Chapter 33

Battlefield Transfusions

Introduction
About 87% of battlefield deaths occur in the prehospital environment. Of these, 24% have been deemed to be potentially survivable, with over 90% of this potentially preventable mortality occurring due to hemorrhage. Prehospital blood transfusion administered within 30-40 minutes of injury has been shown to dramatically reduce combat casualty mortality from hemorrhagic shock. In addition, of the patients dying of wounds after reaching an MTF, about 51% were found on autopsy to have had potentially survivable injuries, and 80% of these died of hemorrhage. Hemorrhage is thus the main cause of potentially preventable death on the battlefield.

Treatment of hemorrhage requires aggressive control of bleeding and blood transfusion. Considering the patients in the prehospital setting who bled to death before reaching an MTF over the course of recent conflicts in Iraq and Afghanistan, as well as the patients arriving directly to MTFs without prior resuscitation who either received a massive transfusion (>10 units of red blood cells and/or whole blood in 24 hours) or who died of hemorrhage in the course of resuscitation, then a total of at least 10% of all casualties were at risk of exsanguination at point of injury and required substantial blood transfusion support beginning as close as possible to point of wounding. Indeed, data from the Joint Trauma System and Armed Services Blood Program indicate that these patients received 90% of all blood transfused in theater.

Another perspective on the need for battlefield transfusion stems from the observation that 13.6% of all casualties admitted to Role 3 combat support hospitals in Iraq and Afghanistan between 2003 and 2012 required transfusion, almost half of these being massive transfusions. Considering that these recent conflicts occurred
with reduced overall battlefield lethality due to weapons systems used and troop protective measures (conditions that have not been prevalent in conflicts since World War II), it is easy to see that need for transfusion may affect up to 20% of casualties.

The 10%-20% of patients likely to require massive transfusion are at high risk of early mortality, generally occurring within the first 6 hours after injury. These patients require immediate resuscitation with blood, preferably starting within 30 minutes of injury, especially in the prehospital setting. In cases of massive blood loss, there is no substitute for the transfusion of blood.

This chapter will briefly address early control of hemorrhage, blood products and their availability by role, ABO Rh matching of blood products, massive transfusion and its specific complications/management, emergency fresh whole blood collection, and transfusion reactions/management relevant to the field.

**Early Control of Hemorrhage**

- Patients who do not lose large amounts of blood following injury will not likely need blood products. Although this is an obvious statement, it highlights the point that every attempt to control external bleeding should be made during initial care.
- Tourniquets should be applied immediately to extremities with potential for life-threatening blood loss, such as with traumatic amputation, active/ongoing bleeding, or suspected vascular injury (ie, pulsatile bleeding or expanding hematoma formation).
- Advanced bandages or topical hemostatic agents approved for use in theater should be used to help control sites of external bleeding.
- For proximal extremity bleeding (eg, in the groin, axilla, and neck), junctional tourniquets or hemostatic pressure should be applied, and every attempt at hemorrhage control should be made in the prehospital environment while not delaying rapid transport to surgical care.
- Patients with non-compressible torso hemorrhage will likely require rapid surgical intervention to survive; however, adjuncts for hemorrhage control include the anti-fibrinolytic tranexamic acid (TXA) and blood transfusion, preferably whole blood.
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- Early control of extremity and external hemorrhage with tourniquets, bandages, and direct manual pressure is essential.
- Patients with suspected thoracic, abdominal, or pelvic bleeding must be evacuated quickly to medical units with surgical capability.

Blood Products Available by Role
- Damage control resuscitation initiated in the prehospital phase of care must include the use of blood products.
- Blood products fielded with Role 2 surgical units are predominantly low titer group O whole blood (LTOWB) (whole blood with low titers of anti-A and anti-B antibodies that can be transfused to any patient), group O stored RBCs and AB or A plasma (fresh frozen plasma [FFP] that is thawed and stored at 1°–6°C for up to 5 days as thawed plasma, or never frozen liquid plasma, or freeze-dried plasma).
- Role 3 combat support hospitals have a much larger inventory of ABO type-specific blood products that also include apheresis platelets (aPLTs) and cryoprecipitate.
- Role 1 through Role 3 facilities must have the ability to perform emergency fresh whole blood drives.
- Availability, storage, and shelf-life of these products are outlined in Table 33-1.

