The Art and Science of Infusion Nursing

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Transfusion Reaction Identification and Management at the Bedside

ABSTRACT

Blood product transfusion is one of the most common invasive procedures performed in the health care setting. In contrast to pharmaceuticals, blood is actually a liquid transplant. Transfusion complications consequently encompass complex biological processes and infectious possibilities. Changes in vital signs are regularly seen during transfusion. Knowledge of common transfusion reaction signs and symptoms enables the clinical team to differentiate a normal patient response from a life-threatening reaction. Direct care nurses responsible for this procedure play a vital role in its success. Understanding the possible complications of transfusion and how to quickly recognize reactions at the bedside helps ensure the best patient outcomes.

Key words: blood transfusion, transfusion reactions, transfusion-related acute lung injury

Transfusion can be lifesaving. Blood product transfusion is performed millions of times each year. It is one of the most common invasive procedures performed in the modern health care setting. The vast majority of transfusions are performed by the direct care nurse without incident. However, there is an important difference between administering blood and giving a drug: blood transfusion is more like a liquid transplant from 1 individual to another. Transfusion involves the introduction of active biological products (cells and proteins) from a living donor to a patient. As such, there are many complex biological possibilities that may result. The immediate and long-term consequences of a blood "transplant" are very different from those of giving a typical drug. Complications include reactions to the transfusion, as well as transmissible diseases and other long-term effects that are not well understood.

This article will emphasize complications of transfusion that may occur at the bedside, meaning reactions that are recognized during the transfusion or in the following hours. It is the responsibility of the direct care nurse to recognize an abnormal response to blood administration and to identify any potential reaction. Even in cases when a patient is transfused in the operating suite, it is often recovery room or intensive care nurses who deal with potential reactions.

To be prepared to recognize a reaction at the bedside, it is important to understand blood transfusion in context. The following will be considered:

- the place of the transfusion recipient in the blood donation process

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The authors have no conflicts of interest to disclose.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (http://journals.lww.com/journalofinfusionnursing).

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DOI: 10.1097/NAN.0000000000000097

- an overview of the various types of transfusion-related complications, allowing bedside reactions to be put into context
- the relative frequency of reactions and the time course of presentation, so the transfusionist will know what to expect when performing a blood transfusion
- normal and abnormal changes to patient signs and symptoms seen during transfusion, to illustrate how a normal response to transfusion can be differentiated from a possible transfusion reaction
- the specific etiologies of important reactions, which have an impact on the differential diagnosis and bedside treatment
- management of transfusion reactions, along with the possible role of prophylactic medication

There are many ways to approach a discussion about transfusion complications. For instance, complications may be organized according to the order of importance of morbidity and mortality. Alternatively, they may be classified by which reactions are seen most commonly, or which are associated with fever, or simply by listing them in alphabetical order. The authors have attempted to arrange the material in several different ways that might prove useful to the patient care team at the bedside. This discussion is heavily dependent on figures to help put the topic in context. It is hoped that these figures may serve as useful summaries for the reader and also valuable educational materials for the clinical staff.

Entire books have been dedicated to a discussion of transfusion reactions,[1] so some generalization was necessary to present this vast amount of material in a manner that might be useful at the bedside. The reader is encouraged to consult other references for a detailed discussion of any particular complication.[2-4] Analogous to pharmaceuticals, blood has a package insert that describes the various formulations, administration guidelines, and possible adverse reactions. It includes an extensive bibliography of educational references. The most recent blood product Circular of Information can be downloaded from the AABB Web site at http://www.aabb.org/tm/coi/Documents. Some institutions summarize local transfusion indications and reaction information on pocket cards for staff. An example of the card used at the authors' institution is included (Supplemental Digital Content 1; http://links.lww.com/JIN/A65). This can be modified for use at other institutions.

THE TRANSFUSION RECIPIENT: JUST 1 LINK IN THE BLOOD TRANSFUSION CHAIN

Transfusion is a set of processes, not just infusion of a product. An understanding of how blood is obtained from donors and prepared for patient transfusion provides important background to a discussion of transfusion reactions.

Blood is an altruistic gift given freely from 1 individual to another.[5] Donors are not paid for their blood. However, the cost of collection, testing, preparation, and administration of the product is significant. Transfusion complications add dramatically to that cost.

Figure 1 illustrates 9 key elements of the system that ensures that safe and effective blood is available when it is needed by the patient. Blood transfusion into the patient is the second-to-last step. This step includes positive identification and monitoring for reactions. Absolute confirmation of the patient identity and the correct labeling of the blood are 2 of the most important elements of the transfusion chain. The risk of an adverse event resulting from getting the wrong unit of blood is greater than the risks of all of the commonly feared transmissible infections combined.

