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Trauma Resuscitation: The Use of Blood and Blood Products

Trauma is the most common cause of death for young people, with hemorrhage being a substantial cause of the mortality. The best resuscitative fluid and amount of fluid that is appropriate in the trauma setting is controversial. This issue explores the use of blood and blood products in a trauma resuscitation.

— Ann M. Dietrich, MD, Editor

Introduction

In the United States, trauma is the leading cause of death for people younger than age 45 years.[1] Hemorrhage is the second leading cause of mortality following injury, behind only traumatic brain injury.[2]

Classifications of shock have traditionally been defined by vital signs and physiologic parameters. Based on these definitions, the severity of shock can be determined prior to any laboratory data, and appropriate resuscitation can be initiated. The American College of Surgeons Committee on Trauma has defined the classes of shock as follows (*see Table 1*):

- Class I shock is characterized by 750 mL of blood loss or 15% of blood volume, pulse rate < 100, normal blood pressure, a normal or increased pulse pressure, urine output of > 30 mL/hour, slightly anxious mental status, and a respiratory rate of 14-20.
- Class II shock is characterized by 750-1500 mL of blood loss or 15-30% of blood volume, pulse rate 100-120, normal blood pressure, decreased pulse pressure, urine output of 20-30 mL/hour, mildly anxious mental status, and a respiratory rate of 20-30.
- Class III shock is characterized by 1500-2000 mL of blood loss or 30-40% of blood volume, pulse rate 120-140, decreased blood pressure, decreased pulse pressure, urine output of 5-15 mL/hour, anxious or confused mental status, and a respiratory rate of 30-40.
- Class IV shock is characterized by > 2000 mL of blood loss or > 40% of blood volume, pulse rate > 140, decreased blood pressure, decreased pulse pressure, negligible urine output, confused or lethargic mental status, and a respiratory rate of > 35.

Undifferentiated shock in trauma should be assumed to be hemorrhagic until proven otherwise. Hemorrhage represents 30-40% of mortality of trauma and may require significant volume to resuscitate.[2] Classic crystalloid resuscitation has been called into question because it is associated with a metabolic acidosis,[3,4] and blood components may offer a superior option to reverse shock. In this paper, the authors discuss the use of blood and blood products during a trauma resuscitation.

Resuscitative Goals: To What End?

While blood pressure is one of the most readily available measurements in the resuscitative environment, it may provide false reassurance of end organ perfusion. Markers that reflect tissue perfusion may facilitate initial assessment and

Executive Summary

- Undifferentiated shock in trauma should be assumed to be hemorrhagic until proven otherwise. Hemorrhage represents 30-40% of mortality from trauma and may require significant volume to resuscitate.
- One pre- and post-intervention of a massive transfusion protocol showed improved outcomes with the 1:1 FFP:PRBC transfusion protocol for critically ill trauma patients at 24 hours and 30 days, and lower bleeding complications, with 18% and 21% absolute mortality reduction, respectively.
- Rapid depletion of fibrinogen has been shown in patients with significant blood loss exceeding 20% of their calculated blood volume, and fits within the conceptual understanding of the mechanism of traumatic consumptive coagulopathy.
- If thromboelastography can identify specific functional deficiencies of the traumatic coagulopathy, one can adapt the massive transfusion to simultaneously reverse the coagulopathy and shock while limiting the exposure to harm from excessive utilization of blood components.
- The most common side effects associated with PRBC transfusions reported in the CRIT trial were fever (1.9%), fluid overload (1.7%), and hypotension (1%). A pooled meta-analysis showed that the risk of developing an infectious complication was 1.8 times more likely and ARDS 2.5 times more likely with transfusion of blood.
- Clinical findings of TRALI are tachypnea, cyanosis, frothy pulmonary secretions, dyspnea, hypotension, tachycardia, and fever within 6 hours of transfusion, although most cases occur within 1-2 hours.

monitoring of a patient's response to resuscitation. Goals for a successful response to therapy are as follows:[8]

- arterial lactate < 2
- urinary output > 0.5 mL/kg/hr
- hematocrit > 25%
- normal arterial base deficit.

One study found a base deficit > 8 mEq/L or lactate > 2.5 mmol/L was an independent predictor of developing multisystem organ failure (MSOF).[9] While those who achieve optimal markers of perfusion have a better survival rate, a landmark trial found age alone is the strongest predictor of whether a patient will respond optimally to resuscitation or not. Additional attempts to resuscitate to supranormal levels (i.e., systolic blood pressure > 100 mmHg, hematocrit > 30%, base deficit < 3, or urinary output > 1 mL/kg/hr) resulted in more blood components and inotrope utilization without improving mortality.[10]

Table 1. Shock Classification

Class I

- **Shock is characterized by 750 mL of blood loss or 15% of blood volume, pulse rate < 100, normal blood pressure, a normal or increased pulse pressure, urine output of > 30 mL/hour, slightly anxious mental status, and a respiratory rate of 14-20.**

Class II

- **Shock is characterized by 750-1500 mL of blood loss or 15-30% of blood volume, pulse rate 100-120, normal blood pressure, decreased pulse pressure, urine output of 20-30 mL/hour, mildly anxious mental status, and a respiratory rate of 20-30.**

