Severe Trauma and Hemorrhagic Shock

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LESSON OBJECTIVES
Upon completion of this lesson, the reader should be able to:

1. Describe the classification of hemorrhage in trauma patients.
2. Define massive transfusion in trauma resuscitation.
3. Describe common patterns of clinical presentations of trauma hemorrhage.
4. Identify hypothermia as a major component of ongoing hemorrhage in trauma.
5. Explain the lethal triad in severe trauma.
6. Describe the coagulopathy of acute trauma shock.
7. Discuss the impact on acidosis with massive bleeding.
8. Explain damage control surgery and damage control resuscitation.
9. List all relevant blood products used in massive transfusion.
10. Discuss the necessity to implement a massive transfusion protocol.

Current Reviews for Nurse Anesthetists® designates this lesson for 1 CE contact hour in Clinical pharmacology/therapeutics.

Introduction
Severe trauma is the leading cause of mortality in patients under the age of 45. Two reasons account for the majority of these deaths: traumatic brain injury and hemorrhagic shock. Mortality can occur early, within 24 hours after severe trauma, or late, some days after the traumatic event. The most common cause of early mortality is exsanguination and the subsequent hemorrhagic shock; the mortality of patients who develop hemorrhagic shock is about 50% in the prehospital phase and nearly 80% in the operating room. In contrast, after the first 24 hours, traumatic brain injury replaces hemorrhage as the leading cause of trauma-related mortality. Early hypotension, the amount of hemorrhage, multiple organ failure and infection are all predictors of late mortality (Table 1). Early hypotension is defined as a systolic blood pressure less than 90 mmHg in the prehospital phase or in the emergency room. The amount of blood loss is the volume of hemorrhage as measured by blood pressure and the number of blood units replaced. Multiple organ failure is a direct consequence of protracted organ hypoperfusion. Infection mostly presents as sepsis or severe pneumonia with development of acute respiratory distress syndrome (ARDS).
Early resuscitation of severely traumatized patients is of paramount importance to assure the best possible outcome. Resuscitation comprises damage control surgery and damage control resuscitation. The trauma surgeon performs damage control surgery and focuses on surgical hemostasis. The surgeon's efforts are supported by damage control resuscitation, meaning the restoration of circulating intravascular volume. This includes the administration of blood products and the treatment of coagulopathy, acidosis, and hypothermia. In most cases, massive transfusion is necessary and a massive infusion protocol must be initiated to treat the impending hemorrhagic shock.

Classification of Hemorrhage

According to the American College of Surgeons, hemorrhage is broken down into the following four classes (Table 2):

- **Class I hemorrhage** involves loss of up to 15% of the circulating blood volume. There is typically no change in vital signs and fluid resuscitation is not usually necessary.

- **Class II hemorrhage** involves loss of 15-30% of the circulating blood volume. A patient is often tachycardic with a narrowing of the pulse pressure. Peripheral vasoconstriction ensues. Volume resuscitation with crystalloids is required. Blood transfusion is not typically required.

- **Class III hemorrhage** involves loss of 30-40% of the circulating blood volume. The patient's blood pressure drops, the heart rate increases, peripheral perfusion—such as capillary refill—worsens, and the mental status worsens. Fluid resuscitation with crystalloids and blood transfusion are usually necessary.

- **Class IV hemorrhage** involves loss of > 40% of the circulating blood volume. The limit of the body's compensation is reached making blood transfusion mandatory.

**Table 2**

<table>
<thead>
<tr>
<th>Classification of Hemorrhage</th>
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<tbody>
<tr>
<td>Class I hemorrhage blood loss &lt; 15%</td>
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<tr>
<td>Class II hemorrhage blood loss 15-30%</td>
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<tr>
<td>Class III hemorrhage blood loss 30-40%</td>
</tr>
<tr>
<td>Class IV hemorrhage blood loss &gt; 40% → blood transfusion mandatory</td>
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Patients with class IV hemorrhage are subject to massive transfusion.

