Canine and equine textbooks still report that animals with DIC show bleeding signs only with catheter-induced thrombophlebitic events. However, until now, DIC has not been assessed as having a relationship with multiorgan failure syndrome in dogs and horses. A current study is demonstrating that DIC and multiorgan failure syndrome are significantly related (Monreal and a new study by Cotovio et al undergoing final revision for publication in J VetIntern Med).

In human and experimental literature, DIC is already associated with multiorgan failure syndrome (the most common signs), and bleeding signs are very uncommon (<5%). Thus DIC is underrecognized in veterinary clinical settings.

Luis Monreal, DVM, PhD, DECEIM
Universitat Autònoma de Barcelona
Barcelona, Spain

Disseminated intravascular coagulation (DIC) is a syndrome characterized by marked activation of the intravascular coagulation system, resulting in massive thrombin activation, fibrin formation, and subsequent, widespread microvascular clot deposition. Marked activation of the coagulation system can be mainly counteracted by different anticoagulation mechanisms, such as the activation of coagulation inhibitors (antithrombin, protein C) and the fibrinolytic system. However, subsequent platelet and coagulation protein depletion resulting from ongoing coagulation may induce severe consumption coagulopathy and, secondarily, severe bleeding disorder (hemorrhagic diathesis). In addition, when fibrin formation is severely increased and fibrinolysis is reduced or suppressed (i.e., endotoxemia), widespread fibrin formation and deposition may cause small and midsize blood vessel thrombosis, ischemic tissue lesions, and multiorgan dysfunction/failure syndrome. 

DIC is always secondary to a severe clinical condition and is the most common hemostatic disorder in horses because it occurs in many septic newborn foals (>50%), in horses with inflammatory (36%) and ischemic (55%) gastrointestinal (GI) tract disorders, and in horses with other systemic conditions (Box 1). Therefore, most horses hospitalized in a critical care unit may be at risk for DIC.

**CLINICAL FEATURES**

According to veterinary textbooks, the most common clinical signs associated with DIC are prolonged bleeding after minor surgery or wounds as well as petechiation and/or spontaneous hemorrhage (i.e., epistaxis, hemorrhagic diathesis) from mucous membranes. These clinical signs constitute the bleeding form of DIC, where marked consumption of platelets and coagulation factors may lead to a secondary hypocoagulable state (coagulation deficiency) and to bleeding complications. This form is very easy to recognize clinically but, once established, is very difficult to treat and resolve, and the associated mortality rate is very high. This clinical form is very uncommon in humans (<5% of patients with DIC).

However, when the excessive amount of fibrin formation overwhelms the inhibitory system because of suppression of fibrinolysis, massive fibrin deposition in different tissues leads to multiorgan dysfunction syndrome and, possibly, multiorgan failure syndrome. Renal failure, hypoxia (respiratory failure), liver failure, colic, cardiac arrhythmia, shock, and death

---

4 Canine and equine textbooks still report that animals with DIC show bleeding signs only with catheter-induced thrombophlebitic events. However, until now, DIC has not been assessed as having a relationship with multiorgan failure syndrome in dogs and horses. A current study is demonstrating that DIC and multiorgan failure syndrome are significantly related (Monreal and a new study by Cotovio et al undergoing final revision for publication in J Vet Intern Med). In human and experimental literature, DIC is already associated with multiorgan failure syndrome (the most common signs), and bleeding signs are very uncommon (<5%). Thus DIC is underrecognized in veterinary clinical settings.
Treating Disseminated Intravascular Coagulation

Box 1. Clinical Conditions Associated with DIC in Horses

- Sepsis or severe infections (gram-negative and gram-positive bacteria, viruses)
- Ischemic GI disorders
- Inflammatory GI disorders
- Endotoxemia
- Malignancy
- Immunologic disorders (severe hemolytic reactions)
- Trauma
- Heatstroke
- Obstetrical complications
- Systemic inflammatory response syndrome

**DIAGNOSIS**

The bleeding form of DIC can be detected by observation of prolonged bleeding in at-risk patients. A basic laboratory investigation can rapidly confirm the diagnosis. In contrast, specific clinical skills are needed to recognize that organ dysfunction is caused by DIC in the multiorgan failure syndrome form, although laboratory testing can rapidly confirm the diagnosis.

**Laboratory Diagnosis**

DIC can be easily diagnosed when at least three of the following laboratory abnormalities are detected together:

- Thrombocytopenia
- Decreased mean platelet component (MPC)
- Prolonged clotting times (prothrombin time and activated partial thromboplastin time)
- Decreased fibrinogen concentration

DIC may be diagnosed in the laboratory in many horses with ischemic (55%) or inflammatory (36%) gastrointestinal disorders as well as in septic foals (>50%).

**TREATMENT**

The goals of treating DIC are as follows:

- Control the underlying disease that is inducing excessive intravascular activation of the coagulation system.

- Stop severe hypercoagulation, thereby reducing further thrombin and fibrin formation.
- Reduce fibrin deposition and multiorgan dysfunction or failure.
- Replace depleted platelets and coagulation factors in patients with the bleeding form of DIC.

**Postmortem Diagnosis**

If the patient dies, DIC may also be diagnosed by histologic observation of fibrin deposits within capillaries of different tissues (reportedly in lung, kidney, and liver tissue). However, the use of fibrin-specific staining (e.g., phosphotungstic acid hematoxylin) or immunohistochemical techniques is required to reliably visualize fibrin depositions in tissue samples.

