TRAUMA-ASSOCIATED COAGULOPATHY
Christa Bernhard, DVM, MS, DACVECC
VCA Veterinary Care, Albuquerque, NM

Massive hemorrhage following trauma is one of the leading causes of death in people with traumatic injury. Trauma-associated coagulopathy (TAC) is a state of hypocoagulability and hyperfibrinolysis that occurs in the immediate posttraumatic period (within an hour or less). There are many contributing factors to TAC. Early recognition and intervention of TAC are vital to decreasing mortality in patients suffering from severe trauma.

Review of the Coagulation Pathway (Cell Based Model)
The cell based model of the coagulation pathway contains much of the same components as the cascade model, but emphasizes the role of cells (especially platelets and endothelial cells) in the process of normal coagulation. The cell based model consists of the following three phases:

1. **Initiation.** Initiation takes place on a cell that is bearing Tissue Factor (TF), such as an endothelial cell, fibroblast, or monocyte. TF interacts with coagulation factor VIIa, eventually forming thrombin (factor IIa). This results in the activation of platelets at the site of damage.

2. **Amplification.** This phase of coagulation takes place on a platelet. During activation of the platelet, coagulation factors V and VIII are activated to set the stage for the coagulation complex.

3. **Propagation.** On the surface of an activated platelet, factor Xla activates factor IXa, which then interacts with factors Va and VIIIa. The end result is activation of thrombin, which forms large complexes to form fibrin, thereby forming a stable thrombus. During this stage, there is also recruitment of additional platelets.

Mechanisms of TAC
There are many factors that contribute to a hypocoagulable state following trauma. Direct tissue injury and a state of shock lead to multiple abnormalities in the coagulation system. In addition, there are iatrogenic effects secondary to treatment of the trauma patient which also cause complications.

1. **Tissue Trauma.**
Trauma to tissue itself (skin, muscle, connective tissue, vital organs) results in direct damage to the endothelium locally. Secondary to trauma, there is often a state of systemic hypoperfusion and tissue hypoxia. Both the tissue injury and resulting hypoxia lead to a significant ramping up of the sympathetic nervous system. The massive release of neurotransmitters such as norepinephrine leads to systemic injury to endothelial cells. This injury can lead to both a hyper- and hypocoagulable state. The hypercoagulable state occurs due to the release of TF from the endothelium, which eventually leads to the formation of fibrin. As thrombi form throughout the body, it leads to consumption of coagulation factors and platelets, and the thrombi themselves lead to organ damage.

At the same time coagulation is being initiated with endothelial injury, there are other processes occurring which directly lead to a hypocoagulable state. First, the injury of the endothelial cells
results in increased amounts of tissue-type plasminogen factor (tPA), which promotes fibrinolysis (clot breakdown). Protein C is also activated due to injury; activated protein C (aPC) directly inhibits factors Va and VIIIa. The endothelium releases nitric oxide and heparan sulfate when injured, which contribute to hypocoagulability. Lastly, there is evidence of platelet dysfunction (via platelet aggregometry), even with normal platelet numbers, although the exact mechanism of this is not well elucidated.

This platelet dysfunction and other anti-coagulation processes, combined with the consumption of coagulation factors and platelets, can lead to a systemic state of severe hypocoagulability within minutes or hours of the inciting trauma.

2. Iatrogenic Effects
Patients with severe trauma are treated with large amounts of fluids and often are in a state of metabolic acidosis. Fluid therapy in large boluses leads to dilution of blood and therefore dilution of clotting factors. Metabolic acidosis and the resulting low blood pH lead to impairment of normal coagulation factor activity. Often, trauma patients are also hypothermic during the initial resuscitation phase of treatment. This hypothermia causes reduced activity of coagulation factors. These three main factors – dilution, acidosis and hypothermia – are the main components of iatrogenic effects of trauma treatment. These effects, when combined with the direct effects of tissue trauma and a state of shock, result in wide-spread coagulopathy.