Class III

- **Shock is characterized by 1500-2000 mL of blood loss or 30-40% of blood volume, pulse rate 120-140, decreased blood pressure, decreased pulse pressure, urine output of 5-15 mL/hour, anxious or confused mental status, and a respiratory rate of 30-40.**

Class IV

- **Shock is characterized by > 2000 mL of blood loss or > 40% of blood volume, pulse rate > 140, decreased blood pressure, decreased pulse pressure, negligible urine output, confused or lethargic mental status, and a respiratory rate of > 35.**

Permissive Hypotension in Penetrating Trauma

In the setting of trauma, the body's earliest response is an attempt to form a clot to stop hemorrhage. In penetrating trauma, a focal site of hemorrhage is likely, and preventing clot disruption can reduce the overall blood loss a patient has before hemorrhage control can be achieved. Elevated blood pressures may disrupt the clot. Therefore, in penetrating trauma, practice tolerates a lower blood pressure to protect the tenuous clot providing hemostasis.

This is of greatest value in

hemorrhagic lesions in which rapid hemostasis is more difficult to achieve, such as liver or pelvic fractures.[8] Resuscitative hypotension tolerates a systolic blood pressure between 70 and 90 until source control of hemorrhage has been achieved, generally in the operating room (OR).[8,11] The physiology underlying resuscitative hypotension strategies optimizes perfusion without blunting compensatory mechanisms or disrupting early hemostatic control from initial clot formation at the source of bleeding.

In studies, resuscitative hypotension did not result in worse outcomes for patients and prevented the use of higher blood component volumes transfused with no significant difference in incidence or severity of coagulopathy, anemia, or thrombocytopenia, while encouraging the preservation of native hemostatic mechanisms, such as early clot formation, until hemorrhagic source control can be achieved.[8] Lower volumes of resuscitative fluids may maintain physiologic mechanisms such as endogenous catecholamines and vasoconstriction to prevent the lethal triad of hypothermia, coagulopathy, and acidosis.[12,13] (*See Figure 1.*)

Traumatic brain injury should not be resuscitated with permissive hypotension, as studies excluded this population, and hypotension in traumatic brain injury may aggravate anoxic brain injury.[14]

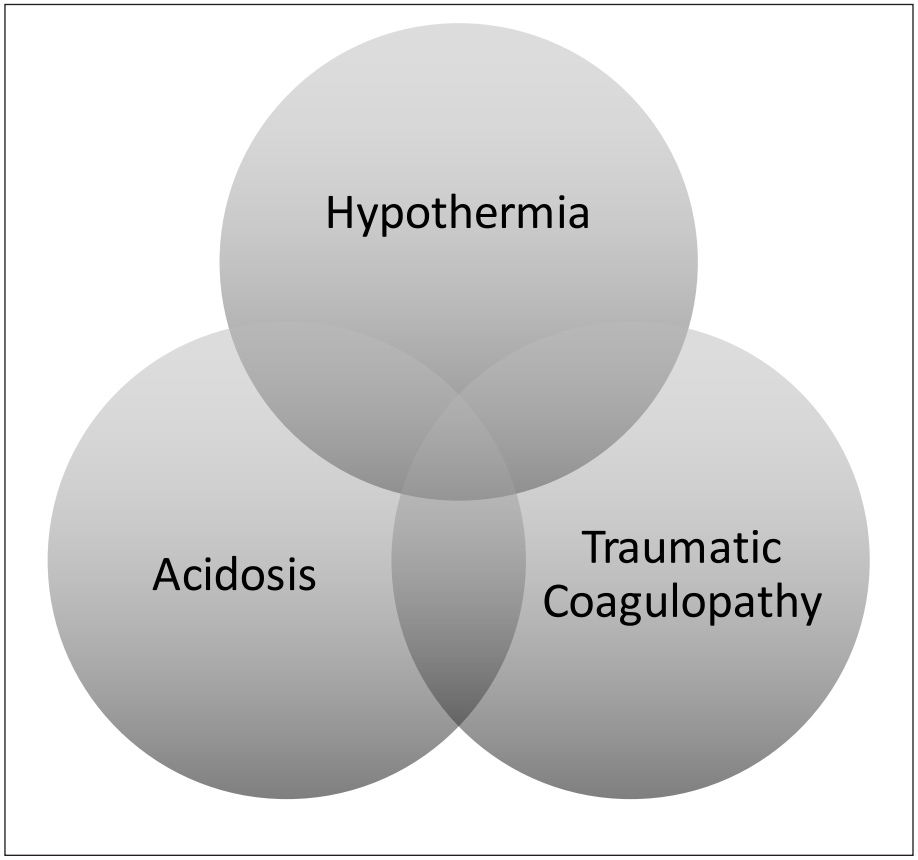
Traumatic Coagulopathy

Traumatic coagulopathy occurs in 25% of trauma patients.[6,15] The cause is multifactorial, including depletion and consumption of coagulation factors, dilution from resuscitative crystalloid, platelet dysfunction, and increased fibrinolysis ultimately compromising the coagulation system.[5,16,17] (*See Figure 2.*) Resuscitation should be tailored to restore function of the coagulation system, strengthen the clot, slow hemorrhage, replace volume losses, and improve oxygen delivery to tissues.[18]

The cell-based model defines three critical activation steps of primary hemostasis in trauma: initiation, amplification, and propagation.[19] The initiation phase of the traumatic coagulopathy is in response to endothelial injury exposing subendothelial prothrombogenic surface to platelets, which in turn form a loosely adherent plug. This plug acts as a catalyst for coagulation proteins: factor VII activates factors IX and X that convert prothrombin to thrombin. Thrombin subsequently activates factors V, VIII, and XI, amplifying the production of thrombin to sufficient levels to activate factor XIII, which forms fibrin cross-links to stabilize the clot.[18] This describes primary hemostasis in trauma with the initial clot formation of a "sticky platelet clot" on the endothelial surface at the site of injury.