Patient transfusion is just 1 part of an entire quality procurement system. Each of these steps involves elements intended to make the product safer. Modifications such as leukoreduction and gamma irradiation are performed to reduce the possibility of certain transfusion reactions. Screening of donors using laboratory testing, as well as intrusive donor interview questions, are attempts to limit infectious risks. The last step in the chain is relatively new. Hemovigilance is a clinical quality improvement system most familiar in the United Kingdom, but becoming more common in North America. Hemovigilance is a set of quality improvement surveillance procedures covering the whole 9-step transfusion chain. The intent is to collect and assess information on unexpected or undesirable events resulting from the use of blood products. The goal is to reduce or eliminate these in the future. Complementing hemovigilance is the current hospital movement toward integrated programs of "patient-centered blood management."[6] The clinical nursing staff is poised in an ideal position to provide leadership in these areas.

THERE ARE MANY POSSIBLE COMPLICATIONS OF TRANSFUSION

The shadow cast by the AIDS crisis of the 1980s still taints the public understanding of blood transfusion. Remarkably, HIV and similar infectious risks are now very rare complications of blood transfusion in developed countries. Figure 2 outlines the acute complications of transfusion most commonly seen at the bedside. The importance of hypothermia, volume overload, and metabolic abnormalities should not be overlooked, even though these may not be the first things to come to mind in a discussion of transfusion reactions.

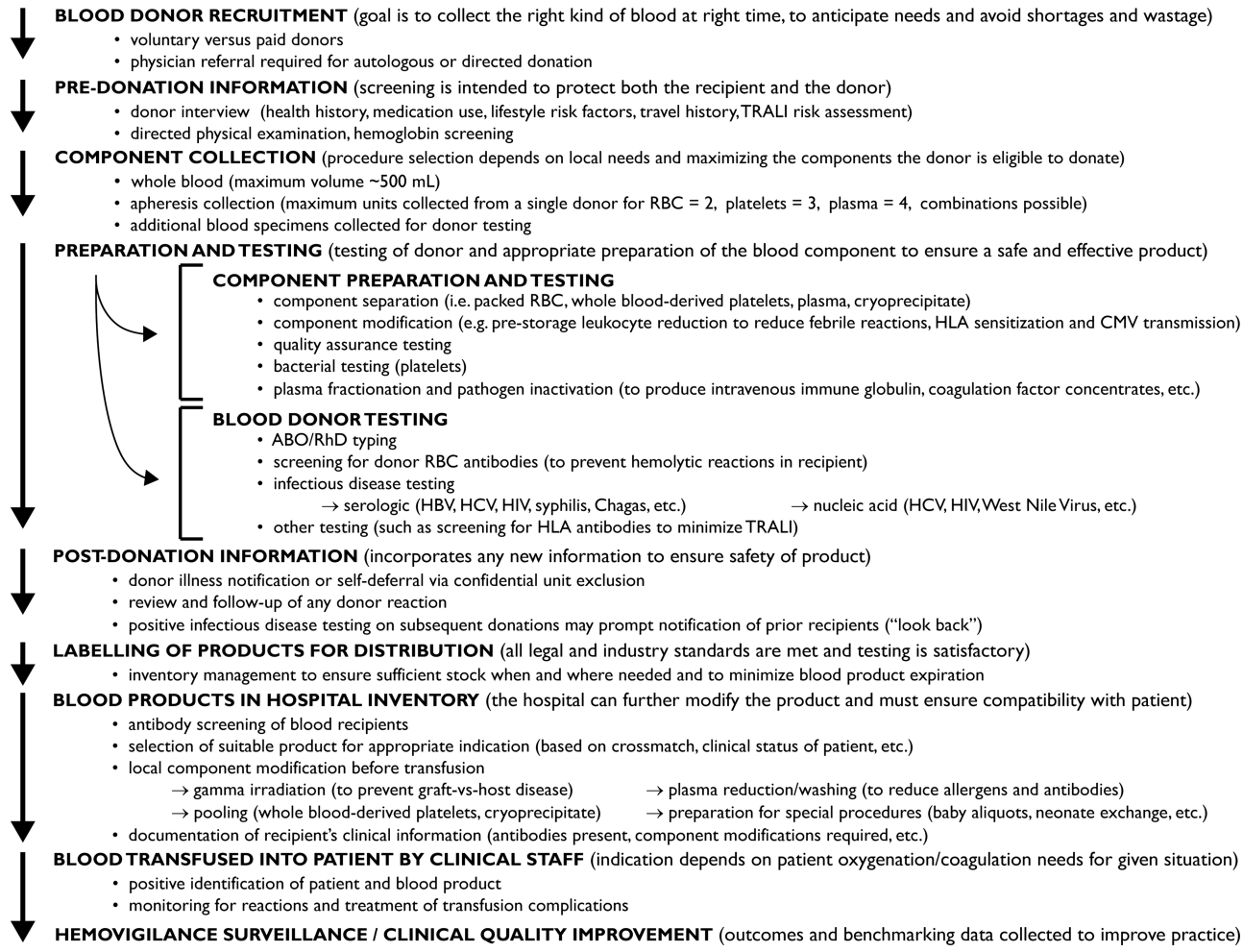

Figure 1 The blood transfusion chain: from donor arm to patient vein. The bold arrows outline 9 important stages in the system that ensure safe and effective patient blood transfusions. (Graphic design by Kimberly E. Crookston.) *Abbreviations: TRALI, transfusion-related acute lung injury; HLA, human leukocyte antigen; CMV, cytomegalovirus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.*

Figure 3 lists delayed complications that are seen in days to months following transfusion. These are of both infectious and noninfectious etiologies. The impact of patient sensitization to red blood cell (RBC) antigens and other antigens should not be overlooked. This makes life difficult for patients who become refractory to platelet transfusion. Patients who have developed RBC antibodies experience a delay in the issuing of blood because of increased difficulty finding and cross-matching compatible units. In rare instances, nation-wide searches are needed to find compatible units.