ABO Matching of Blood Products
- Until the ABO type of the casualty is known, type O RBCs and LTOWB are safe and recommended for emergency transfusion.
- AB plasma (which contains neither anti-A nor anti-B antibodies) is safe for emergency transfusion. However, AB plasma is a scarce resource because only 4% of the population has this blood type, so AB plasma is frequently unavailable. Reactions against the A antigen tend to be more severe; therefore, A plasma (which does not contain anti-A antibodies) is also recommended for emergency transfusion and is used in patients of all blood types (Table 33-2).
- Once the ABO typing of the casualty is known, type-specific blood products should be used if available.
<table>
<thead>
<tr>
<th>Roles Blood Product</th>
<th>ABO and Rh Groups</th>
<th>Storage Capacity</th>
<th>Storage</th>
<th>Shelf-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Fresh whole blood</td>
<td>Type-specific or LTOWB</td>
<td>Emergency collection only</td>
<td>Room temp or 1°C–6°C</td>
<td>24 hours at room temp / 21 or 35 days at 1°C–6°C</td>
</tr>
<tr>
<td>2 RBCs</td>
<td>O Rh+/–</td>
<td>50–100 U</td>
<td>1°C–6°C</td>
<td>42 days</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>AB, A</td>
<td>50–100 U</td>
<td>≤–18°C</td>
<td>1 yr/5 days post-thaw</td>
</tr>
<tr>
<td>Fresh whole blood*</td>
<td>Type-specific or LTOWB</td>
<td>Emergency collection only</td>
<td>Room temp or 1°C–6°C</td>
<td>24 hours at room temp / 21 or 35 days at 1°C–6°C</td>
</tr>
<tr>
<td>LTOWB (stored)</td>
<td>O Rh+/–</td>
<td>2–10 U</td>
<td>1°C–6°C</td>
<td>21 or 35 days</td>
</tr>
<tr>
<td>Never frozen liquid plasma</td>
<td>AB, A</td>
<td>10–20 U</td>
<td>1°C–6°C</td>
<td>26 or 40 days</td>
</tr>
<tr>
<td>3 RBCs</td>
<td>O Rh+/–</td>
<td>50–100 U</td>
<td>1°C–6°C</td>
<td>42 days</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>AB, A</td>
<td>50–100 U</td>
<td>≤–18°C</td>
<td>1 yr/5 days post-thaw</td>
</tr>
</tbody>
</table>

(Table 33-1 continues)
### Table 33-1 continued

<table>
<thead>
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<th>Storage Capacity</th>
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<th>Shelf-Life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh whole blood*</td>
<td>Type-specific or LTOWB</td>
<td>Emergency collection only</td>
<td>Room Temp or 1°–6°C</td>
<td>24 hours at room temp / 21 or 35 days at 1°–6°C</td>
</tr>
<tr>
<td>LTOWB (stored)</td>
<td>O Rh+/−</td>
<td>2-10 U</td>
<td>1°–6°C</td>
<td>21 or 35 days</td>
</tr>
<tr>
<td>Never frozen liquid plasma</td>
<td>AB, A</td>
<td>10-20 U</td>
<td>1°–6°C</td>
<td>26 or 40 days</td>
</tr>
<tr>
<td>Apheresis platelets</td>
<td>O, A, B Rh+/−</td>
<td>Up to 24 U</td>
<td>20°–24°C or 1-6°C</td>
<td>5 days</td>
</tr>
<tr>
<td>Cryoprecipitate</td>
<td>N/A</td>
<td>50–100 U</td>
<td>≤−18°C</td>
<td>1 yr/4 h</td>
</tr>
</tbody>
</table>

CCMD: combatant command; LTOWB: low titer group O whole blood; N/A: not applicable; RBCs: red blood cells; U: units.