This amplification of thrombin, however, also activates a counter-regulatory fibrinolytic process to prevent overactivation of the coagulation system. In normal settings, this breaks up fibrin to prevent excessive coagulation. In massive hemorrhage, the coagulation process capacity is overwhelmed and unable to maintain this balance, leading to the traumatic coagulopathy and uncontrollable hemorrhage associated with trauma.[17] Current evidence suggests that traumatic coagulopathy exists early in injury independent of clotting factor deficiency and may be a result of an injury complex triggered by tissue injury, cellular ischemia, dilution of clotting factors, hypocalcemia, hypothermia, acidosis, inflammation, and fibrinolysis, which the resuscitation should seek to reverse or contain early.[18]

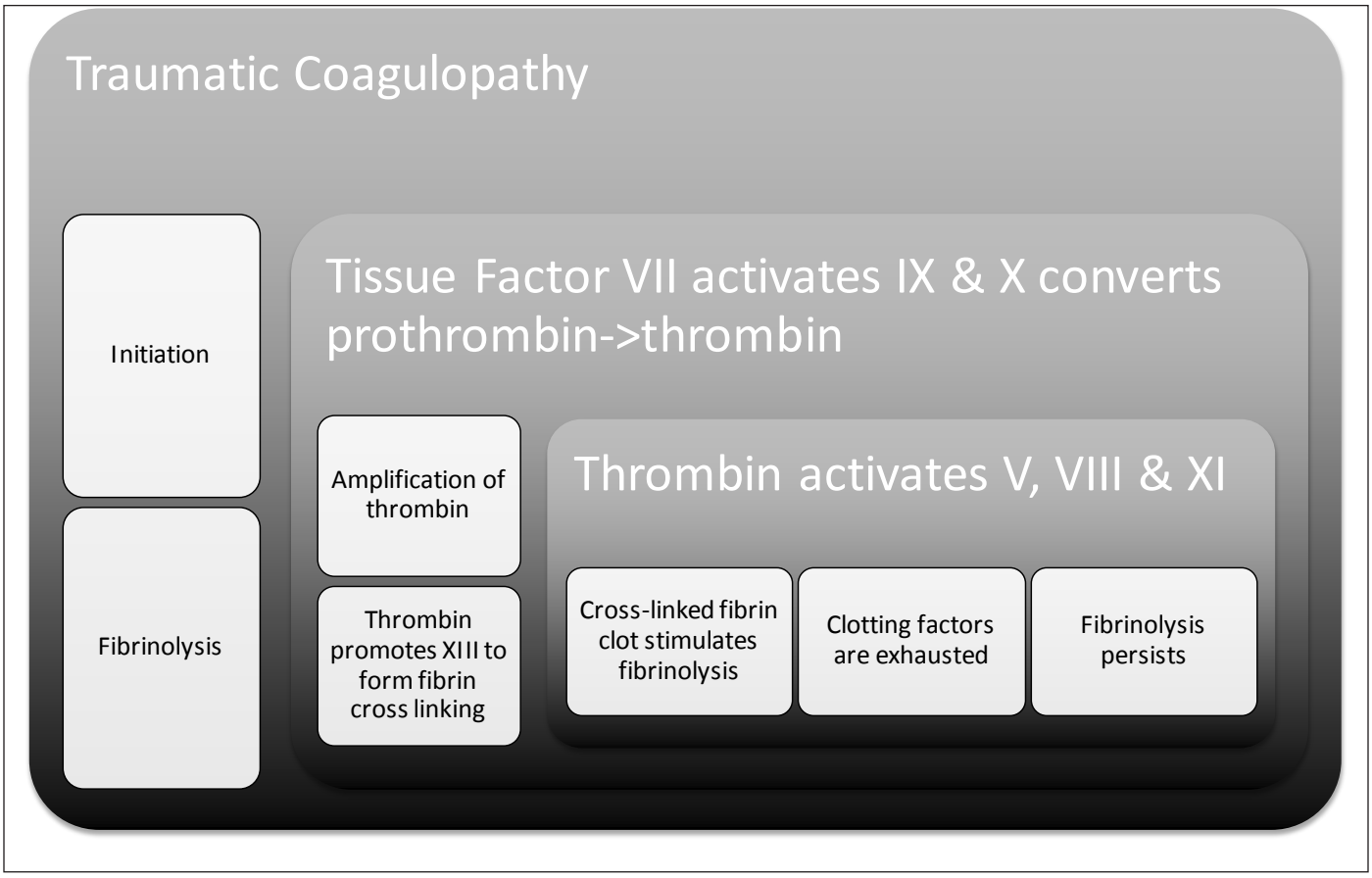
Figure 1. Lethal Triad



Balanced Resuscitation

Early in resuscitation, reversal of the traumatic coagulopathy improves patient outcomes and lessens the

