

## Battlefield Transfusions

### Introduction

About 75% of all trauma casualties requiring evacuation do not require any blood product transfusion, and, for the remaining 25%, most only require 1–4 units of blood. However, **exsanguinating hemorrhage is the leading cause of preventable deaths during war**. Between 5%–8% of evacuated casualties will lose large volumes of blood during initial care and require “massive transfusion” (10 or more units of red blood cells [RBCs] in 24 hours), which is associated with a high mortality. Such deaths occur early, generally within the first 6–12 hours following injury. In cases of massive blood loss, there is no substitute for the transfusion of blood. It is critical to recognize such casualties because transfusion support for massively transfused patients must be managed differently than for other casualties.

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.
  - Proximal extremity bleeding (eg, in the groin, axilla, and neck) is not amenable to tourniquet application; therefore, direct manual pressure should be applied as best as possible during evacuation.
  - Control of severe bleeding at “noncompressible” sites in the thorax, abdomen, and pelvis can only be accomplished with surgery. Therefore, patients with suspected bleeding from injuries to the thorax, abdomen, and/or pelvis must be evacuated quickly to medical units with surgical capability.
- 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**

- Blood product transfusion is an essential component for the management of exsanguinating hemorrhage, but is insufficient without definitive surgical control of bleeding.
- Damage control resuscitation initiated in the prehospital phase of care may include the use of blood products.
- Because no surgical assets are available at Role 1, blood products may not be available.
- Blood products fielded with forward surgical units are predominantly group O-stored RBCs and AB plasma (fresh frozen plasma [FFP] that is thawed and stored at 1°–6°C for up to 5 days as thawed plasma).
- Combat Support Hospitals have a much larger inventory of ABO type-specific blood products that also includes apheresis platelets (aPLTs) and cryoprecipitate.
- Availability, storage, and shelf-life of these products are outlined in Table 33-1.

Table 33-1. Blood Products by Role of Care

Roles	Blood Product	ABO and Rh Groups	Storage Capacity	Storage	Shelf-Life
1	None	—	—	—	—
2	RBCs	O Rh+/-	50-100 U	1°-6°C	42 days
	Fresh frozen plasma	AB, A	25-50 U	≤ -18°C	1 yr/5 days postthaw
3	Fresh whole blood*	<b>Type-specific</b>	Emergency collection only	20°-24°C	24 h
	RBCs	O, A, B Rh+/-	300-500 U	1°-6°C	42 days
	Fresh frozen plasma	AB, A, B, O	100-200 U	≤ -18°C	1 yr/5 days postthaw
	Apheresis platelets	O, A, B Rh+/-	24 U	20°-24°C	5 days
	Cryoprecipitate	N/A	100-200 U	≤ -18°C	1 yr/4 h postthaw
	Fresh whole blood†	<b>Type-specific</b>	Emergency collection only	20°-24°C	24 h

N/A: not applicable; RBCs: red blood cells; U: units.

\***Type-specific** fresh whole blood collection is performed when plasma/RBC products are exhausted or when platelets are required.

†**Type-specific** fresh whole blood collection is performed when blood products are exhausted or in critical shortage (ie, type O RBCs that are needed in reserve for emergency release).

### ABO Matching of Blood Products

- Once the ABO typing of the casualty is known, type-specific blood products should be used if available.
- Until the ABO type of the casualty is known, **type O RBCs are safe for emergency transfusion.**
- Only AB plasma (which contains neither anti-A nor anti-B antibodies) is considered 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 the next safest alternative for emergency transfusion (Table 33-2).
- At Role 2 surgical units, platelets are generally not available, and plasma products may be in short supply. In such cases, if such products are needed (as in massive transfusion), emergency collection of **type-specific** fresh whole blood is necessary.
- Given the time that it takes to collect fresh whole blood from the time it is requested (30–45 minutes at best), it would be a very uncommon circumstance that the ABO type of the casualty would be unknown. If ABO typing is unavailable, **type O fresh whole blood is not safe** and can only be

**Table 33-2. ABO Matching for Transfused Blood Products\***

Recipient Group	Unknown	O	A	B	AB
RBCs					
1st choice	O	O	A	B	A, B, or AB
2nd choice			O	O	O
Fresh frozen plasma					
1st choice	AB	O	A	B	AB
2nd choice	A <sup>†</sup>	A	AB	AB	A <sup>†</sup>
3rd choice	B <sup>†</sup>	B	B <sup>†</sup>	A <sup>†</sup>	B <sup>†</sup>
Whole blood <sup>‡</sup>	Type-specific	O	A	B	AB

RBCs: red blood cells.