**Clinical Relevance of TAC**
In human trauma patients, TAC is recognized as a preventable cause of mortality for patients post-trauma. Massive hemorrhage is a leading cause of death (40-70%) in traumatic injury. Ongoing hemorrhage also leads to hypovolemia, hypoxia, and consumption of coagulation factors and platelets. As these processes occur, and are subsequently treated, this becomes a vicious cycle leading to progressive life-threatening coagulopathy.

While TAC is fairly well-documented in human literature, the evidence is still limited in veterinary patients. In 2013, Holowaychuck et al. published a study looking at 40 dogs within 12 hours of severe trauma. In this study, TAC was identified in 50% of dogs, evidenced by prolonged coagulation times (PT, aPTT) and changes in thromboelastography (TEG) variables. TAC was associated with higher incidence of cavitory hemorrhage, requirement for blood product transfusion, and increased mortality. In this study, patients were treated with crystalloid fluids and coagulation parameters were assessed several hours after injury. Therefore, it is likely that at least some of the coagulopathy noted was due to iatrogenic effects of treatment, as well as consumption and increased fibrinolysis.

Unlike the findings of Holowaychuck et al., another 2013 study by Abelson et al. found that 30% of dogs with traumatic injury showed a hypercoagulable state. However, this population of subjects had less severe injury (per scoring systems) and were also assessed for coagulation prior to any fluid therapy. This may support a theory that these patients are initially hypercoagulable, but may become hypocoagulable due to iatrogenic causes and consumption of factors.
Despite the paucity of evidence in veterinary patients, it seems reasonable that TAC is worth considering and assessing in trauma patients. Early detection of TAC may be vital to guiding therapy and even preventing morbidity and mortality. There are many diagnostic tests that can be useful in identifying TAC. Some tests are difficult or impossible to perform in most veterinary practices (e.g. platelet aggregometry and viscoelastic testing such as TEG), while others are more reasonable (aPTT, fibrinogen levels, and platelet count).

**Therapeutic Interventions for TAC**

Blood product therapy is a mainstay of treating patients with TAC. Patients suffering from massive hemorrhage require RBC transfusions to maintain normal oxygen delivery. Fresh frozen plasma or fresh whole blood transfusions may be necessary to replace coagulation factors in patients with evidence of hypocoagulability. Platelet transfusions are commonly used in human medicine, but are more difficult to obtain and administer in veterinary patients.

Specific medications such as anti-fibrinolytics (e.g. aminocaproic acid and tranexamic acid) may be beneficial in patients with TAC by decreasing breakdown of clots. In the 2010 CRASH-2 trial of more than 20,000 human trauma patients, the patients receiving tranexamic acid (half of all patients) had lower overall mortality and less death due to bleeding, compared to those receiving a placebo.

Other considerations for trauma patients include modification of resuscitation strategies. It is important to realize that crystalloid fluids, while often vital to restoring vascular volume, may have deleterious effects. Studies have shown that strategies of hypotensive resuscitation improve outcomes (decreased mortality) in patients that are at high risk for hemorrhage. This involves providing fluids, blood products, or vasopressors to achieve a target goal of a systolic BP of around 90 mmHg and a MAP of around 60 mmHg. At these pressures, until definitive hemostasis is achieved, you can provide adequate oxygen delivery to tissues while also minimizing blood loss.

It is also important that the trauma patient be reassessed frequently. Maintaining normal core body temperature and blood pH are essential to preventing further injury and worsening of coagulation disorders. Frequently monitoring PE parameters, oxygenation status, lactate, and coagulation status is extremely important to providing interventional therapy at its most treatable stage.

**Key Points**

1. Trauma-associated coagulopathy is a complicated process in which multiple factors are at play. There are intrinsic effects of tissue injury that result in a hypocoagulable state. Iatrogenic effects of fluid resuscitation and initial treatment of trauma also contribute to coagulopathy.
2. Early recognition and intervention of TAC is essential to decreasing morbidity and mortality in patients with traumatic injury. In-house parameters such as aPTT and platelet count should be monitored serially.
3. Blood product therapy is often necessary to prevent or treat hemorrhage associated with shock. Anti-fibrinolytics and conservative resuscitation strategies are also important considerations.
References