Figure 2. Traumatic Coagulopathy



total blood components required. Trauma patients post-resuscitation had less coagulopathic problems in the ICU with early administration of higher plasma:PRBC ratios.[17,20,21] The likely benefit of plasma comes from replacing coagulation factors, which prevent or correct the coagulopathy that occurs in hemorrhage and shock. Rapid depletion of fibrinogen has been shown in patients with significant blood loss exceeding 20% of their calculated blood volume,[22] and fits within the conceptual understanding of the mechanism of traumatic consumptive coagulopathy.[17] Each unit of fresh frozen plasma (FFP) contains fibrinogen, and is an essential element of coagulation factor replenishment.[23] Plasma may also function as a buffer to help to counter the acidosis of traumatic shock.[7]

The literature is consistent that early reversal of traumatic coagulopathy improves outcomes. Recent literature has promoted a ratio between FFP to packed red blood cells (PRBCs) as close as possible to 1:1.9.[24-26] One study showed a survival difference of approximately 20%, with the majority of the difference occurring within the initial 6 hours and persisting through 30 days.[7] Another prospective, observational study showed no difference in mortality or ICU and hospital days,[27] while a third prospective cohort study showed that a high FFP:PRBC ratio (> 1:1.5) produced a significantly lower mortality risk within the first 24 hours in blunt trauma patients requiring more than 8 units of PRBC.[28] While the higher FFP:RBC ratio showed improved mortality, the study attributed this to reversal of traumatic coagulopathy and also found a higher incidence of ARDS. Other retrospective studies have shown a preferable FFP:PRBC ratio of 1:1 to 2:3 to improve mortality.[29] One of these studies showed an absolute mortality reduction of 55%.[30] One retrospective study of 252 soldiers receiving massive transfusion showed higher fibrinogen:PRBC ratios were independently associated with improved survival (odds ratio 0.37, $p = 0.013$).[23] While exact ratios are unclear, the evidence clearly supports that use of blood components in as close to a 1:1 to 2:3 FFP:PRBC ratio is preferable over crystalloid for the initial traumatic resuscitation. All studies to date are subject to survivor bias — those who receive the plasma survive long enough for it to thaw and become available.[31] To date, no prospective, randomized, controlled trial has investigated the optimal ratio; however, the PROPPR trial,[32]

a prospective, multi-center, randomized trial, is currently underway. While we await these results, the literature favors 1:1 FFP:PRBC ratios in those with massive PRBC transfusion requirements.[16,33]

The benefits of balanced transfusion show that the composition of blood components transfused in traumatic resuscitation may be as important as the volume itself. As soon as a patient is stabilized and hemorrhagic source control is achieved, one should attempt to avoid excessive transfusion of blood component therapy.[34]

Massive Transfusion Protocols

In an effort to pursue balanced resuscitation while avoiding overexposure to blood products and the associated risks, utilization of massive transfusion protocols (MTP) at many hospitals has been implemented for patients requiring in excess of 6-10 PRBC units. MTPs have decreased the incidence of transfusion-associated complications, reduced delays to activate massive transfusion protocols, reduced total volumes of blood products transfused, and improved patient mortality.[9,20,35-38] One pre- and post-intervention of a massive transfusion protocol showed improved outcomes with the 1:1 FFP:PRBC transfusion protocol for critically ill trauma patients at 24 hours and 30 days, and lower bleeding complications, with 18% and 21% absolute mortality reduction, respectively. The same study also showed a significant reduction in the incidence of traumatic coagulopathy.[20]

Research has sought to identify earlier the patients who require massive transfusion to improve the delivery of blood transfusion within the "golden hour" of trauma resuscitation.[39,40] The largest prospective, observational study of 1103 patients, identified the following variables that independently predicted the need for a massive transfusion (defined as greater than 10 units PRBC within the first 24 hours). Using regression analysis, they found significant correlation between systolic blood pressure (SBP) < 90 mmHg, SBP 90-120, free fluid in the peritoneum on FAST, clinically unstable pelvic ring fracture, and age older than 60 years increased the likelihood of requiring a massive transfusion.[41,42]

Thromboelastography (TEG)

The properties of an individual patient's ability to produce a clot can be assessed by thromboelastography,[43] allowing the resuscitation to adapt to a patient's coagulopathy. Additional research in trauma-associated coagulopathy advocates a resuscitation balancing blood components based on a specific patient's ability to form and maintain clot integrity using thromboelastography.[18,44,45] Thromboelastography assesses parameters of clot initiation, maximum strength, and rates of lysis in a more real-time manner to determine the strength and duration of clot in traumatic hemorrhage.[46] Resuscitation practices that have evolved to pursue a more physiologic balancing of blood components can now employ new laboratory data to tailor resuscitative strategies to the patient being treated.[18,46,47]

Existing laboratory coagulation studies were originally designed to evaluate for hemophilia and monitoring anticoagulation therapy. Furthermore, laboratory in vitro coagulation studies are buffered to a normal pH and a temperature of 37°C, which will not reflect the in vivo status of coagulation in a bleeding trauma patient.[17] Thus, these tests have not been proven in trauma and frequently take longer than is clinically useful for prompt correction of coagulopathy in traumatic resuscitations.[18]

Massive transfusion protocols have allowed for more rapidly balanced resuscitations and resulted in less total blood products, and, thus, fewer transfusion-related risks.[18,48] However, a predetermined ratio may result in higher proportionate use of FFP without benefit, as found in one center that combined TEG with their MTP.[29,43] While not statistically significant, this same center found a trend that their patients received less FFP in penetrating trauma than blunt trauma.[46] These findings support that massive transfusion protocols and TEG in trauma are not mutually exclusive but complementary.