\*Platelets and cryoprecipitate do not need to be type-specific.

<sup>†</sup>Only suitable for emergency use when other plasma types are unavailable.

<sup>‡</sup>Fresh whole blood MUST be type-specific.

considered in extreme circumstances after at least 10 U of type O RBCs have been transfused (ie, after the native blood of the patient has been largely replaced with transfused type O RBCs).

- **Type O RBC is 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, it MUST be ABO type-specific.**

### 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 80%) 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. Chronic hemolytic disease of the newborn may result, which can be fatal to the fetus in 50% of pregnancies without modern treatments (which have reduced the mortality down to 16%).
- 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 aPLTs (due to a small amount of RBCs in the unit), Rh incompatibility should not influence transfusion. **If Rh+ platelets are transfused to a 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

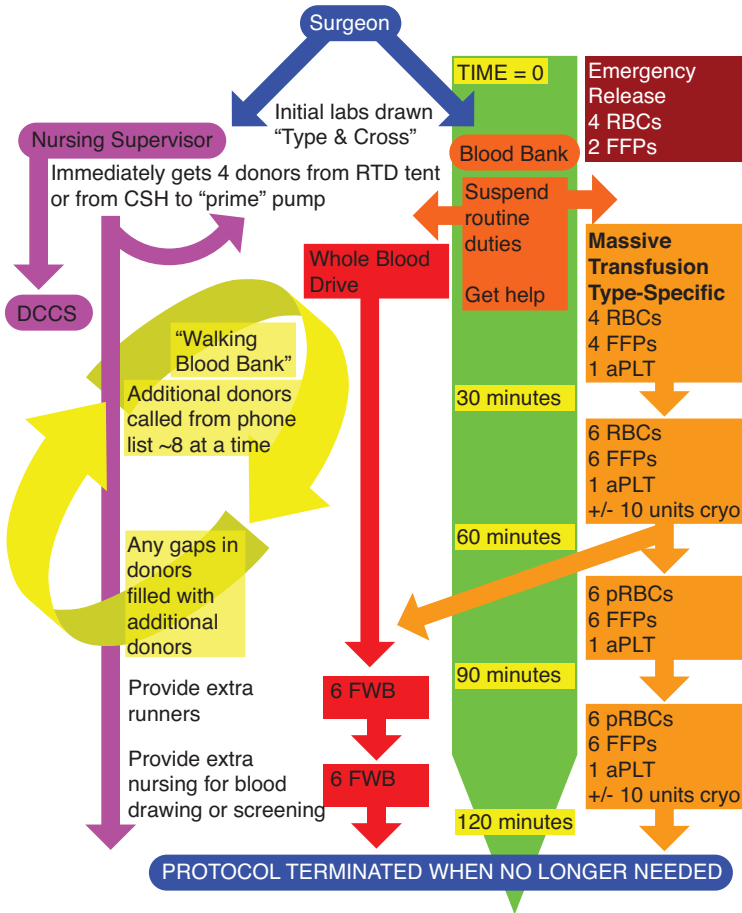
- Massive transfusion has been defined in various ways, but the most common definition is the need for **≥10 U of blood in 24 hours**. (This is based on the estimate of 1 blood volume for an average adult male. Small individuals and pediatric patients have a lower blood volume that should be considered when deeming a patient as needing a massive transfusion.)
- **Survival in massively transfused combat casualties is higher in patients who are transfused with increased amounts of plasma and platelets.** Based on these observations, prior to definitive surgical control of bleeding, massively bleeding patients should be transfused in fixed ratios of blood products aiming at a ratio of **6 RBCs:6 FFPs:1 aPLT**. It is reasonable to consider transfusing 10 U of cryoprecipitate along with this ratio.
- **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.
- If platelets or plasma are unavailable, **type-specific fresh whole blood** (which provides all the blood components in a fixed ratio) should be collected and transfused to provide these critical components.

- **Survival in massively transfused combat casualties is higher in patients who are transfused with increased amounts of plasma and platelets.**
- **Crystalloid use should be minimized to avoid dilution.**
- **Goal blood pressure is systolic blood pressure ~90 mm Hg (in patients without central nervous system injury) until surgical control of bleeding is established.**
- **Blood products should be transfused with a goal ratio of 6 RBCs:6 FFPs:1 aPLT.**
- **If plasma or platelets are unavailable, type-specific fresh whole blood should be collected/transfused.**

### 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 RBCs 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 33-3.
  - Currently, the goal during resuscitation is normalization of body temperature, 37°C.