Over the past 2 decades, it has become increasingly clear that patients may benefit from fewer transfusions than traditionally have been given in the past.[7] The recommended hemoglobin levels used to trigger RBC transfusion have been declining. Although triggers are useful talking points, the real indication for RBC transfusion is to improve patient oxygenation so that it is *sufficient to meet the demands of a given clinical situation*.[8] This remains largely a clinical decision that should be made for each patient, rather than by adhering to a specific hemoglobin level learned during past training. In an analogous manner, the indication for most plasma or platelet transfusions is to improve patient hemostasis so that it is sufficient for a given clinical situation.

The move toward fewer transfusions is not just based on cost. Complications are more than just an expensive annoyance during blood infusion: they may be matters of life and death. Among the transfusion complications listed in Figures 2 and 3 are impaired oxygen delivery and immunosuppression. The jury is still out on the importance of these topics, awaiting the completion of solid randomized controlled studies. However, it is becoming increasingly accepted that negative outcomes can be associated with unnecessary transfusion. These vary from increased postoperative infections to increased length of hospital stay to increased mortality.[3]

WHICH TRANSFUSION REACTIONS ARE MOST COMMON?

While much of the bedside transfusion process is optimized to detect the potentially lethal acute hemolytic reaction, the

Acute Complications of Transfusion

(During Transfusion or Within Hours)

COMPLICATION	SYNONYM or RELATED	COMMENTS	POSSIBLE SIGNS & SYMPTOMS	INCIDENCE*†
Acute Hemolytic Reaction	Immune mediated hemolysis, acute febrile hemolytic, ABO incompatibility	Patient antibody reacts with transfused RBC, often IgM toward ABO antigen caused by giving incorrect unit of blood; can be from certain non-ABO antibodies	Fever ≥ 1˚C, chills, nausea, hypotension, back/chest pain, hemoglobinuria seen in urinary catheter, hematuria, shock	Uncommon, but deadly (1/76,000)
Acute Lung Injury	Transfusion related acute lung injury (TRALI)	New onset of acute lung injury within 6 hours of transfusion not otherwise explained (rule out pneumonia, sepsis, volume overload, etc.), usually from blood products high in plasma, as most cases are caused by donor antibody to patient leukocytes, more often in the critically ill	Dyspnea, hypoxemia, hypotension, pulmonary infiltrates--similar to acute respiratory distress syndrome (ARDS)	Uncommon (1,5,000)
Air Embolism		Typically due to infusion of large amount of air (> 200 mL) during rapid transfusion under pressure		Very rare during a simple transfusion
Anaphylaxis	Severe allergic reaction Anaphylactoid reaction	Typically patient antibody to donor blood proteins (e.g. IgA, haptoglobin)	Respiratory distress, hypotension, flushing, shock/circulatory collapse, nausea	Uncommon (1/30,000)
Bacterial Contamination	Transfusion-associated sepsis	Bacterial contamination of blood product, usually platelets, less common in RBC	Sepsis (shaking chills, fever ≥ 2˚C, hypotension, etc.) generally early in the in transfusion	Uncommon (~1/5,000 in bacterial- tested platelets)
Febrile Non-Hemolytic Reaction	Simple febrile reaction	Unexplained temperature rise ≥ 1˚C, MUST be evaluated to rule-out hemolytic	Fever, chills	Common (0.5-1%)
Hypothermia		Decreased body temperature due to infusion of cold blood components	Decreased temperature, coagulopathy	Common when many blood products are transfused
Metabolic Abnormalities		Metabolic and electrolyte changes resulting from large volume of blood products and preservatives	Cardiac arrhythmias	Common with large volumes transfused and in tiny patients
• Citrate Toxicity	Hypocalcemia	More common with liver failure; seen more often in neonates / infants and massive transfusion	Numbness, tingling, nausea, hypotension; decreased ionized calcium level	Common with large volumes transfused
• Hyperkalemia	Transfusion-associated hyperkalemia	Can be avoided in infants by using fresher blood and irradiating just prior to issue	Nausea, bradycardia, cardiac arrest, increased potassium level	Uncommon if safeguards followed
•Impaired Oxygen Delivery	Blood storage defect	Stored blood not as efficient as native blood	Poor tissue oxygenation	Common
Mild Allergic Reaction	Urticarial, Hypersensitivity	Hypersensitivity to protein or other substance in blood product	Itching, hives, local edema	Common (1-3%)
Volume Overload	Transfusion-associated circulatory overload (TACO)	Acute pulmonary edema due to too excessive fluids transfused, most common in patients with decreased cardiac reserve	Shortness of breath, orthopnea, hypertension, severe headache, tachycardia, congestive heart failure	Common (up to 1%) in cardiac and renal patients

