.<sup>50</sup> Current guidelines for the transfusion of packed red blood cells from the AABB (formerly the American Association of Blood Banks) support the use of a restrictive approach that uses a hemoglobin concentration of less than 7 g/dL in conjunction with clinical judgment as a transfusion threshold.<sup>23</sup>

and mortality focus on early recognition of shock, implementation of massive transfusion protocols, and control of factors that may worsen coagulopathy. The primary goal in resuscitation following trauma is to control and stop the source of bleeding. However, transfusion therapy is often necessary to save lives, and nurses are essential in identifying the patients who require transfusion, reducing risks of complications, and safely administering transfusions in accordance with current recommendations.

Other considerations include availability of resources. In the setting of mass casualties or in cases in which one critically injured patient taxes the institution's supply of transfusion products, consideration must be given to strategies that benefit the greatest number of patients.<sup>40-43</sup>

### THE ESSENTIAL ROLE OF NURSING IN TRANSFUSION

Nurses are essential to the success of transfusion therapy in the emergency care setting and throughout all hospital units that receive transfusion recipients. Ongoing assessment and recognition of the patient's history are important factors in determining appropriate use of blood products and in assessing patient risk of both short- and long-term complications of transfusion. Current guidelines and recommendations support the use of a more restrictive approach to replacing blood products (see *Restrictive Transfusion Strategies: The TRICC Trial*<sup>6,23,44-50</sup>), but clinical judgment is crucial in determining whether the risks associated with transfusion outweigh the patient's need for this lifesaving therapy. As with nearly all aspects of health care,

the nurse's assessment and therapeutic skills are a critical component of management. ▼

For 10 additional continuing nursing education activities on blood transfusion and transfusion reactions, go to [www.nursingcenter.com/ce](http://www.nursingcenter.com/ce).

*Margaret Carman is an associate professor at the Georgetown University School of Nursing and Health Studies, Washington, DC. Jennifer Schieferle Uhlenbrock is a clinical nurse III in the ED at the Duke University Health System, Durham, NC. Sara Marie McClintock is a critical care advanced practice provider in the neurosciences ICU at Wake Forest Baptist Medical Center, Winston-Salem, NC. Contact author: Margaret Carman, mc2300@georgetown.edu. The authors and planners have disclosed no potential conflicts of interest, financial or otherwise.*

### REFERENCES

1. American Red Cross. *Blood facts and statistics*. n.d. <http://www.redcrossblood.org/learn-about-blood/blood-facts-and-statistics>.
2. New York Blood Center. *Donate blood: blood facts*. n.d. <http://nybloodcenter.org/donate-blood/blood-facts>.
3. Lieberman L, et al. A retrospective review of patient factors, transfusion practices, and outcomes in patients with transfusion-associated circulatory overload. *Transfus Med Rev* 2013; 27(4):206-12.
4. Muszynski JA, et al. Transfusion-related immunomodulation: review of the literature and implications for pediatric critical illness. *Transfusion* 2017;57(1):195-206.
5. Pavenski K, et al. HLA alloimmunization against platelet transfusions: pathophysiology, significance, prevention and management. *Tissue Antigens* 2012;79(4):237-45.
6. Roubinian NH, Murphy EL. Transfusion-associated circulatory overload (TACO): prevention, management, and patient outcomes. *International Journal of Clinical Transfusion Medicine* 2015;3:17-28.