**Fig. 33-1.** Combat surgical 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; pRBCs: packed red blood cells; RBCs: red blood cells; RTD: return to duty.

- **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.
- 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 standstill.
  - 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 33-3.
- **Hypocalcemia** occurs in massive transfusion due to the citrate (anticoagulant) in plasma and platelet products. Under normal physiological conditions, citrate is rapidly metabolized by the liver. Metabolism can also be overwhelmed by rapid infusion of plasma-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.
  - If labs are not immediately available, 1 amp of calcium chloride should be administered with every 8 units of plasma.

**Table 33-3. Management/Prevention of Complications of Massive Transfusion**

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**Hypothermia**

- Prehospital active/resistive warming with hot packs/heating blankets
- High-capacity fluid warmers
- Warmed trauma suites/operating rooms
- Forced-air warming blankets
- Warmed/humidified oxygen
- Limit surgical exposure (eg, damage control techniques)

**Acidosis**

- Restoration of adequate tissue perfusion
- Sodium bicarbonate

**Hyperkalemia**

- Transfuse fresher blood (<14 days)
- Transfuse blood from lines farther away from the right atrium
- Calcium chloride (1 amp) to stabilize the myocardium
- Shift extracellular potassium into the intracellular space
- Correction of acidemia/alkalinizing solutions
- Regular insulin 10 units with 1 amp (50 mL) 50% dextrose
- Inhaled beta-agonists

**Hypocalcemia**

- Calcium chloride (1 amp) based on measurement of serum ionized calcium levels or with every 8 units of plasma

**Coagulopathy/Microvascular Bleeding**

- Goal temperature > 37°C
- Goal pH > 7.2
- Goal ratio of transfused blood products of **6 RBCs:6 FFPs: 1 aPLT**.
- Type-specific fresh whole blood should be used if some or all of these blood products are unavailable
- rFVIIa 7.2 mg IV if persistent microvascular bleeding, despite other measures

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aPLT: apheresis platelet; FFPs: fresh frozen plasmas; RBCs: red blood cells; rFVIIa: recombinant factor VIIa.

- **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.
  - 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 due to the addition of preservative solutions to stored blood products following collection. Transfusion of stored 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  $80 \times 10^9/L$ .
  - Limit 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 blood products.
    - ◆ If blood products are not available, volume replacement with 6% Hetastarch (Hextend) 500–1,000 mL can be considered to achieve goal systolic blood pressure ~90 mm Hg.
  - Recombinant factor VIIa (rFVIIa) can reduce blood loss in blunt trauma, although its benefit is less clear for penetrating trauma. The off-label use of rFVIIa (100  $\mu\text{g}/\text{kg}$  or 7.2 mg) is still considered controversial, and should only be used with sound clinical judgment and after optimal management of hyperthermia, acidosis, and dilutional coagulopathy.
  - If rFVIIa is used, adequate platelet counts and fibrinogen levels are necessary (managed with transfusion) prior to rFVIIa administration; otherwise, it will be much less effective.

- In stabilized patients, standard transfusion thresholds should be adopted for patients.
  - **RBC transfusion.**
    - ◆ Hemoglobin <7.0 g/dL.
    - ◆ Hemoglobin <9.0 g/dL with anticipated blood losses from planned surgery.
    - ◆ Hemoglobin <10.0 g/dL for patients with myocardial ischemia.
  - **Plasma transfusion.**
    - ◆ No bleeding or planned invasive procedures: No specific transfusion trigger.
    - ◆ Active bleeding or planned invasive procedure: Transfuse for prothrombin >18.0 or International Normalized Ratio >1.5.
  - **Platelet transfusion.**
    - ◆ Platelet count <50 with active bleeding or for invasive procedures: Higher for neurosurgical injuries as directed by the surgeon.
    - ◆ Platelet count <30 for patients requiring therapeutic anticoagulation (with heparin or Coumadin).
    - ◆ Platelet count <20 for febrile or “ill” patients.
    - ◆ Platelet count <10.

### **Emergency Collection of Fresh Whole Blood in the Field (“Walking Blood Bank”)**

- Fresh whole blood collection should be reserved for when standard blood products are exhausted or unavailable (eg, when aPLTs are unavailable to support a massive transfusion at Role 2).
- Current Clinical Practice Guidelines and Department of Defense (Health Affairs) policy for the use of fresh whole blood in theater also include that fresh whole blood can be requested on clinical grounds when other blood products are unable to be delivered at an acceptable rate to sustain the resuscitation of an actively bleeding patient, or when stored components are not adequately resuscitating a patient with an immediately life-threatening injury.
- Emergency collection and transfusion of fresh whole blood should not be performed at Role 1. For Roles 2 and 3, fresh

whole blood collection should not be performed in lieu of securing blood products through normal channels.