Figure 2 Acute complications of blood transfusion. This figure lists complications typically seen during transfusion or in the hours following transfusion.*The descriptors of incidence (common, uncommon, rare, etc) refer to how often the complication is seen by clinical and blood bank staff in an average hospital. The risk to an individual patient is expressed numerically on a per unit basis. Specific patient risk is addressed more fully in Figure 4.†Roback JD, ed. *AABB Technical Manual.* 17th ed. Bethesda, MD: AABB; 2011:429-433.

clinical nurse is much more likely to see other reactions. Figure 4 illustrates the relative frequency of transfusion reactions and viral infection. Mild allergic reactions are most commonly seen. With the introduction of universal leukoreduction, the incidence of febrile nonhemolytic reactions has decreased, although they are relatively common still.

WHEN DO TRANSFUSION REACTONS TYPICALLY HAPPEN?

Figure 5 illustrates the presentation time course for selected reactions, many of which start during the transfusion or within several hours. When caring for a

Delayed Complications of Transfusion

(Days to Months After Transfusion)

COMPLICATION	SYNONYM or RELATED	COMMENTS	POSSIBLE SIGNS &	INCIDENCE*†
Infectious: Parasite				Very rare (< 1/1 million)
• Babesiosis				
• Malaria				
•Treponema pallidum	Syphilis			
•Trypanosoma cruzi	Chagas Disease			
Infectious: Prion				Very rare (< 1/1 million)
• Creutzfeldt-Jakob Disease	CJD	Heriditary, but can be transmitted by transfusion		
• Variant CJD	vCJD, mad cow disease	Typically acquired by consumption of meat of infected animal, can be transmitted by transfusion		
Infectious: Virus				
• Cytomegalovirus	CMV	Typically a concern transfusing immuncompromised patients, leukoreduction or serologic screening of blood prevents most infections	Usually subclinical	Common, even in CMV reduced-risk products (>1%)
• Hepatitis B	HBV			Rare (< 1/500,000)
• Hepatitis C	HCV			Very rare (< 1/1 million)
• Human Immunodeficiency	HIV, AIDS			Very rare (< 1/1 million)
• Human T-cell Lymphotropic	HTLV			Very rare (< 1/1 million)
• West Nile	WNV			Very rare (< 1/1 million)
Iron Overload	Transfusion-related hemochromatosis	From break down of transfused blood in chronically transfused patients, typically occurs after receiving a total of more than 100 units of RBC	Increased serum ferritin, dysfunction of heart, liver, and endocrine system	Common in transfusion-dependent thalassemia patients & sickle cell disease (up to 23%)
Sensitization to Non-RBC Antigens				
• HLA Alloimunization		Sensitization to HLA or other leukocyte antigens	May lead to febrile reaction when receiving future blood products	Common (up to 10%)
• Platelet Refractoriness		Rapid clearance of transfused platelets due to sensitization to HLA or platelet antigens (must rule out other causes of platelet destruction, e.g. sepsis)	Lack of anticipated rise in platelet count after platelet transfusion	Common in multiply transfused cancer patients (up to 27%)
• Post-Transfusion Purpura	PTP	Patient makes antibodies against foreign antigens in transfused blood, these antibodies cross-react with patient's own platelets	Precipitous fall in platelet count > 1 week after transfusion, generalized bruising	Uncommon (1/50,000-1/100,000)
Sensitization to RBC Antigens	RBC alloimmunization	Immune response to foreign antigens on donor RBC		
• Delayed Hemolytic Reaction		Clinically significant rise in antibody level, usually anamnestic (3-10 days) but can be *de novo* (2-3 weeks)	Fever, falling hematocrit, jaundice, can be similar to acute hemolytic reaction	Uncommon (1/2,500 to 1/11,000)
• Subclinical Antibody Formation	Serological reaction	Usually discovered by blood bank during routine type and screen testing	Positive antibody screen, may contribute to minor decrease in hematocrit	Common (1%)
Transfusion-Associated Graft Versus Host Disease	TA-GVHD	Donor lymphocytes proliferate in the recipient, eventually attacking the recipient, almost always fatal	Fever, gastrointestinal symptoms, macular-papular rash	Very rare when products are irradiated appropriately
Transfusion-Associated Immunosuppresion	Transfusion-associated immunomodulation (TRIM)	Unknown level of immunosuppression after receiving donor blood, transfusion of leukocytes thought to play a role	Transient immunosupression, possible increase in post-operative infection, cancer, and short-term mortality	Difficult to quantitate, subclinical effects likely common, RBC transfusion may increase patient risk of infection 5-fold

Figure 3 Delayed complications of blood transfusion. This table lists complications typically seen in the days to weeks following transfusion. Some complications may not become evident until months to years. (See Figure 2 for footnote annotations.)