Thus, in the appropriate population, a TEG tailored massive transfusion protocol resuscitation in trauma could theoretically offer real-time understanding of which blood product a patient needs next. If thromboelastography can identify specific functional deficiencies of the traumatic coagulopathy, one can adapt the massive transfusion to simultaneously reverse the coagulopathy and shock while limiting the exposure to harm from excessive utilization of blood components.[18,46-47]

Blood Components: Potential Harms

The above discussion has illustrated clearly that blood components have significant benefit in the appropriate ratios to resuscitate patients; however, these benefits are not without possible harms. All studies of blood component therapy suggest some immunomodulating effect as a possible cause of adverse outcomes. Collectively, they are known as Transfusion Related Immunomodulatory Response (TRIM), but the specific mechanism is not known. The risks associated with each blood component are discussed below. (*See Table 2.*)

Fresh Frozen Plasma and Cryoprecipitate

Fresh frozen plasma is the portion of blood that remains when whole blood is centrifuged and red blood cells removed. Each unit of FFP contains approximately 400 mg of fibrinogen.[23] Cryoprecipitate is the cold insoluble fraction formed when FFP is thawed at 4°C. Rich in factors VIII, XIII, vWF, and fibrinogen, the fibrinogen contained in one pooled cryoprecipitate pack is roughly equivalent to four units of FFP.

As the administration of FFP increases with the balanced blood component transfusions, so do the

Table 2. Blood Components and Potential Harms

Blood Component	Product Contents	Indications and Thresholds	Considerations and Volume	Complications
FFP	Contain all clotting factors	Most useful for traumatic coagulopathy	400 mg of fibrinogen Volume = 300 mL	Infectious and inflammatory complications
Cryoprecipitate	Contain factor 8, vWF, fibrinogen	Smaller volumes with focused delivery of specific clotting factors	250 mg of fibrinogen/ unit	Infectious and inflammatory complications
PRBC	Red blood cells improve oxygen-carrying capacity	TRIC trial transfusion threshold: hgb > 7.0 g/ dL TRACS and CCP establish threshold for cardiac patients hematocrit > 24%	Citrate solution can cause hypocalcemia. Cell lysis can cause hyperkalemia and acidosis. Volume = 250-330 mL	Fever, fluid overload, hypotension Infectious risk 4%/unit transfused
Platelets	Typically transfused in 6 packs of single-donor platelets	Function ultimately more important than total number	Thrombocytopenia occurs late in the course of hemorrhage	Most likely to cause TRALI

incidents of complications. A retrospective, case-control study showed an increased relative risk of infections with the transfusion of FFP, specifically severe ventilator associated pneumonia (VAP) (RR = 5.42), simple VAP (RR = 1.91), severe blood stream infection (RR = 3.35), simple blood stream infection (RR = 2.12), and undifferentiated sepsis (RR = 3.32).[49]

Platelets

Initially, ratios favored a higher ratio of platelet transfusion attempting to approximate ratios of components of whole blood.[7] However, this 1:1 ratio of platelets:PRBC has been criticized for excessive exposure to risk of transfusion-related adverse reactions, specifically Transfusion Related Acute Lung Injury (see below), and some have advocated a much reduced ratio of 1:5 for platelets:PRBC.[24,34] A significant relationship between platelet count and mortality from hemorrhage has not been shown,[6] and thrombocytopenia occurs late in the course of bleeding and massive transfusion.[50,51] The count itself may not be as relevant as the function, and this could be better assessed by thromboelastography.[18]

Packed Red Blood Cells (PRBC)

PRBCs are an important component of hemorrhagic resuscitation, as hemoglobin improves the blood's oxygen-carrying capacity to body tissues essential to maintain perfusion. PRBCs are the best initial transfusion to reverse shock, as they improve oxygen-carrying capacity while simultaneously providing volume that will not extravasate (in contrast to crystalloid) through permeable capillary membranes. In the initial trauma resuscitation, one should resuscitate to hemodynamic stabilization, hemorrhage control, and the physiologic end goals of resuscitation described above.