*Type-specific or LTOWB collection is performed when plasma/RBC products are exhausted or when platelets are required. Type-specific or LTOWB collection is performed when blood products are exhausted or in critical shortage (i.e., type O RBCs that are needed in reserve for emergency release).
Table 33-2. ABO Matching for Transfused Blood Products*

<table>
<thead>
<tr>
<th>Recipient Group</th>
<th>Unknown</th>
<th>O</th>
<th>A</th>
<th>B</th>
<th>AB</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBCs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st choice</td>
<td>O</td>
<td>O</td>
<td>A</td>
<td>B</td>
<td>A, B, or AB</td>
</tr>
<tr>
<td>2nd choice</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st choice</td>
<td>AB</td>
<td>O</td>
<td>A</td>
<td>B</td>
<td>AB</td>
</tr>
<tr>
<td>2nd choice</td>
<td>A</td>
<td>A</td>
<td>AB</td>
<td>AB/A</td>
<td>A</td>
</tr>
<tr>
<td>Whole blood</td>
<td>Type-specific</td>
<td>O</td>
<td>A</td>
<td>B</td>
<td>AB</td>
</tr>
</tbody>
</table>

RBCs: red blood cells

*Low titer O whole blood (LTOWB) may be transfused regardless of recipient ABO type. Platelets and cryoprecipitate do not need to be type-specific.

†Fresh whole blood MUST be type-specific if no group O prescreened donors are available (preferably low titer Group O). If group O, prescreened low titer (anti-A / anti-B) donors are drawn, then see LTOWB for ABO matching guidance.

- At Role 2 surgical units, cold stored LTOWB may be available. RBCs and plasma should be readily available. However, if blood product support is not adequate, emergency collection of type-specific whole blood or LTOWB is necessary.
- LTOWB drawn from pre-screened donors may be transfused to a patient regardless of patient’s blood type. If pre-screened, low titer group O donors are unavailable, collected whole blood must be an ABO type-specific match with the patient’s blood type. If ABO typing and low titer group O donors are unavailable, type O fresh whole blood (unknown titer levels) can be used as a last resort.

- LTOWB or type O RBCs are safe for emergency transfusion.
- AB plasma (or A plasma as the next safest alternative) is used for emergency transfusion.
- If fresh whole blood is required:
  - Group O low titer donors are preferred.
  - If whole blood is not group O (low-titer group O is preferred); then it MUST be ABO type-specific whole blood.
**Rh Blood Matching for Female Casualties**

- Women, military and civilian, are becoming more frequent victims of conflict. Serious consequences to Rh incompatible blood are rare in men who have no previous history of transfusions.
- Rh– women transfused with Rh+ blood are very likely (approximately 20%) to produce anti-D (Rh+) antibodies. This seroconversion can jeopardize a subsequent pregnancy when this Rh– mother, now sensitized by Rh+ transfusion, conceives an Rh+ fetus. Hemolytic disease of the fetus and newborn (HDFN) may result, which can be fatal to the fetus. With current therapy for HDFN, serious adverse events occur in approximately 6% of affected pregnancies.
- When the supply of group O blood permits, **group O Rh– blood for emergency release should be reserved for women of child-bearing potential** (age <50) until their ABO and Rh types are known. If Rh– blood is not available, Rh+ blood should **NOT** be withheld (saving a life takes precedence over risk of Rh immunization).
- Although there is a risk of Rh seroconversion with apheresis platelets (due to a small amount of RBCs in the unit), Rh incompatibility should not influence transfusion. If **Rh+ platelets are transfused to an Rh– woman, this can be mitigated by use of Rh immunoglobulin (RhoGAM) within 72 hours of platelet transfusion.**
- Rh seroconversion from FFP and cryoprecipitate is rare, and these products are not generally Rh matched.

**Under no circumstances should a lifesaving transfusion be withheld because of Rh incompatibility. Saving a life takes precedence over Rh immunization.**

**Massive Transfusion**

- Massive transfusion has been defined in various ways, but the most common definition is the need for **≥10 U of blood in 24 hours.** This definition is far from perfect in that it does not account for the rate of transfusion. For example a casualty receiving 8 units of blood in the first hour of resuscitation will likely have worse anatomic and physiologic insults than a
casualty who receives ½ unit of blood every hour for 20 hours. Therefore, this definition is under scrutiny, but is still widely accepted.