Massive transfusion has been defined as the loss of 50% of the circulating blood volume in 3 hours or less. Another definition is the administration of more than 10 units of packed red blood cells (PRBC) within 24 hours. For example, a male patient with a hematocrit of 40% has a red blood cell (RBC) volume of 2000 ml, which is the equivalent of 10 units of PRBC.

**Early mortality is mainly caused by traumatic hemorrhage and traumatic brain injury or a combination of both.**

Clinical Presentation of Trauma Hemorrhage

Most trauma patients present to the emergency room with a mild or moderate trauma score corresponding to class I-III hemorrhage. These patients are usually in a hypercoagulable state. However, a small portion of patients suffer severe trauma and require massive blood transfusion (Class IV hemorrhage). This small segment of trauma patients accounts for 75% of the overall blood utilization and is typically hypocoagulable.

Evidence suggests that patients with severe trauma and massive hemorrhage have some coagulopathy when admitted to the hospital. This coagulopathy occurs very early in about 25% of admitted patients. This condition is referred to as acute coagulopathy of trauma shock (ACoTS). ACoTS is not a simple dilution coagulopathy that occurs in injured patients, but a complex problem with multiple factors. The key initiators to the process of ACoTS are shock and hypoperfusion. Besides early coagulopathy, shock causes acidosis and hypothermia. The combination of coagulopathy, acidosis, and hypothermia is called the lethal triad as illustrated in Figure 1. The lethal triad is associated with a significant increase of mortality.
Coagulopathy

Acute coagulopathy of trauma shock is characterized by activation of protein C and hyperfibrinolysis. As hemorrhagic shock advances, excessive activation of coagulation ensues. This results in the development of disseminated intravascular coagulation (DIC) and the exaggerated generation of thrombin and fibrin with consumption of platelets and coagulation factors.

In addition to the consumption of coagulation factors and platelets, coagulation factors are lost directly through hemorrhage. Frequently, early blood loss is replaced by crystalloids, colloids and (RBCs). This replacement promotes dilution of coagulation factors thereby further reducing the ability to form blood clots.

Even if fresh frozen plasma (FFP) has been ordered early in the treatment of hemorrhage, it takes about 20-30 minutes to thaw FFP before it can be infused. This delay may result in additional reduction in coagulation factors.

Acidosis

Hemorrhagic shock leads to hypoperfusion of body tissues, causing a switch from aerobic to anaerobic cellular metabolism because of the lack of oxygen transfer to the tissues. Anaerobic metabolism causes accumulation of lactic acid. This lactic acidosis induces a drop in pH and increases negative base excess values. Depending on the degree of base excess, acidosis is classified as mild, moderate, or severe acidosis (Table 3).

Acidosis impairs essential parts of the hemostatic process. Acidosis inhibits the activity of coagulation enzyme complexes on lipid surfaces. When pH is reduced from 7.4 to 7.0, the activity level of Factor VIIa is reduced by 90%, factor VIIa/tissue factor (TF) complex is reduced by 55%, and pro-thrombin activation by factor Xa/factor Va complex is reduced by 70%. Acidemia also leads to increased degradation of fibrinogen.

Increased levels of plasminogen activator causing hyperfibrinolysis further enhance dysregulation of coagulation. Thus, blood clots once formed may be dissolved again and contribute to ongoing bleeding. Furthermore, acidosis contributes to a change in the shape of platelets. Thrombocytes become spherical and lose their pseudopodia. This change causes an impaired capacity of platelets to adhere to vascular injuries.

Overall, acidosis causes an impairment of thrombin formation, which can be seen as one of the major reasons for the ongoing coagulopathic bleeding. It is important to note that correction of acidemia per se does not reverse the coagulopathy.

Markers for late mortality are early hypotension, volume of hemorrhage, multiple organ failure, and infections such as pneumonia and sepsis.