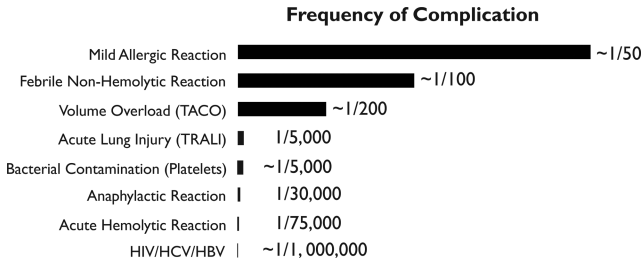

Figure 4 Relative frequency of complications associated with blood transfusion. The approximate incidence is given per unit transfused. Note that some reactions are more likely to be associated with certain components (eg, bacterial contamination → platelets; acute hemolytic reactions → RBC). The graph is not drawn to scale. (Graphic design by Kimberly E. Crookston.) *Abbreviation: RBC, red blood cell.*

patient who has been transfused recently, it is important for the direct care nurse to remember that acute reactions may sometimes present after the conclusion of the transfusion.

PATIENT SIGNS AND SYMPTOMS HELP IDENTIFY ACUTE TRANSFUSION REACTIONS

Patient vital signs are monitored at the initiation of the transfusion and frequently thereafter to detect serious transfusion reactions. Changes in vital signs are often seen during routine transfusion. This may be because of an underlying disease or a transfusion reaction, or it may just represent an expected response to transfusion. Differentiation of a "normal" response from an abnormal response is the prime responsibility of the transfusionist.

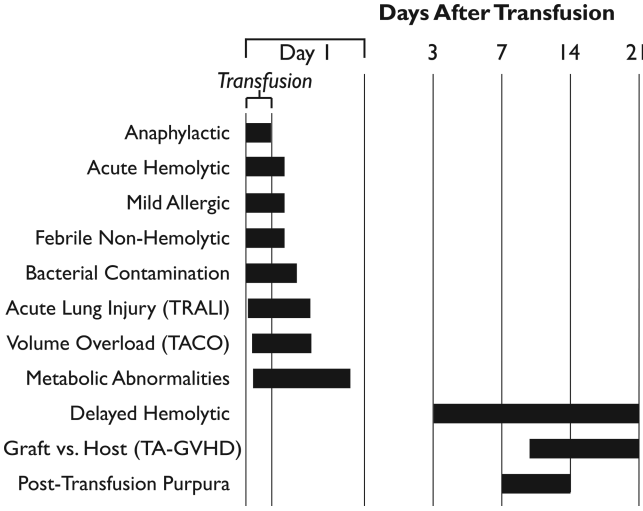

Figure 5 Time course for the typical presentation of transfusion reactions. The bracket emphasizes those reactions that begin during transfusion or later on day 1. Refer to Figures 2 and 3 for specific information on each type of reaction. (Graphic design by Kimberly E. Crookston.)

One study reported vital sign variations in patients during routine transfusion with no suspicion of transfusion reaction.[9] Vital sign changes were evaluated separately for RBC, plasma, whole blood-derived platelets, and apheresis platelets. There were differences in vital sign changes based on the blood product transfused, but not huge differences. The maximum changes in patients not experiencing a reaction were seen in RBC transfusion, with the exception of change in respiration and diastolic blood pressure, which were slightly greater in patients receiving whole-blood platelets. The maximum changes from baseline among any of the products follow, derived from the reported mean and standard deviation. About two-thirds of patients not experiencing a reaction fell within these parameters (± 1 standard deviation): for temperature, 0 ± 0.5°C; respiratory rate, −0.9 ± 4 respirations per minute; heart rate, −1 ± 8 beats per minute; systolic blood pressure, 3 ± 15 mm of mercury; and diastolic blood pressure, 2 ± 13 mm of mercury.

Figure 6 suggests a simplified rule of thumb for remembering normal vital sign variations during transfusion. This is useful as long as it is realized that these parameters are not meant as triggers for diagnosing an abnormal response to transfusion. They are intended to give the direct care nurse an idea of a normal vital sign response to transfusion. About one-third of "normal" patients may fall outside these ranges, and some reactions may occur without major changes in vital signs. If 1 vital sign falls outside these ranges, then extra attention must be given toward patient monitoring. If 2 or more vital signs fall outside these parameters, a mental review of the possible reactions should be done. Figure 6 demonstrates that understanding the relationship between the prominent presenting signs and symptoms of reactions can help in establishing a differential diagnosis:

Hives and/or Itching

Hives and/or itching typically are the presenting signs of an allergic reaction, but in rare cases, these symptoms may progress rapidly into a life-threatening anaphylactic reaction. Signs of an anaphylactic reaction may include swelling of the throat or tongue, flushing, and hypotension. Because it is not possible to distinguish between a mild, self-limited allergic reaction and the early signs of a more serious reaction, the first response to itching and hives should always be to stop the transfusion. If the symptoms are limited to itching and hives and the patient responds to treatment with diphenhydramine, some hospitals will allow the transfusion to resume. The patient should be carefully monitored throughout the remainder of the transfusion.