- The massive transfusion definition based on 10 units in 24 hours is based on the estimate of 1 blood volume for an average adult male. Small individuals and pediatric patients have a lower blood volume that should be considered when deciding whether a patient needs a massive transfusion. Massive transfusion in pediatric patients is defined as exceeding 40 mL/kg of combined blood products in 24 hours.

- **Survival in massively transfused combat casualties is higher in patients who are transfused with increased ratios of plasma and platelets in relation to RBCs.** Based on these observations, prior to definitive surgical control of bleeding, massively bleeding patients should be transfused with whole blood or with component therapy aiming at a ratio of 6 RBCs:6 FFPs:1 aPLT. It is reasonable to consider trans-fusing 10 U of cryoprecipitate along with this ratio. Whole blood is the preferred therapy.

- **Early recognition (on admission) of need for massive transfusion.**
  - Systolic blood pressure <110 mm Hg.
  - Heart rate >105 beats per minute.
  - Hematocrit <32%.
  - pH <7.25.
  - Patients with three of the above four risk factors have approximately a 70% risk of massive transfusion.
  - Patients with all four of the above risk factors have an 85% risk of massive transfusion.

- Laboratory-directed transfusion thresholds should **not** be used in massively bleeding patients until the patient has been stabilized (because of the significant time lag between drawing labs and receiving their results).

- The rate and volume of blood products to transfuse should be determined **clinically,** until surgical correction of hemorrhage has been established. Goals include clinical factors supporting adequate perfusion, restoration of hemodynamic physiology, mentation, skin color, and urine output > 0.5 mL/kg/h.
• Massive transfusion protocols (Fig. 33-1) and good communications between providers in the ER, OR, ICU, and blood bank are essential.

**Fig. 33-1.** Role 3 combat support hospital example of massive transfusion protocol. aPLT: apheresis platelet; cryo: cryoprecipitate; CSH: combat support hospital; DCCS: Deputy Commander for Clinical Services; FFP: fresh frozen plasma; FWB: fresh whole blood; LTOWB: low titer O whole blood; RBCs: red blood cells; RBCs: red blood cells; RTD: return to duty.
If whole or component therapy including platelets and plasma are unavailable, fresh whole blood from a walking blood bank collecting LTOWB or type-specific fresh whole blood should be transfused.

- Survival in massively transfused combat casualties is higher in patients who are transfused with whole blood or component therapy with increased ratios of plasma and platelets in relation to RBCs.
- Whole blood is the transfusion therapy of choice.
- Neither crystalloid nor colloid should be administered. The standard of care is resuscitation with blood, not crystalloid or colloid.
- Goal blood pressure is systolic blood pressure ~90–110 mm Hg (target 100).
- In patients with central nervous system injury, goal blood pressure should be 110 mm Hg.
- If whole blood is not available, blood components should be transfused with a goal ratio of 6 RBCs:6 FFPs:1 aPLT.

Refer to Table 33-3 and Chapter 7, Shock, Damage Control Resuscitation, and Vascular Access, for further information on transfusion and resuscitation.

**Table 33-3. Battlefield Transfusion and Damage Control Resuscitation Principles**

**Prehospital**
- Rapid recognition of life-threatening hemorrhagic shock
  - Point of care measurements: near infrared spectroscopy, INR, lactate level may be of value
- Prevent hypothermia
- Hemorrhage control with mechanical hemostatic adjuncts:
  - Tourniquet / junctional tourniquet
  - Pressure dressings / thrombin- and fibrin-impregnated gauze
  - REBOA
  - Intraabdominal foams (investigational)
- Hemostatic resuscitation
  - Whole blood is optimal

(Table 33-3 continues)
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Component therapy with plasma (dried, liquid, or thawed), RBCs, and platelets in 1:1:1 ratio
Permissive hypotension for patients without traumatic brain injury*
Avoid crystalloid resuscitation
Consider TXA administration if less than 3 hours from time of injury†
Consider source of fibrinogen (fibrinogen concentrate or cryoprecipitate)
Avoid hypocalcemia
In prolonged evacuations, empiric calcium administration for every 4–6 units of RBCs or WB