- **Risks:** Even with soldiers who are immunized against hepatitis B virus (HBV) and screened for human immunodeficiency virus (HIV) predeployment, there is a real risk for transmission of hepatitis C virus (HCV), HIV, syphilis, human T-cell leukemia virus I/II, and endemic diseases (eg, malaria, dengue, and leishmaniasis). Additionally, cases of transfusion-associated graft-versus-host disease (a fatal, although rare complication) have occurred following fresh whole blood transfusion.
- Despite these potential risks, fresh whole blood is a **LIFESA-VING** product that should not be withheld when standard blood components are **unavailable**.
- Fresh whole blood **must be ABO type-specific** to the patient.

Trying to collect blood at a time of extreme emergency, with little time, is very difficult and stressful. It cannot be mastered for the first time on actual casualties. Emergency fresh whole blood collection at best takes 30–45 minutes from request to its availability at bedside. It requires coordination between clinicians, nursing staff, and the blood bank. Variations will exist depending on blood product inventory, frequency of resupply, availability of donors, size and capability of medical unit, number of personnel (in clinical areas, as well as in the lab/blood bank), casualty flow, and mass casualty situations. Planning and hands-on training are critical. The medical unit should practice with realistic training exercises, including mass casualty situations, to walk through/simulate the entire process. The boxed information that follows below and on the next few pages is a template to organize an emergency fresh whole blood collection program that will need to be individualized to the specific tactical situation and environment:

### 1. Clinical Determination of the Need for Fresh Whole Blood

- When will we use it?
  - Only to provide platelets during massive transfusion because aPLTs are unavailable? (at Role 2)

- Only for mass casualty situations because of small inventory? (at Role 2 or 3)
  - Only to manage low inventory of type O blood because of the need to reserve for emergency release? (Role 2 or 3)
  - Will providers be able to request if they clinically determine that standard blood products are not adequate for resuscitation?
  - How often do we anticipate the need to collect fresh whole blood?
  - How early do I need to initiate a fresh whole blood drive?
    - How long will it take to get fresh whole blood? 45 minutes or several hours?
    - Do I have a process in place to facilitate ordering from the ER, as well as from the OR and ICU?
- 2. Request/Notification for Emergency Collection of Type-Specific Fresh Whole Blood**
- Who is authorized to initiate a whole blood drive?
    - Surgeon?
    - Deputy Commander for Clinical Services (DCCS) and/or Hospital Commander?
    - Blood Bank Director?
  - Who must be contacted to initiate the process (to mobilize resources)?
    - Nursing Supervisor and/or Deputy Commander of Nursing (DCN)?
    - Blood Bank Director/Lab Director?
    - Hospital S-3 to announce the blood drive outside the hospital?
- 3. ABO Typing of the Casualty**
- Who will perform ABO Rh typing, and how long will it take to get a result?
    - Dog tags are only a last resort because they cannot be relied on. Dog tags have a 3% error rate in either ABO or Rh, and civilian casualties will not have known ABO Rh.
- 4. Identification of Potential Donors**
- Who will be available to donate?

- Medical Personnel—usually only to start the process / provide the first couple of donor units.
- Soldiers awaiting return to duty—if holding area for healthy troops awaiting return to duty is available.
- Local troops—if US soldiers are reasonably close by to be called on to provide donors.
- How will we notify / request donors?
  - Overhead announcement in the hospital?
  - Runner to go to the “return-to-duty” area to ask for volunteers?
  - Tactical communications to local military units?

#### **5. Screening of Donors**

- Will we only have blood type screening with dog tags (3% error rate in either ABO or Rh)?
- Can we establish in advance formal ABO Rh typing and a donor roster?
- Do we have donor screening questionnaires readily available?
- Where will we screen with donor questionnaires? (History of IV drug use, history of hepatitis, history of high-risk sexual behavior, recent febrile illness, use of aspirin or NSAIDs [nonsteroidal antiinflammatory drugs] within the last 72 hours.)
- Will we need to modify donor screening to account for endemic diseases (eg, malaria, dengue, or leishmaniasis)?
- Do we have or can we get “pedigree” donors with recent testing for transfusion transmitted viruses?
- If donor roster is created, who will keep this roster up-to-date with changes in personnel and when they last donated (can only donate once every 8 weeks)?