Hypothermia

Hypothermia, which occurs frequently during severe trauma, is associated with an increased risk of uncontrolled bleeding and increased mortality. Hypothermia impairs platelet function, including platelet adhesion, aggregation, and thrombin generation. In addition, the function of enzymes involved in the coagulation cascade is reduced by 10%, when the temperature drops by 1°C.

Also, fibrinolysis is altered in a temperature-dependent manner. In elective surgery, blood loss is increased by 16% during mild hypothermia (35°C). In contrast to acidosis-related coagulopathy, bleeding problems secondary to hypothermia are reversible with normalization of the temperature. This suggests that inadvertent hypothermia should be prevented and treated aggressively.

Damage Control Resuscitation

Patients with life-threatening hemorrhage should be identified as early as possible. Typically, these patients have penetrating and blunt trauma. Trauma can occur in the abdominal cavity or the
with major extremity trauma always triggers massive hemorrhage, and coagulopathy are subject to damage control surgery and damage control resuscitation. Often patients present with inaccessible major anatomic injury and the need for time-consuming procedures concomitant with major injury outside the abdomen. This acute state prompts damage control surgery as part of the resuscitation efforts.

Three Components of Damage Control Resuscitation

Three components comprise the resuscitation efforts. First, an abbreviated resuscitative laparotomy or thoracotomy for control of bleeding is undertaken. This procedure is followed by restitution of blood flow where necessary and simultaneously there is an ongoing effort to control contamination. The primary surgery should be achieved as quickly as possible without spending unnecessary time on traditional organ repairs that can be deferred to a later time. The abdomen, thorax, or both are packed, and temporary closure is performed. After hemodynamic and metabolic stabilization, the patient is taken back to the operating room for removal of packs and definitive surgical repair. When the patient is admitted to the emergency room, damage control resuscitation is started immediately and continues throughout surgery and postoperative critical care.

The damage control resuscitation performed by the anesthesia provider in the operating room consists of two components: hypotensive resuscitation and hemostatic resuscitation.

The lethal triad consists of hypothermia, acidosis, and coagulopathy and is associated with a significant increase in mortality.

Hypotensive Resuscitation. During hypotensive resuscitation, low volumes of fluids are administered to achieve a safe but below normal blood pressure until operative control of bleeding can be established. The goal is to minimize rebleeding by avoiding dislodging newly formed blood clots while tissue perfusion is maintained. This process is also referred to as permissive hypotension. However, the low-volume approach has its limits. It is contraindicated in traumatic brain injury and spinal injuries. Likewise, elderly patients and patients with chronic hypertension might not tolerate permissive hypotension.

Hemostatic Resuscitation. Hemostatic resuscitation is started simultaneously with hypotensive resuscitation. It involves aggressive delivery of blood products, which begins prior to any laboratory-defined anemia or coagulopathy. Blood components are given early in the resuscitation process to restore both perfusion and normal coagulation function, while minimizing crystalloid use. Restricting infusion of crystalloids prevents further dilution of already deficient coagulation factors.

The following blood components must be available to successfully perform massive transfusion: red blood cells (RBCs), fresh frozen plasma (FFP), platelet concentrate, cryoprecipitate, and, under certain circumstances, factor VII(a). As an alternative to blood components, whole fresh blood can be infused. Auto-transfusion devices like cell savers are useful to reduce the transfusion of allogenic RBCs.

Damage control resuscitation is performed by rewarming the core, by correcting the acid-base imbalance, by correcting the coagulopathy, and by optimizing the ventilation and hemodynamic status.

Blood Components for Massive Transfusion

Red Blood Cells. RBCs are the most utilized component during massive transfusion. RBCs have a hematocrit of about 55% and a volume of about 355 ml. If time allows, RBCs should be typed and crossed for the patient. If transfusion must be started immediately, O negative blood should be administered. RBCs are stored at refrigerator temperatures. Thus, they need to be rewarmed during transfusion. All rapid infusion devices used during massive transfusion automatically warm blood components to core body temperature. This prevents further aggravation of inadvertent hypothermia.