Fever and/or Chills

Fever and/or chills are most commonly associated with a febrile nonhemolytic reaction. However, fever is often

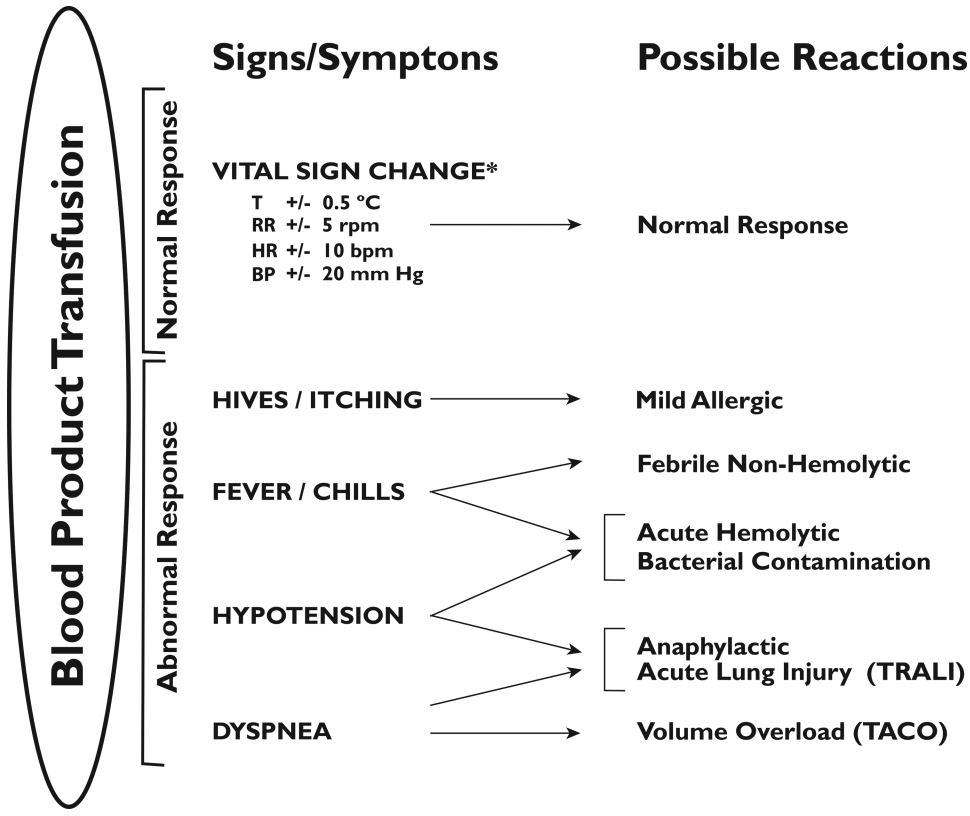

Figure 6 Transfusion reaction recognition at the bedside. Signs and symptoms help the clinical team differentiate a normal patient response to transfusion from a potential transfusion reaction. (Graphic design by Kimberly E. Crookston.) *Abbreviations: T, temperature; RR, respiratory rate in respirations per minute (rpm); HR, heart rate in beats per minute (bpm); BP, either systolic or diastolic blood pressure in millimeters of mercury (mm Hg).* *The "normal" vital sign changes during transfusion are approximated for use as a "rule of thumb" to help in recognition of a possible transfusion reaction. When changes fall outside these parameters, then special vigilance is needed to assess for possible reactions (see text).

the first sign of an acute hemolytic reaction, and this is why transfusions are typically stopped after a temperature rise of 1°C. (Refer to local hospital guidelines.) This prevents infusion of additional incompatible blood in the event of a hemolytic reaction. Shaking chills and fever greater than 2°C are often seen when transfusing a blood product into a patient containing bacterial endotoxin and other microbial by-products. This may prompt the laboratory to perform additional microbiology studies during the transfusion reaction workup. Because platelets are not refrigerated like RBC, they are more likely to support bacterial growth. Bacterial testing of platelets during the production process is now standard practice, so the incidence of bacterial contamination has declined.

Hypotension

Hypotension may also be seen with acute hemolytic reactions and bacterial contamination. In addition, low blood pressure is a sign associated with anaphylaxis and often with transfusion-associated acute lung injury (TRALI). TRALI results in noncardiogenic pulmonary edema with a presentation indistinguishable from acute respiratory distress syndrome.[10] Other potential causes should first be ruled out because TRALI is treated by supportive care only. TRALI is typically attributed to donor antibodies transfused within plasma-rich products, such as platelets or plasma, but RBC units also have been implicated. Donors who have been pregnant have a much higher likelihood of developing antibodies against foreign leukocyte antigens that may contribute to the pathogenesis of TRALI. For TRALI to occur, however, the recipient must possess the antigens to which the donor antibodies are targeted.

Dyspnea

Dyspnea during transfusion is sometimes a result of the patient's underlying condition. Shortness of breath is a concerning sign when due to the transfusion itself. It is a prominent sign of an anaphylactic reaction and also accompanies TRALI. Anaphylaxis is a severe allergic reaction that leads to shortness of breath and hypotension (analogous to a severe bee-sting reaction). The most common transfusion-related cause of dyspnea, however, is not directly related to the specific blood product itself, but due to an increase of fluid in a susceptible patient. The elderly are susceptible to volume overload, as well as patients with heart failure,

chronic anemia, or renal disease. Transfusion-associated volume overload (TACO) is fairly common. It is sometimes unavoidable in susceptible patients who need an acute increase in RBC mass to ensure adequate oxygenation. It is important to distinguish between volume overload and TRALI because diuretics effectively treat TACO but may worsen TRALI.[1]

Knowledge of these common signs and symptoms combined with vigilant monitoring during and immediately after transfusion enables the clinical team to differentiate a normal patient response from a life-threatening reaction.