Hospital
Rapid surgical correction of bleeding
Hemostatic resuscitation
Whole blood is optimal
Component therapy: plasma (dried, liquid, thawed, FFP/FP24), RBCs, platelets in 1:1:1 ratio
Shift from empiric whole blood based resuscitation to goal-directed resuscitation when feasible
Permissive hypotension prior to surgical control of bleeding for patients without TBI*
Intravenous hemostatic adjuncts:
Consider TXA administration indicated either empirically or guided by functional viscoelastic studies demonstrating LY30 > 3%†
Source of fibrinogen for reduced fibrinogen function
PCC for patients taking vitamin K antagonist
Avoid crystalloid resuscitation
Blood pressure goals after hemorrhage control
MAP ≥ 60; SBP >100 mm Hg and evidence of improved end organ perfusion
Monitor CBC, electrolytes, and blood gas hourly
Calcium administration for every 4–6 units of RBC or WB; follow ionized calcium concentration
Treat hypomagnesaemia
Avoid/treat hyperkalemia

(Table 33-3 continues)
Emergency War Surgery

Table 33-3 continued

CBC: complete blood count; FP24: frozen plasma, frozen within 24 h; FFP: fresh frozen plasma, frozen within 8 h; INR: international normalized ratio; LY30: percent of clot lysed after 30 minutes; MAP: mean arterial pressure; PCC: prothrombin complex concentrates; RBCs: red blood cells; REBOA: resuscitative endoscopic balloon occlusion of the aorta; SBP: systolic blood pressure; TBI: traumatic brain injury; TXA: tranexamic acid; WB: whole blood

*Conventional goal is systolic blood pressure >90 mm Hg. Recent concept indicates a higher goal of 90–110 mm Hg due to shift toward blood-based resuscitation and concern for prolonged hypoperfusion, especially for patients with long transport times.

†Military policy currently is to empirically administer 1 g of TXA for severe bleeding in both prehospital and in hospital settings.

Management of Complications During Massive Transfusion

- **Hypothermia** in trauma patients develops from conductive, convective, evaporative, and radiative losses due to environmental and surgical exposure.
  - Because whole blood, RBCs, and plasma are stored at 4°C, hypothermia can develop quickly during massive transfusion.
  - Hypothermia contributes to coagulopathy (impaired clotting factors and platelets) and increased risk of cardiac dysrhythmias.
  - Fluid warmers are absolutely essential for preventing or limiting hypothermia, along with other measures listed in Table 33-4.
  - Currently, the goal during resuscitation is normalization of body temperature, 37°C.

- **Acidosis** in massively transfused patients is largely due to hypoperfusion, but can be exacerbated by crystalloids and stored RBCs. (RBCs become progressively more acidic during storage due to cellular metabolism.)
  - Acidemia contributes to coagulopathy and can cause dysrhythmia, hypotension, and decreased responsiveness to catecholamines.
  - Reversal of acidosis is primarily accomplished through restoration of adequate tissue perfusion.
  - The best way to reverse acidosis is resuscitation; however, in extreme circumstances (eg, cardiac dysfunction),
bicarbonate or tromethamine (THAM) can be used as necessary to achieve an arterial blood gas pH >7.2.

- **Hyperkalemia** is a common complication due to extracellular potassium that increases over time in stored RBCs.
  - During massive transfusion, blood can be administered rapidly through central lines without sufficient time or mixture to prevent this extracellular potassium from reaching the right heart and result in ventricular arrhythmia and cardiac arrest.
  - Limit effects by transfusing blood from lines farther away from the right atrium.
  - Hyperkalemia can also be limited with the use of fresher blood (<14 days).
  - Vigilance for this complication is necessary (with labs and EKG monitoring).
  - Management of hyperkalemia is listed in Table 33-4.