7. Goforth CW, et al. Fresh whole blood transfusion: military and civilian implications. *Crit Care Nurse* 2016;36(3):50-7.
8. Kauvar DS, et al. Fresh whole blood transfusion: a controversial military practice. *J Trauma* 2006;61(1):181-4.
9. Hillyer CD. Component preparation and manufacturing. In: Shaz BH, et al., editors. *Transfusion medicine and hemostasis: clinical and laboratory aspects*. 2nd ed. Amsterdam: Elsevier Science; 2013. p. 61-7.
10. Whitaker BI, et al. *The 2013 AABB blood collection, utilization, and patient blood management survey report: final*. Bethesda, MD: American Association of Blood Banks (AABB); 2015 Dec 18. <http://www.aabb.org/research/hemovigilance/bloodsurvey/Documents/2013-AABB-Blood-Survey-Report.pdf>.
11. American Association of Blood Banks (AABB). *Circular of information for the use of human blood and blood components*; 2013 Nov. <http://www.aabb.org/tm/coi/Documents/coi1017.pdf>.
12. Sharma RR, Marwaha N. Leukoreduced blood components: advantages and strategies for its implementation in developing countries. *Asian J Transfus Sci* 2010;4(1):3-8.
13. Simancas-Racines D, et al. Leukoreduction for the prevention of adverse reactions from allogeneic blood transfusion. *Cochrane Database Syst Rev* 2015(12):CD009745.
14. Baysinger K, et al. What's in the box? The effectiveness of a low-volume massive transfusion protocol. *Am Surg* 2016; 82(7):602-7.
15. Hussmann B, et al. Does increased prehospital replacement volume lead to a poor clinical course and an increased mortality? A matched-pair analysis of 1896 patients of the Trauma Registry of the German Society for Trauma Surgery who were managed by an emergency doctor at the accident site. *Injury* 2013;44(5):611-7.
16. Sisak K, et al. Acute transfusion practice during trauma resuscitation: who, when, where and why? *Injury* 2013;44(5):581-6.
17. Xi CY, et al. [Investigation and analysis of blood transfusion in 1 766 hospitalized trauma patients.] *Zhongguo Shi Yan Xue Ye Xue Za Zhi* 2015;23(1):228-33.
18. Tseng E, et al. An order set and checklist improve physician transfusion ordering practices to mitigate the risk of transfusion-associated circulatory overload. *Transfus Med* 2016;26(2): 104-10.
19. Gorgas DL, Kaide CG. Transfusion therapy: blood and blood products. In: Roberts JR, et al., editors. *Roberts and Hedges' clinical procedures in emergency medicine*. 6th ed. Philadelphia: Elsevier Saunders; 2014. p. 496-517.
20. Centers for Disease Control and Prevention, National Healthcare Safety Network. *Biovigilance component hemovigilance module surveillance protocol*. Atlanta; 2017 Jan. Protocol vol 2.4. <https://www.cdc.gov/nhsn/pdfs/biovigilance/bv-hv-protocol-current.pdf>.
21. Ellsworth B, et al. Adverse reaction case definition criteria. In: American Association of Blood Banks (AABB), editor. Bethesda, MD; 2011. [http://www.aabb.org/research/hemovigilance/Documents/diagnose\\_full.html](http://www.aabb.org/research/hemovigilance/Documents/diagnose_full.html).
22. Vlaar AP, Juffermans NP. Transfusion-related acute lung injury: a clinical review. *Lancet* 2013;382(9896):984-94.
23. Carson JL, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. *Ann Intern Med* 2012;157(1): 49-58.
24. Sahu S, et al. Adverse events related to blood transfusion. *Indian J Anaesth* 2014;58(5):543-51.
25. Paglino JC, et al. Reduction of febrile but not allergic reactions to RBCs and platelets after conversion to universal prestorage leukoreduction. *Transfusion* 2004;44(1):16-24.
26. Alam A, et al. The prevention of transfusion-associated circulatory overload. *Transfus Med Rev* 2013;27(2):105-12.
27. Hendrickson JE, et al. Incidence of transfusion reactions: a multicenter study utilizing systematic active surveillance and expert adjudication. *Transfusion* 2016;56(10):2587-96.