PRBC Side Effects

The accompanying fluid transfused alongside the red blood cells is by no means inert. The storage of blood exposes the red blood cells to "age lesions,"[52] leading to hyperkalemia with cell breakdown in some populations, and the anticoagulant citrate binds to the patient's calcium and may cause tetany, QT prolongation, and decreased myocardial contractility and should be monitored closely with an ionized calcium. Finally, the actual storage of blood leads to a pH of 7.0 in fresh units and decreases to 6.6 to 6.8 with age, which could in fact worsen acidosis.[13]

Another study examined 15,534 trauma patients over three years controlling for confounding shock variables and found transfusion to be an independent predictor of mortality with an odds ratio of 2.83 (1.82-4.40).[53] The risk of PRBC transfusions has been replicated in the CRIT trial, a prospective, multicenter, observational study among ICU patients showing PRBC transfusions were independently associated with worse clinical outcomes. The authors demonstrated a 15% increased incidence of death among those who received six or more units of PRBC as compared to those who received no transfusion.[54]

The most common side effects reported in the CRIT trial were fever (1.9%), fluid overload (1.7%), and hypotension (1%).[54] A pooled

meta-analysis showed that the risk of developing an infectious complication was 1.8 times more likely and ARDS 2.5 times more likely with transfusion of blood.[55] Another study found a 4% cumulative risk of infection for each unit of PRBC transfused.[49]

Complications of Transfusion

Aside from the risks associated with the specific blood components, complications of transfusing donor products can occur. Vigilance can assist with early recognition and management of these complications post-resuscitation. These complications broadly fall into the categories of pulmonary and hemolytic reactions, transmission of blood-borne pathogens, and problems associated with preparation and storage of blood products.

Transfusion Related Acute Lung Injury (TRALI)

Transfusion Related Acute Lung Injury (TRALI) is the leading cause of transfusion-related morbidity and mortality in the United States.[56] Clinical findings of TRALI are tachypnea, cyanosis, frothy pulmonary secretions, dyspnea, hypotension, tachycardia, and fever within 6 hours of transfusion, although most cases occur within 1-2 hours. Physiologic findings include PaO_2/FiO_2 ratios of < 300 mm Hg and decreased pulmonary compliance despite normal cardiac function. Chest radiographs will frequently show bilateral infiltrates.[48,56] Diagnosis is based on clinical criteria consistent with acute lung injury and treated similarly. In practice, it can be difficult to differentiate TRALI from Transfusion Associated Circulatory Overload (TACO), although a B-natriuretic peptide level more than 100 pg/dL and a post-transfusion to pre-transfusion ratio more than 1.5 can be suggestive of TACO over TRALI.[56] Generally, fluid management and volume adjustments are sufficient to address TACO.

TRALI is now the most frequent cause of transfusion-related mortality reported to the FDA. It is estimated to occur approximately 1 in every 5000 blood component transfusions, with mortality from 5-25%.[48,57] Two predominant theories exist. The first suggests the presence of leukocyte alloantibodies, cytokines, lipid or human leukocyte antigen (HLA) class I and II that accompany transfused blood components prime neutrophils and cause pulmonary damage.[48,58,59] The second theory suggests a predisposing condition such as surgery, trauma, infection, or proinflammatory event stimulates the release of cytokines and encourages neutrophils to attach to the vascular endothelium, particularly in the pulmonary capillaries. The second step is the same as the first theory except that the belief is that TRALI is a two-step process requiring the initial priming of the patient's baseline condition upon transfusion.[48,59,60]

FFP should be ABO typed as the first choice, but can be given to a different ABO group so long as it does not possess anti-A or anti-B activity.[58] Increasingly, the importance of HLA screening has been emphasized. The presence of leukocyte alloantibodies in donor plasma appears to contribute significantly to the development of the syndrome. Such alloantibodies develop most frequently in women after pregnancy and are entirely absent from male blood unless the patient has had prior transfusions. As a result, the United Kingdom has disqualified multiparous females from plasma donation, and the United States uses primarily males.[48,56,58]

The TRICC trial found an OR 1.5 (0.97-2.49) of developing TRALI with PRBC transfusion.[61] The largest retrospective study of 14,070 trauma patients found patients receiving 1-5 and 6-10 units of PRBC had an odds ratio of 1.70 and 2.24, respectively, to develop ARDS and TRALI. The study also found a 6% higher risk of ARDS for each unit of PRBCs transfused, although the ARDS group was more severely injured than the non-ARDS group prior to developing the syndrome. This same study found that receiving more than five units of FFP also had an odds ratio of 2.55 for development of ARDS.[62] High ratios of FFP:PRBC early in resuscitation were associated with almost a twofold higher risk of acute lung injury.[28] Additionally, a retrospective analysis focused on the incidence of TRALI in association with transfusions found FFP (OR = 2.48, 1.29-4.74) and platelets (OR = 3.89, 1.36-11.52) to be more likely than PRBCs to contribute to the development of TRALI.[63] Other series have found the following transfusion to be most contributory, in descending order of likelihood: whole blood platelets, FFP, PRBCs, whole blood, apheresis platelet concentrates, and intravenous immunoglobulin (IVIG).[48,60]

Hemolytic Reactions

Acute hemolytic transfusion reactions are estimated at approximately 1 in 76,000, and mortality related to transfusions at 1 in 1.8 million units transfused.[57]

Delayed hemolytic transfusion reactions are more common than acute reactions, occurring days after a transfusion, and they have an incidence of 1 in 6000 units transfused.[57] They frequently go unrecognized and are characterized by fever, declining hemoglobin, and mild jaundice. Delayed reactions occur when a patient previously sensitized by pregnancy or transfusion receives "incompatible red cells" because the low titer of circulating alloantibody escapes detection by pre-transfusion screening.