### Table 33-4. Management/Prevention of Complications of Massive Transfusion

<table>
<thead>
<tr>
<th>Hypothermia</th>
<th>Acidosis</th>
<th>Hyperkalemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehospital active/resistive warming with hot packs/heating blankets</td>
<td>Restoration of adequate tissue perfusion</td>
<td>Transfuse fresher blood (&lt;14 days)</td>
</tr>
<tr>
<td>High-capacity fluid warmers</td>
<td>Sodium bicarbonate</td>
<td>Transfuse blood from lines farther away from the right atrium</td>
</tr>
<tr>
<td>Warmed trauma suites/operating rooms</td>
<td>Forced-air warming blankets</td>
<td>Calcium chloride (1 amp) or calcium gluconate (30 ml of 10% solution) to stabilize the myocardium</td>
</tr>
<tr>
<td>Forced-air warming blankets</td>
<td>Warmed/humidified oxygen</td>
<td>Correction of acidemia/alkalinizing solutions</td>
</tr>
<tr>
<td>Limit surgical exposure (eg, damage control techniques)</td>
<td>Limit surgical exposure (eg, damage control techniques)</td>
<td>Regular insulin 10 units with 1 amp (50 mL) 50% dextrose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inhaled beta-agonists</td>
</tr>
</tbody>
</table>

(Table 33-4 continues)
Hypocalcemia
Calcium chloride (1 amp) or calcium gluconate (30 mL of 10% solution) based on measurement of serum ionized calcium levels or with every 4 units of blood products.

Coagulopathy/Microvascular Bleeding
Goal temperature > 37°C Goal pH > 7.25
Whole blood (LTOWB) or type-specific whole blood is the preferred therapy
Goal ratio of transfused blood components of 6 RBCs:6 FFPs:1 aPLT.

- Hypocalcemia occurs in trauma patients even before transfusion, and is exacerbated by massive transfusion due to the citrate (anticoagulant) in blood products. Under normal physiological conditions, citrate is rapidly metabolized by the liver. Metabolism can be overwhelmed by rapid infusion of citrate-containing components (>100 mL/min). It is also dramatically impaired in hypoperfused patients or those with advanced liver disease.
  - Hypocalcemic/citrate toxicity manifests by decreased myocardial contractility and increased susceptibility to arrhythmia from coexisting hyperkalemia.
  - Monitor for/anticipate hypocalcemia based on the pace of plasma transfusion, electrocardiographic changes, or ionized calcium levels.
  - Treat with intravenous calcium chloride or calcium gluconate.
  - If labs are not immediately available, 1 amp of calcium chloride should be administered as soon as the decision to transfuse blood is taken and then with every 4 units of citrated blood products.

- Coagulopathy (trauma-induced and dilutional).
  - Trauma-induced coagulopathy is frequently present on admission in severely injured patients, and it is correlated with the need for massive transfusion, as well as increased mortality.
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- Dilutional coagulopathy develops in massive transfusion as a consequence of the replacement of shed whole blood with factor and platelet-poor fluids like crystalloids, colloids, and stored RBCs.
- Dilutional coagulopathy may be inevitable in patients requiring a massive resuscitation with blood components due to the addition of preservative solutions to stored blood products following collection. Transfusion of RBCs, plasma, and platelets—even in a 1:1:1 ratio—results in a solution with a hematocrit of 30%, coagulation factor levels of about 60%, and platelets of \(80 \times 10^9/L\). This is why whole blood is preferred over component therapy!
- Do not give crystalloids or colloids; they greatly intensify dilutional effects.
  ♦ Primarily used only as a carrier for medications.
  ♦ Additional administration of crystalloids to restore volume should be avoided in preference to whole blood or blood components.
- TXA should be given within 3 hours of injury to reduce fibrinolysis and stabilize clots. Use of TXA has been shown to reduce mortality in bleeding trauma patients.
- Refer to Chapter 36, Emergency Whole Blood Collection.

Transfusion Reactions in the Field

Transfusion reactions may be difficult to recognize in severely or multiply injured casualties. Regardless, clinicians should be aware of the potential complications of transfusion and their management in the deployed environment.

<table>
<thead>
<tr>
<th>Treatment Plan for Transfusion Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>● STOP the transfusion.</td>
</tr>
<tr>
<td>● Disconnect tubing from infusion site; flush IV site with NS; send blood product to blood bank for testing.</td>
</tr>
<tr>
<td>● Keep IV line open with NS.</td>
</tr>
<tr>
<td>● Assess the patient: review vitals and auscultate lungs. If patient is conscious, ask about subjective complaints.</td>
</tr>
<tr>
<td>● If fever and unexplained hypotension, consider ABO mismatch and bacterial contamination/sepsis.</td>
</tr>
</tbody>
</table>
• ABO mismatch can cause disseminated intravascular coagulation (DIC) and diffuse bleeding, which may be the only intraoperative manifestation of ABO mismatch and hemolysis.