28. Serious Hazards of Transfusion (SHOT). *Definitions of current SHOT reporting categories and what to report*. Plymouth Grove, Manchester, UK; 2017 Apr. <https://www.shotuk.org/wp-content/uploads/SHOT-Definitions-Jan-2016-1.pdf>.
29. Vamvakas EC, Blajchman MA. Transfusion-related immunomodulation (TRIM): an update. *Blood Rev* 2007;21(6):327-48.
30. Vamvakas EC, Blajchman MA. Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. *Blood* 2009;113(15): 3406-17.
31. Murthi SB, et al. Transfusion medicine in trauma patients. *Expert Rev Hematol* 2008;1(1):99-109.
32. Murthi SB, et al. Transfusion medicine in trauma patients: an update. *Expert Rev Hematol* 2011;4(5):527-37.
33. Gajic O, et al. Pulmonary edema after transfusion: how to differentiate transfusion-associated circulatory overload from transfusion-related acute lung injury. *Crit Care Med* 2006; 34(5 Suppl):S109-S113.
34. Andrzejewski C, Jr., et al. How we view and approach transfusion-associated circulatory overload: pathogenesis, diagnosis, management, mitigation, and prevention. *Transfusion* 2013;53(12):3037-47.
35. Kim KN, et al. The usefulness of a classification and regression tree algorithm for detecting perioperative transfusion-related pulmonary complications. *Transfusion* 2015;55(11):2582-9.
36. Brand A. Immunological complications of blood transfusions. *Presse Med* 2016;45(7-8 Pt 2):e313-e324.
37. Hess JR. Massive blood transfusion. New York, NY: UpToDate, 2017. <https://www.uptodate.com/contents/massive-blood-transfusion>.
38. World Health Organization. *Injuries and violence: the facts 2014*. Geneva, Switzerland; 2014. [http://apps.who.int/iris/bitstream/10665/149798/1/9789241508018\\_eng.pdf?ua=1&ua=1&ua=1](http://apps.who.int/iris/bitstream/10665/149798/1/9789241508018_eng.pdf?ua=1&ua=1&ua=1).
39. Gando S, Hayakawa M. Pathophysiology of trauma-induced coagulopathy and management of critical bleeding requiring massive transfusion. *Semin Thromb Hemost* 2016;42(2): 155-65.
40. Doughty H, et al. Mass casualty events: blood transfusion emergency preparedness across the continuum of care. *Transfusion* 2016;56 Suppl 2:S208-S216.
41. National Advisory Committee on Blood and Blood Products. *Emergency framework for rationing of blood for massively bleeding patients during a red phase of a blood shortage*. Winnipeg, MB; 2012 Apr 14. <http://www.nacblood.ca/resources/shortages-plan/emergency-framework-final.pdf>.
42. National Advisory Committee on Blood and Blood Products. *Emergency framework for rationing of blood for massively bleeding patients during a red phase of a blood shortage—synopsis for triage team*. Winnipeg, MB; 2012 Oct 11. <http://www.nacblood.ca/resources/shortages-plan/synopsis-triage-team.pdf>.
43. Smith LB, et al. How do I allocate blood products at the end of life? An ethical analysis with suggested guidelines. *Transfusion* 2013;53(4):696-700.
44. Hébert PC, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. *N Engl J Med* 1999;340(6):409-17.
45. McIntyre L, et al. Is a restrictive transfusion strategy safe for resuscitated and critically ill trauma patients? *J Trauma* 2004; 57(3):563-8.
46. Dutton RP, et al. Hypotensive resuscitation during active hemorrhage: impact on in-hospital mortality. *J Trauma* 2002;52(6): 1141-6.
47. Dutton RP, et al. Trauma mortality in mature trauma systems: are we doing better? An analysis of trauma mortality patterns, 1997-2008. *J Trauma* 2010;69(3):620-6.
48. Handel J, Lang E. Transfusion strategy for acute upper gastrointestinal bleeding. *CJEM* 2015;17(5):582-5.
49. Michetti CP, et al. Reducing transfusions in critically injured patients using a restricted-criteria order set. *J Trauma Acute Care Surg* 2016;81(5):889-96.
50. ARISE Investigators, et al. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med* 2014;371(16): 1496-506.