WHAT CAUSES TRANSFUSION REACTIONS?

To know how to treat transfusion reactions, it helps to understand the causes. Figure 7 lists causes of transfusion reactions that may develop acutely, along with representative examples of possible pathophysiology. Grouping together reactions with similar mechanisms helps understand them. Preexisting antibodies made by the transfusion recipient may account for a number of reactions, such as mild allergic, febrile nonhemolytic, acute hemolytic, and anaphylactic.

In contrast, TRALI is due to the antibodies from the blood donor that are transfused into the patient. They are directed toward patient leukocytes. Donor antibodies directed toward patient RBCs are not usually an issue because blood collection agencies screen for these antibodies.

Acute reactions caused by contamination of blood products are usually due to bacteria. Other infectious agents such as viruses do not typically present acutely. The bacteria may come from the donor during collection or from contamination of the collected blood product as the result of manipulation. This is why there are strict rules about how long RBCs may be left outside of refrigeration and the maximum time over which a product may be transfused.

Reactions may occur because of factors that are not intrinsic to any particular unit of blood. These include volume overload (TACO) and hypothermia. Metabolic abnormalities are linked to metabolism of blood storage solutions and with factors released from RBCs during storage.

WHAT DO I DO WHEN I SUSPECT A TRANSFUSION REACTION?

The most important thing to do when a transfusion reaction is suspected is to *stop the transfusion immediately and keep the line open*. Table 1 outlines additional actions. A transfusion reaction evaluation request form typically is used to document signs and symptoms of a suspected reaction so that the blood bank can use this information, in conjunction with laboratory testing, to arrive at a likely diagnosis. The blood bag, along with the infusion set and anything else attached to the set, should be sent with the transfusion reaction evaluation request. These items are examined by medical technologists for causes of acute RBC hemolysis not related to antibodies, such as thermal damage to RBC from a blood warmer, lysis due to administration of a hypotonic solution, or lysis due to improper blood storage or product contamination. One of the most sensitive tests

Causes of Acute Transfusion Reactions

Reaction		Typical Etiology
Caused by Antibodies in the Recipient	→	***Recipient* Antibody Directed Toward Blood *Donor* . . .**
• Mild Allergic		Plasma Proteins
• Febrile Non-Hemolyic		Leukocytes
• Acute Hemolytic		ABO Blood Group (or certain other RBC antigens)
• Anaphylactic		Immunoglobulin A
Caused by Antibodies from the Donor*	→	**Blood *Donor* Antibody Directed Toward *Recipient* . . .**
• Acute Lung Injury (TRALI)		Leukocytes
Caused by Contamination of Blood Product	→	**Bacteria from . . .**
• Bacterial Contamination		Donor's Blood or Skin; Product Manipulation
Cause Not Intrinsic to the Unit of Blood	→	**Due to Transfusion to a Patient That Cannot . . .**
• Volume Overload (TACO)		Tolerate Extra Fluid Volume
• Hypothermia		Compensate for Volume of Cold Blood
• Metabolic Abnormalities		Metabolize Blood Product Anticoagulants

Figure 7 Acute transfusion reactions grouped by etiology. It should be noted that not all reactions are caused by factors intrinsic to a particular donor unit. *Abbreviation: RBC, red blood cell.* *Donor antibodies directed toward patient RBC are not usually an issue because blood collection agencies screen for these. Anti-A present in plasma-incompatible platelet transfusions can cause hemolysis in rare instances (eg, blood group O platelet to group A patient).

TABLE 1

Bedside Protocol for a Suspected Transfusion Reaction

Stop the transfusion immediately and keep the line open.[a]
Perform a clerical check of blood component labeling and patient identification.
Notify the clinical team.
Complete a transfusion reaction evaluation request form.
Send the blood bag, infusion set, and anything else connected to it except the needle, as well as a newly drawn blood specimen, to the laboratory, usually in a lavender-top EDTA tube.
If the patient has a urinary catheter, examine the urine for free hemoglobin.
In consultation with the blood bank physician, the clinical team may order ancillary tests on the patient. For example, for hemolysis, lactate dehydrogenase and bilirubin may be evaluated (haptoglobin is sometimes evaluated, but may not be as useful); for shortness of breath, a chest x-ray and BNP; for anaphylaxis, an immunoglobulin A level; for bacterial contamination, patient blood culture.