• If unexplained hypoxia, consider volume overload and TRALI (transfusion-related acute lung injury).

• If unexplained hypotension/shock without fever, consider severe allergic reaction/anaphylaxis.

• If bronchospasm or angioedema, consider anaphylactoid reaction.

• If only urticaria, likely urticarial reaction.

• If only fever in stable patient, consider febrile reaction, but still send unit to blood bank to rule out ABO mismatch or bacterial contamination.

Acute Hemolytic Transfusion Reaction (ABO Incompatibility)

• Generally develops rapidly (minutes to a few hours) after initiation of an ABO incompatible RBC transfusion.

• Mortality can be >15% and increases with the amount of incompatible blood that is infused.

• The most common cause of hemolytic transfusion reaction is clerical error that occurs outside of the blood bank, or mistyping the patient or donor information inside the blood bank.

• Fever is the most common early sign; thus, a hemolytic transfusion should be considered any time a febrile reaction follows a transfusion.

• In unconscious/sedated patients, the only signs may be:
  o Fever.
  o Inappropriate hypotension.
  o Tachycardia.
  o Dark urine (reflecting hemoglobinuria).
  o Renal failure.
  o Development of generalized/coagulopathic bleeding due to associated diffuse intravascular coagulation (DIC).

• Frequently, such patients are given additional units of incompatible blood before medical personnel realize that a hemolytic transfusion reaction is occurring.
Conscious patients can also report chills, severe low back pain (reflecting renal involvement), dyspnea, apprehension, chest pain, nausea, and vomiting.

To prevent renal failure, administer 0.9% normal saline and intravenous furosemide as needed to maintain urinary output (goal: 100 mL/h or 1–2 mL/kg/h for small patients) until resolution of hemoglobinuria.

If a transfusion reaction occurs during resuscitation for ongoing bleeding, stop transfusion of offending product and switch to emergency release blood.

The coagulation system and platelet count must be monitored for the development of DIC.

FFP and platelet transfusions may be needed if coagulopathic bleeding develops.

**Acute Hemolytic Transfusion Reaction Treatment**

- Stop transfusion and clearly mark the suspected unit.
- If a transfusion reaction occurs during resuscitation for ongoing bleeding, stop transfusion of offending product and switch to emergency release blood.
- If not in active resuscitation, maintain blood pressure and urinary output with 0.9% saline ± intravenous furosemide as needed (goal urine output: 100 mL/h until resolution of hemoglobinuria).
- Observe for coagulopathic bleeding from diffuse intravascular coagulation and monitor coagulation tests/platelet counts. Treat as necessary with fresh frozen plasma and/or platelets.
- Recheck identification of patient and unit for clerical errors and retype to rule out mistyping errors.
- Annotate patient record with description of the suspected reaction and treatments.
- Send all transfused units at the bedside to the blood bank (or to the next echelon of care).

**Bacteremia and Sepsis From Contaminated Blood Products**

Liquid stored blood products (aPLTs and RBCs) are a fertile culture media, and small amounts of contaminating bacteria may grow in blood products during their storage. These bacteria can
cause fevers and bacteremia during or soon after a transfusion. If the bacterial load is sufficiently high or gram-negative organisms are present, frank sepsis (hypotension/shock) can develop.

- Room temperature-stored platelets carry the highest risk for bacteremia/sepsis because they are stored for up to 7 days in theater. Cold-stored platelets present a much lower risk of bacterial contamination (similar to red blood cells).
- If fever and hypotension develop during or immediately following a transfusion of room temperature platelets, then broad-spectrum antibiotics should be administered.
- Because fever and hypotension are also signs of ABO mismatch, sepsis often cannot be immediately distinguished from an acute hemolytic transfusion reaction at bedside. The blood bank can clarify/rule out ABO incompatibility. Once ABO mismatch has been excluded by the blood bank, broad-spectrum antibiotics should be considered.