#### **6. Collection of Fresh Whole Blood**

- Do we have the current / standard SOP on Emergency Whole Blood Collection from the theater Blood Program Officer?
- Do we have the necessary equipment, such as the CDPA-1 blood collection bags (equipment listed in SOP)?
- Are there limits to the amount of blood collected because of high altitudes?

- Where will we physically collect blood? Beds? Cots? Chairs?
- How many donors can we collect at a time?
- Where will donors rest after donation?
- Repeat donors should receive iron supplementation. Who will order it for them?
- Are there limits to the number of soldiers from a single unit who can donate? (Performance may be impaired by donation. Large numbers can lead to increased unit ineffectiveness.)

### **7. Processing of the Collected Unit**

- ABO confirmation.
- Unit labeling.
- Rapid screening for infections (pretransfusion): Currently for HIV 1/2, HBV, and HCV.
- Write the expiration of the unit, which is 24 hours from collection. Keep the product at room temperature (20°–24°C) because platelets become inactive in whole blood stored cold.
- Recording of data in the blood inventory and disposition records. (If units are not transfused, input donor information and disposition as “Destroyed/Expired.”)
- Management of units with positive rapid screening for HIV, HBV, or HCV.
  - Destroy unit and place donor on deferral list.
  - Inform Community Health Nurse of positive screening and confirmatory donor infectious disease results.
  - Inform the Blood Program Officer of any donors with a confirmed positive infectious disease marker where the patient received the donor’s blood.
  - Notify donor to seek follow-up with healthcare provider on positive test results and not to donate blood or blood products.
- Process in place to send segments to CONUS for posttransfusion infectious disease testing.

### **8. Release of Fresh Whole Blood to Bedside**

- Additional runners and nursing staff will be needed. Where will they come from?



- Who will run the fresh whole blood to the ER/OR/ICU?
- Will additional standard blood components, such as RBCs and FFP, also be issued if they are available? Will only fresh whole blood be used once a whole blood drive has been initiated?

#### 9. Monitoring of Ongoing Requirements for Fresh Whole Blood

- Who will coordinate with the clinicians to communicate to the blood bank and collection area how many and how fast additional units are needed?

#### 10. Cessation of Fresh Whole Blood Collection

- Who will determine that fresh whole blood is no longer needed (ie, the patient has stabilized or ongoing resuscitation is futile)?

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aPLTs: apheresis platelets; CONUS: continental United States; CPDA-1: citrate-phosphate-dextrose-adenine; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; SOP: standard operating procedure.

### 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.

#### Treatment Plan for Transfusion Reaction

- STOP the transfusion.
- Assess the patient: review vitals and auscultate lungs. If patient is conscious, ask about subjective complaints.
- If fever and unexplained hypotension, consider **ABO mismatch** and **bacterial contamination/sepsis**.
- 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 **allergic 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 reactions is clerical error that occurs outside of 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:
  - **Fever.**
  - **Inappropriate hypotension.**
  - **Tachycardia.**
  - **Dark urine (reflecting hemoglobinuria).**
  - **Renal failure.**
  - **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.
- 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 generally develops rapidly (from minutes to a few hours) after initiation of an ABO incompatible red blood cell transfusion.

### **Acute Hemolytic Transfusion Reaction Treatment**

- Stop transfusion and clearly mark the suspected unit.
- 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.
- Annotate field medical card or 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.
- Platelets carry the highest risk for bacteremia/sepsis because they are stored at room temperature for up to 5 days.
- If fever and hypotension develop during or immediately following a transfusion of 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 or with acetaminophen prior to transfusion (unlikely to mask fevers from hemolytic reactions or bacterial contamination).
- 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.
- Whole blood, platelets, packed RBCs, and FFP are most commonly implicated.
- 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).
  - 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.
  - A key feature of TRALI is that noncardiogenic pulmonary edema 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.
- ◆ If volume status of the patient cannot be determined, administration of furosemide can be considered. If the clinical status of the patient does not improve with diuresis, then TRALI is more likely.
- 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.

### **Allergic Transfusion Reactions**

- Mild allergic reactions involve dyspnea, bronchospasm/wheezing, and/or abdominal pain (intestinal edema).
- More severe allergic 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 allergic 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://usaisr.amedd.army.mil/clinical\\_practice\\_guidelines.html](http://usaisr.amedd.army.mil/clinical_practice_guidelines.html)