[a] *Some hospitals allow the transfusion to be restarted when clinical examination suggests only a simple allergic reaction. Typically, an antihistamine is administered and the infusion rate is slowed. A transfusion reaction evaluation request should still be sent to the lab to allow hemovigilance tracking.*

Abbreviations: EDTA, ethylenediaminetetraacetic acid; BNP, B-type natriuretic peptide.

for a hemolytic transfusion reaction is centrifuging a fresh blood specimen from the patient and visually examining the plasma supernatant for hemolysis (free hemoglobin makes the plasma red). Laboratory evaluation is outlined in Table 2.

There are 3 reasons why a transfusion reaction evaluation request should always be submitted, even if the clinical team is confident in their assessment of the reaction and patient risk. First, the workup may affect future care of the patient because special blood products or product modifications may be needed. Second, the workup may affect other patients because certain reactions require that other components from that donation be removed from the blood bank inventory to prevent a similar, or perhaps more severe, reaction in another patient. Third, reporting is an important step in the quality assurance/hemovigilance process to allow tracking and better recognition of how to prevent similar reactions in the future.

HOW DO I TREAT A TRANSFUSION REACTION?

Transfusion reaction treatment varies with the reaction. Diphenhydramine and acetaminophen are some of the most commonly used drugs for treating mild allergic and febrile nonhemolytic reactions. For other reactions,

TABLE 2

Laboratory Investigation of a Suspected Transfusion Reaction

The laboratory will centrifuge a posttransfusion patient blood specimen and evaluate for free hemoglobin. This result is typically called urgently to the clinical team.
The blood bank will perform a serologic investigation, if RBC, which includes confirmation of the patient's blood type and that of the unit, repeat patient antibody screen, and a direct antiglobulin test (DAT; Coombs' test) to look for foreign antibodies attached to blood cells circulating in the patient.
If any testing is abnormal, the pretransfusion blood specimen stored in the blood bank is evaluated for comparison.
If RBC, the transfusion administration set is examined for hemolysis in the tubing that might be due to a blood warmer or nonisotonic solution being infused with the blood.
If RBC, the blood bag is examined for possible hemolysis from contamination or mishandling before the transfusion.
Other testing may be done by request of the blood bank physician. The blood bank may be asked to perform additional tests, such as cross-matching and RBC phenotyping. Table 1 outlines clinical tests that may be done on the patient who received the blood product. Other testing may be done in specialized laboratories. For example, for a suspected bacterial contamination, gram stain and culture of any remaining product in the blood component bag; for TRALI, testing of the blood donor for antibodies to human leukocyte and neutrophil antigens; for anaphylaxis in patients that are IgA deficient, antibodies directed toward IgA.

Abbreviations: RBC, red blood cell; TRALI, transfusion-associated acute lung injury, IgA, immunoglobulin A.

expert consultation should be considered. In cases of acute hemolytic reaction, baseline laboratory tests should be performed and urine should be kept flowing, possibly with alkalinization. Volume overload may require diuretics. TRALI is treated with oxygen and supportive care, which may involve intubation. Bacterial contamination may involve blood pressure support and antibiotics. Because anaphylaxis is treated emergently according to hospital protocol, usually with epinephrine and diphenhydramine, there may not be time for consultation until after the patient is stabilized.

CAN I RESTART A TRANSFUSION AFTER IT IS STOPPED?

The potential restarting of transfusion is a critical question. On one hand, a bleeding patient may desperately need a lifesaving transfusion. On the other hand, if the patient is experiencing a serious reaction, giving the rest of the unit may lead to death. As a rule, once a reaction is suspected, the transfusion is stopped and never restarted. Another unit of blood is requested from the blood bank. The only exception is that some hospitals allow restarting products after a diagnosis of a mild allergic reaction has been made. These hospitals typically have transfusion medicine experts on the staff who can assist with this decision when necessary.

IS THERE A ROLE FOR PREMEDICATION IN PREVENTING TRANSFUSION REACTIONS?

Administering drugs in an attempt to prevent a possible transfusion reaction is becoming controversial. Hospitalists covering inpatient services at night may elect to premedicate before transfusion to lessen the chance of getting awakened during the night. Oncologists may not have time in their busy clinic schedules to deal with "nuisance" reactions, such as mild allergic and febrile nonhemolytic reactions. When rapid RBC exchange is performed for sickle cell patients using apheresis technology, many practitioners choose to premedicate to avoid having to stop an urgent procedure and possible loss of special phenotype-matched RBC units.

Although diphenhydramine and acetaminophen are effective for treating mild allergic and febrile reactions once they occur, it is a subject of debate whether they can prevent reactions. Three controlled trials consisting of 462 total patients suggest that premedication does not prevent mild allergic or febrile nonhemolytic transfusion reactions.[11] It is unlikely that premedication will obscure a true hemolytic reaction, so the issue is primarily one of administering drugs that may not be indicated, a question of both cost and risk-benefit ratio. A certain amount of flexibility is required of the clinical nursing staff, particularly when choosing how to follow a transfusion protocol allowing for *pro re nata* (prn) use of premedications.

CONCLUSION

The safe transfusion of a blood product into a patient who needs it is the ultimate goal of a complex blood procurement system. The direct care nurses responsible for this procedure play a vital role in its success. Understanding the possible complications of transfusion and how to quickly recognize and manage reactions ensures an optimal patient outcome.

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