**Febrile Nonhemolytic Transfusion Reaction**
- Approximately 1% of all transfusions are accompanied by a temperature elevation (defined as an increase of 1°C above normal within 1 hour of transfusion), which can be with or without chills.
- Prevented by use of leuko-reduced blood products.
- There is no definitive test with which to make the diagnosis of a benign febrile reaction, which may also be the first sign of a hemolytic reaction or the infusion of a unit contaminated with bacteria. For this reason, if a fever occurs, management involves:
  - Immediate cessation of the transfusion.
  - Evaluation/consideration for ABO mismatch or bacteremia.

**Transfusion-Related Acute Lung Injury**
- Transfusion-related acute lung injury (TRALI) is manifested by rapid onset of “noncardiogenic” pulmonary edema with dyspnea, hypoxemia, and pulmonary infiltrates within 6 hours after transfusion.
- The estimated mortality rate for recognized TRALI is 5%–8%, although most patients recover completely with appropriate supportive care.
- Recognition.
TRALI in trauma patients can be challenging to distinguish from concomitant pulmonary contusions, blood aspiration, fat embolization, and/or inhalational injury (particular mechanism of injury is an important consideration) and is a diagnosis of exclusion.

- Chest radiography is similar to acute respiratory distress syndrome, with bilateral patchy alveolar infiltrates, typically with a normal cardiac silhouette and without effusions.
- Patients who require intubation have elevated peak airway pressures and frothy pink airway secretions.
- TRALI is noncardiogenic pulmonary edema and must be differentiated from volume overload or heart failure.
  - At Role 2, evaluation is guided by clinical evaluation, exam, and transduced central venous pressure.
  - At Role 3, bedside ECHO may further assist in evaluation of volume status.

- Management of TRALI:
  - Supportive.
  - Milder cases may only require supplemental oxygen as required to maintain oxygen saturation.
  - Intubation with mechanical ventilation is often required.
  - Ventilation is preferably with “lung protective” modes (eg, low tidal volumes and plateau pressures).
  - Unlike adult respiratory distress syndrome, resolution occurs rapidly. Most patients can be extubated within 48 hours, and chest radiographs generally return to normal within 4–7 days.

Urticarial Transfusion Reactions
- Urticaria (hives/itching) is the only transfusion reaction in which the blood product can be continued.
- Thought to occur from an allergenic substance in the plasma of donated blood products.
- Does NOT have wheezing/bronchospasm or inappropriate hypotension (which are allergic reactions).
- Management of urticarial reactions:
  - Hold transfusion.
Treat with diphenhydramine 25–50 mg IV or PO.

If urticaria wanes and neither dyspnea nor hypotension are apparent, the transfusion may be resumed.

**Anaphylactoid Transfusion Reactions**

- Anaphylactoid reactions involve dyspnea, bronchospasm/wheezing, and/or abdominal pain (intestinal edema).
- More severe reactions can include rapid onset of stridor, angioedema, and respiratory failure.
- True anaphylactic reactions (marked by hypotension and shock) are rare.
- **Does not cause fevers.**

Management of anaphylactoid reactions:

- Immediate cessation of the transfusion.

- If only bronchospasm (without stridor, angioedema, or hypotension) is evident:
  - Bronchodilators (albuterol).
  - Diphenhydramine 25–50 mg IV.
  - Consider giving ranitidine 50 mg IV.
  - Oxygen 6–8 L/min via face mask to maintain oxygen saturations >93%.

- If stridor or angioedema is evident, include the measures above and also:
  - Intubation.
  - Epinephrine, 0.3 mL of a 1:1,000 solution intramuscularly (adult dose), repeated every 3–5 minutes as needed.

- If inappropriate hypotension or shock are evident:
  - Fluid resuscitation and vasopressors (eg, dopamine) as needed to maintain blood pressure.
  - Consider giving methylprednisolone 125 mg IV.

For Clinical Practice Guidelines, go to [http://jts.amedd.army.mil/index.cfm/PI_CPGs/cpgs](http://jts.amedd.army.mil/index.cfm/PI_CPGs/cpgs)