Transfusion-associated graft-vs-host disease occurs when immunocompetent allogeneic lymphocytes in transfused blood mount an attack against the host tissues. It occurs between 4 and 30 days after transfusion of any blood component. Diagnosis is suspected when circulating donor lymphocytes are identified in the recipient patient. It is confirmed by detecting donor DNA in the lab or biopsy specimen. Irradiating blood components with at least 25 Gy or chemophototherapy to inactivate donor T lymphocytes can reduce the incidence of transfusion associated graft-versus-host

disease. Nonetheless, if it occurs, treatment ranges from difficult to futile, with morality approaches 90% in full-blown syndromes.[57] Transfusion of FFP will not cause transfusion-associated graft-vs-host disease.[58]

Blood-borne Pathogens

Hepatitis C. In 1990, with the introduction of the first donor screening test for hepatitis C, the transfusion risk of transmission was 4%. Risk of hepatitis C is now calculated to be 1 case in every 1.5 million to 2 million transfusions.[57]

HIV. In 1987, among the known cases of HIV, 2% were from transfused adults. Since the implementation of donor screening, only 49 documented cases of transfusion-associated HIV transmission have occurred. The risk of acquiring HIV infection through blood transfusion is estimated conservatively to be one in 1.5 million.[64]

Bacterial contamination in PRBCs is 0.21 infections per million transfusions. Spirochetes do not survive in citrated blood.[57] The risks of platelet transfusion-associated septic reaction and fatality are 1 in 74,807 and 1 in 498,711 transfusions, respectively.[65]

Age of PRBCS

A recent 2012 meta-analysis reviewing the effects of older blood questioned the effects of age on stored blood.[52] A pooled meta-analysis of six studies with little heterogeneity showed a significant increase in multi-organ dysfunction (OR = 2.26 {1.56-3.25}) and pneumonia (OR = 1.17 {1.08-1.27}) with older blood (> 21 days on average). In another analysis of six papers on trauma patients, the pooled odds ratio of mortality for receiving older blood was 1.18 (1.02-1.35). The analysis showed that the use of "newer" blood would benefit one in 97 patients who received transfusions.

Leukoreduced PRBCS

In 2003, following universal adoption of leukoreduction in Canadian blood storage, Hebert showed a slight mortality benefit of 0.84% to leukoreduction, further suggestive of an immunomodulatory mechanism. This effectively equates to one life saved for every 120 patients who receive leukoreduced blood.[66] The study also showed a reduction in incidence of fever by 2.2%, and use of antibiotics for patients with the use of leukoreduced blood. Another study showed a cumulative risk of infection of 4% per unit of PRBC transfused.[49]

One study in western Europe showed an odds ratio of 1.37 increased mortality with blood transfusion in the ICU.[67] The next study by the same authors found no such increased mortality rate.[68] Both were prospective, multi-center, observational studies of 3534 and 1040 patients, respectively, and the authors attributed the leukodepletion of the transfused PRBC as the only difference supporting the immunomodulatory effect of PRBC units on mortality.[68] While leukoreduction offers benefit, considerable barriers to achieving a sufficient pool of leukodepleted blood globally exist without a significant enough benefit to pursue currently.

Special Populations

Post-resuscitation there are pre-existing conditions that may adjust the transfusion thresholds and end points of resuscitation. The landmark studies TRICC, CCP, and TRACS defined transfusion thresholds and special populations for whom higher hemoglobin levels are beneficial. Please note all these studies occurred after the initial resuscitation in stabilized patients. Moreover, a laboratory transfusion threshold should not exist in initial trauma with hemodynamic instability since the hemoglobin and hematocrit can take some time to equilibrate (even up to 24 hours).

ICU Patients. The landmark Transfusion Requirements in Critical Care (TRICC) established the safety of a hemoglobin level of 7.0 g/dL in critically ill hemodynamically stable patients. The trial randomized patients to a hemoglobin of 7.0 g/dL as a transfusion threshold as compared to the control group with a hemoglobin of 9.0 g/dL and found no difference in outcomes.[61] However, notable exclusions to the study included patients with active acute myocardial infarction.

Acute Myocardial Infarction. The Cooperative Cardiovascular Project (CCP) defined transfusion thresholds in stabilized patients with acute myocardial infarction. A cohort study of 78,974 patients who were 65 years of age or older and hospitalized with confirmed acute myocardial infarction showed transfusion was associated with a reduction in mortality with incrementally increasing hematocrit goals: hematocrit 24.0% or lower (OR 0.36 [0.15-0.83]), hematocrit 24.1-27.0 (OR 0.69 [0.47-1.01]), and hematocrit 27.1-30.0 (OR 0.75 [0.58-0.96]).[69] This is likely from compensatory mechanisms that redistribute coronary blood flow away from the endocardium during low hematocrit levels.[69]

Post-cardiac Surgery. The Transfusion Requirements After Cardiac Surgery (TRACS) randomized, controlled trial of 512 patients post-cardiac surgery randomized patients to a liberal and conservative transfusion goal of hematocrit > 30% and > 24%, respectively, and found no such protective effect of PRBC transfusion.[70] In fact, for each transfused unit, an increased risk of occurrence of respiratory complications (OR 1.27), infectious complications (1.20), and 25% increased likelihood of 30-day mortality, cardiogenic shock, ARDS, or renal injury requiring dialysis or hemofiltration were observed.[70] Since this is the only trial on post-cardiac surgery patients, many now utilize a hematocrit threshold of 24%.