The primary functional role of RBCs is to serve as an oxygen carrier to the tissues due to their content of hemoglobin. Erythrocytes also play an important role in hemoostasis. They allow for marginalization of platelets towards the capillary wall and endothelium. They also modulate the functional responsiveness of activated platelets and support thrombin generation.

A hemoglobin value of 7-9 g/dL (70-90 g/L) should be maintained during massive transfusion. In patients with a history of cardiac disease, the transfusion trigger should be set at hemoglobin values < 10 g/dL (100 g/L).

Fresh Frozen Plasma Each unit of FFP comes at a volume of 200 mL. FFP contains all clotting factors, including fibrinogen. FFP must be compatible with A, B, and O blood types; AB is the universal type since it lacks anti-A and anti-B antibodies.

FFP is stored at -30°C. It takes about 20 minutes to thaw a unit of FFP to get it ready for use. After thawing, the activity of labile clotting factors (such as factor V and VIII) decline gradually. FFP...
can be thawed and stored at 4°C for 24 hours to be available for immediate use without losing most of its hemostatic capacity.

**Platelets.** Thrombocytes are offered as random donor platelets, which are pooled from multiple donors, or single donor platelets separated by apheresis; the volume of a single donor unit equals the volume of 4-6 units of random donor platelets.

Platelets are stored at room temperature and are stirred during storage to prevent clotting. Platelets have a very short shelf life of five days. Each six pack of random donor platelets or one apheresis unit will increase the platelet count by about 20,000/μL, provided there is no further blood loss. A platelet count of more than 50,000/μL should be the goal during massive transfusion. Thus, the transfusion trigger for platelets should be a platelet count below 50,000/μL. Below this, platelet function decreases exponentially. If degradation products are increased or if there is evidence of DIC, a platelet count below 75,000/μL should act as transfusion trigger. Patients with concomitant traumatic brain injury should be given a transfusion if their platelet count is less than 100,000/μL.

Current data suggest to use a FFP:RBC:platelet:cryoprecipitate ratio of 1:1:1:1 in massively transfused patients.

**Fibrinogen (Cryoprecipitate).** Fibrinogen is a protein normally synthesized in the liver. Fibrinogen plays a crucial role in the final steps of the coagulation process. During progressive blood loss, fibrinogen appears to represent the coagulation factor first reaching a critical low threshold level. The decrease in fibrinogen may emerge before the development of significant thrombocytopenia. In addition, hemodilution with colloid plasma expanders predisposes patients to the development of a functional fibrinogen deficiency.

Cryoprecipitate is derived from pooled human plasma. It contains factor VIII, fibronectin, von Willebrand factor, factor XIII, and fibrinogen. Cryoprecipitate will raise critical levels of fibrinogen during massive bleeding. Ten single bags of cryoprecipitate derived from units of whole blood typically raise the patient’s plasma fibrinogen level by 60 to 100 mg/dL (1.8 to 2.9 μmol/L).

Typically, 10 units of cryoprecipitate are administered during massive transfusion. Repeat doses are guided by laboratory assessment of fibrinogen levels.

**Recombinant Factor VIIa.** Factor VII is one of the central proteins in the coagulation cascade. Factor VII is produced in the liver and is Vitamin K dependant. The role of factor VII is to initiate the process of coagulation (the extrinsic pathway) in conjunction with tissue factor (TF). TF is found on the outside of blood vessels so it is normally not exposed to the bloodstream. When a vessel injury occurs, factor VII binds to TF and is activated to factor VIIa.

Factor VIIa is used in treatment of massive hemorrhage. It is effective in reducing blood transfusion requirements modestly in blunt trauma cases. In combat casualties with massive transfusion requirements, the early use of factor VIIa was associated with decreased transfusion requirements.

The rationale for the use of factor VIIa in hemorrhage is that it will only induce coagulation in those sites where TF is also present. Using factor VIIa during massive transfusion is an off-label treatment. However, this treatment has been implemented in both military and civilian massive transfusion protocols. The indication in trauma centers may thus be major bleeding persisting in blunt trauma despite standard attempts to control bleeding and best-practice use of blood components. When the administration of factor VII is considered (see Table 4), platelet levels should be >50,000/μL and fibrinogen levels should be at least 50 to 100 mg/dL (1.5 to 2.4 μmol/L).

**What Is the Optimal Ratio of Blood Products in Massive Transfusion?**

Historically, patients with major bleeding from traumatic injury were treated with an FFP to RBC ratio of 1:3. FFP was recommended if the PTT was 1.5 times the control value or the INR was > 2. The initial recommended dose was 10-15 mL/kg FFP. In addition, crystalloids and colloids were given in large quantities.

Although there are no prospective, randomized controlled trials about the optimal ratio of blood products available, a large number of retrospective analyses in civilian and military trauma patients has demonstrated an increased survival rate with higher ratios of FFP to RBC (FFP:RBC). Since then, transfusion guidelines suggest an “aggressive” ratio of 1:1 (FFP:RBC). This ratio is complemented by one unit

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<thead>
<tr>
<th>Table 4</th>
<th>Factor VIIa Can Be Used If</th>
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<tbody>
<tr>
<td>- Surgical approach is promising to stop surgical bleeding</td>
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<tr>
<td>- Best-practice use of blood products is warranted with RBCs, platelets, FFP, cryoprecipitate/fibrinogen resulting in:</td>
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<tr>
<td>- Hct above 24%</td>
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<tr>
<td>- Platelets &gt; 50,000/μL</td>
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<tr>
<td>- Fibrinogen &gt; 50 to 100 mg/dL (1.5 to 2.4 μmol/L)</td>
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of pooled platelets and 10 units of cryoprecipitate. All blood products should be given early in the course of damage control resuscitation. At the same time, the administration of crystalloids should be minimized. Factor VII is very expensive and should only be used in a civilian setting when all other blood products have been given and surgical bleeding is controlled, but a coagulopathy continues.

**Massive Transfusion Protocols**

Groups that have developed a massive transfusion protocol (MTP) for severe hemorrhage report that an algorithmic, proactive, multidisciplinary approach is more effective than treatment based on the case-by-case discretion of each provider. Several articles have compared transfusion practices before and after implementation of an MTP. Some articles showed a clear decline of mortality, while others did not. Despite this controversy about a reduction in mortality after severe hemorrhage, it seems prudent to implement an MTP, because blood product use and blood bank charges decrease significantly after MTP implementation. This finding may be a consequence of a more rapid and organized delivery of blood products, which may lead to more rapid control of coagulopathy and decreased volumes of crystalloids. See Table 5 for a simple example of an MTP.

**Table 5**

<table>
<thead>
<tr>
<th>Example of a Massive Transfusion Protocol (MTP)</th>
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<tr>
<td>• 6 units of plasma</td>
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<tr>
<td>• 6 units of PRBCs</td>
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<tr>
<td>• 6 packs of platelets</td>
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<td>• 10 units of cryoprecipitate</td>
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*if no concurrent traumatic brain injury has been diagnosed.*

The implementation of an MTP reduces hospital costs and may improve outcome in hemorrhaging patients. An MTP should be a multidisciplinary protocol tailored to the resources of the institution and the needs of the community.

**Bibliography**


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**Summary**

A small portion of civilian trauma victims will require massive transfusion. This group of patients is likely to be coagulopathic on admission to the hospital. Early damage control surgery and damage control resuscitation should be initiated.

Damage control resuscitation includes the administration of FFP and RBC in a 1:1 ratio with additional early administration of platelets and cryoprecipitate. Simultaneously, aggressive treatment of acidosis and hypothermia is a mainstay of damage control resuscitation. Factor VII may be used to further reduce coagulopathy. Administration of crystalloids should be minimized, and the patient’s systolic pressure should be kept at around 90 mmHg.