Conclusion

Early reversal of the shock state with a targeted resuscitation can prevent the lethal triad — acidosis, coagulopathy, and hypothermia — and improve patient outcomes by restoring perfusion and reversing the coagulopathy of trauma.[5,6,7] While

blood component transfusion is not without risk, a variety of components in blood offer the ability to target specific functional deficiencies in a patient's ability to form and maintain a clot or achieve hemorrhage control.

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CME/CNE Questions

1. What is the current ratio of blood products in traumatic resuscitation recommended by the literature?
   A. 1 unit PRBC to 1 unit FFP
   B. 2 units PRBC to 1 unit FFP to 1 pack of single donor platelets
   C. 1 unit of PRBC to 2 units FFP to 1 pack of single donor platelets
   D. 1 unit of PRBC to 1 unit FFP to 2 packs of single donor platelets
2. Permissive resuscitative hypotension should occur in which of the following settings?
   A. penetrating trauma with hemorrhage from easily compressible sites regardless of when hemostatic control is achieved
   B. penetrating trauma in difficult to achieve hemorrhagic lesions such as the liver or pelvic fractures, regardless of when hemostatic control is achieved
   C. penetrating trauma with hemorrhage from easily compressible sites up to the point when hemostatic control is achieved
   D. penetrating trauma in difficult to achieve hemorrhagic lesions such as the liver or pelvic fractures up to the point when hemostatic control is achieved
3. Which of the following patient characteristics predicts the need for massive transfusion?
   A. hypotension (systolic blood pressure < 90)
   B. mechanism of injury
   C. chest injury
   D. no free fluid on the FAST
   E. age younger than 50
4. What is the leading cause of transfusion-related morbidity and mortality in the United States?
   A. transfusion-related acute lung injury
   B. pneumonia
   C. fluid overload
   D. hypotension
5. Which is *not true* regarding Transfusion Related Acute Lung Injury (TRALI)?
   A. Clinical findings include tachypnea, cyanosis, frothy pulmonary secretions, dyspnea, hypotension tachycardia, and fever within 6 hours of transfusion, PaO2/FiO2 ratios of < 300 mm Hg, and decreased pulmonary compliance despite normal cardiac function.
   B. Higher FFP:PRBC ratios are associated with a higher incidence of TRALI.

CNE/CME Objectives

Upon completing this program, the participants will be able to:

- discuss conditions that should increase suspicion for traumatic injuries;
- describe the various modalities used to identify different traumatic conditions;
- cite methods of quickly stabilizing and managing patients; and
- identify possible complications that may occur with traumatic injuries.

C. TRALI occurs with a frequency of 1 in 5000, with morality rates up to 25%.
D. B-natriuretic peptide level more than 100 pg/dL and a post-transfusion to pre-transfusion ratio more than 1.5 indicate TRALI is most likely.

6. Which of the following *inaccurately* describes the risks of blood-borne pathogens from packed red blood cells?
   A. Risk of hepatitis C transmission is 1 in 1.5-2 million transfusions.
   B. Risk of HIV transmission is 1 in 1.5 million transfusions.
   C. Bacterial contamination is 1 in 4.75 million transfusions.
   D. Spirochetes in particular can survive in citrated blood, making these the most common blood-borne pathogen from transfusion.

7. The role of TEG in trauma is best described by which of the following?
   A. TEG identifies when sufficient volume has replaced hemorrhagic losses.
   B. TEG assesses function of the coagulation system to guide a targeted resuscitation of blood components.
   C. TEG assesses oxygen delivery to accurately restore perfusion to end organ tissues.
   D. There is no role for TEG in trauma.

8. Traumatic coagulopathy occurs in trauma as a result of which of the following?
   A. exposure of blood to open air during hemorrhage
   B. mixing of foreign material with blood causes intravascular coagulopathy
   C. infection that occurs after resuscitation causing inability for clotting factors to function
   D. depletion and consumption of coagulation factors and increased fibrinolysis

9. Which of the following correctly describes the transfusion threshold for a patient with cardiac history?
   A. Patients with active cardiac ischemia or recent cardiac surgery should be transfused when their hemoglobin is < 10.0 g/dL or hematocrit < 30%.
   B. Patients with active cardiac ischemia or recent cardiac surgery should be transfused when their hemoglobin is < 8.0 g/dL or hematocrit < 30%.
   C. Patients with active cardiac ischemia or recent cardiac surgery should be transfused when their hemoglobin is < 7.0 g/dL or hematocrit < 21%.
   D. Patients with active cardiac ischemia or recent cardiac surgery should not be transfused, as they are at highest risk of developing volume overload.

10. Which of the following best describes platelets?
    A. Platelets should be transfused to keep above a threshold of 50,000 in hemorrhagic shock.
    B. Platelet function matters more than quantitative volume.
    C. The literature universally indicates platelets should be transfused at a 1:1:1 ratio of PRBC:FFP:platelets.
    D. Platelets carry the least risk of transfusion-related immunomodulatory effects.

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