**Treating the Underlying Disease**

DIC can be controlled only when the underlying disease is adequately treated. Considering the main diseases that can induce DIC in horses (see the box on this page), treatment should include administration of appropriate antimicrobials in septic patients, surgical repair in horses with ischemic GI disorders, and antiendotoxin therapy (i.e., low-dose flunixin meglumine and polymyxin B) in endotoxic animals. In addition, the administration of hydroxyethyl starch solution (10 mL/kg) in horses with DIC (>56% of septic foals with a poor prognosis).
endotoxemia (e.g., horses with inflammatory GI tract disorders) has been shown to be beneficial in restoring endothelial permeability and albumin linking and in reducing platelet activation and subsequent hypercoagulation.

**Treating Severe Hypercoagulation**
Administration of heparin is considered the most effective and safe treatment for reducing severe intravascular hypercoagulation in people, experimental animals, and horses with DIC. Moreover, because thrombin is a strong activator of equine platelets, heparin in horses has not only anticoagulant properties but also antiplatelet aggregation effects. This double action does not occur in humans or other species and makes heparin highly effective in reducing hypercoagulation and DIC in horses.

Two types of heparin can be given:

- **Unfractionated heparin**
  - The recommended dosage is 40 to 100 U/kg q12h SC or IV.
  - The efficacy of this heparin in horses is controversial.
  - Possible detrimental effects:
    - Individual responses to treatment vary; thus there is a high risk for heparin toxicosis (risk for bleeding).
    - The thrombocytopenic effect can increase the risk for bleeding.
    - The dose-dependent erythrocyte agglutination effect can lead to extravascular hemolysis and a severe decrease in the packed cell volume.

- **Low-molecular-weight heparin**
  - Dosages of the most frequently recommended low-molecular-weight heparins (LMWHs; dalteparin and enoxaparin) are shown in Table 1.
  - This heparin is more effective in treating thromboprophylaxis and is safer than unfractionated heparin.
  - This heparin is highly effective in reducing thrombus generation and fibrin deposition.
  - This heparin has no reported detrimental effects (e.g., agglutination, anemia, hemolysis) on erythrocytes, although thrombocytopenia may occur.

The administration of low-dose LMWH for thromboprophylaxis (Table 1) for 3 to 4 days has been very effective in reducing severe hypercoagulation, DIC, and fibrin deposition in horses. In the hospital in which I work, dalteparin (50 IU/kg SC q24h) is routinely administered to patients at risk for DIC; my coworkers and I have observed a clear improvement in the hemostatic derangements (e.g., prolonged clotting times, increased D-dimers, decreased antithrombin activity, thrombocytopenia) detected in these patients and have witnessed no complications related to the treatment. Therefore, this dosage is recommended in any patient at risk for DIC (Box 1).

**Treating Fibrin Deposition and Multiorgan Dysfunction/Failure Syndrome**
The administration of LMWH in horses with severe enteritis was shown to reduce fibrin deposition in differ-
ent tissues (the lungs, kidneys, and liver). In addition, fluid therapy (crystalloids and colloids) may reduce fibrin deposition and improve blood supply to tissue.

Affected horses with clinical signs consistent with multiorgan dysfunction/failure syndrome require supportive care, depending on the organ affected (e.g., intranasal oxygen when hypoxia and respiratory failure are detected; furosemide in a bolus [1 mg/kg] and/or a constant-rate infusion [2 μg/kg/min] and/or a dopamine infusion [3 to 5 μg/kg/min] when renal failure is diagnosed).

**Treating Spontaneous Bleeding Episodes (Bleeding Form of DIC)**

In patients with bleeding diathesis caused by DIC, treatment should also include the replacement of what is being consumed (platelets, coagulation factors, coagulation inhibitors). Transfusion of fresh plasma (15 to 30 mL/kg) provides platelets, coagulation factors, and coagulation inhibitors to replace those that have been consumed in the bleeding form of DIC. Fresh-frozen plasma transfusions (15 to 30 mL/kg) replace coagulation proteins and inhibitors, but not platelets.

Bleeding episodes may be stopped with fresh-frozen plasma transfusions, especially when the underlying disease and the hypercoagulation are efficiently treated. To successfully reduce hypercoagulation in these patients, anticoagulants (heparin) are usually administered together with a fresh-frozen plasma transfusion because plasma antithrombin activity is significantly decreased in these patients and needs to be reestablished in advance for heparin efficacy to be normal.
CONTRAINDICATIONS IN PATIENTS WITH THE BLEEDING FORM OF DIC AND HEMORRHAGIC DIATHESIS

Antifibrinolytics (aminocaproic acid) should not be administered to reduce bleeding because they inhibit the main coagulation inhibitory system (fibrinolysis) and subsequently enhance hypercoagulation, microthrombi deposition, and multiorgan failure syndrome. From a practical point of view, before administering aminocaproic acid, practitioners should first rule out DIC in any horse with a sudden bleeding episode. Thus, in horses with bleeding signs and with any disease associated with DIC (Box 1), antifibrinolytics should never be given.6

Resuscitation fluid solutions, such as hypertonic saline solution (7.5% NaCl), should not be used in patients with the bleeding form of DIC (hemorrhagic diathesis). Administration of these solutions may have detrimental effects in horses with marked consumption coagulopathy because these solutions could cause a hemodilution effect that could enhance the depletion of coagulation factors and, therefore, increase bleeding signs.6

CONCLUSION

Because the mortality rate in patients with clinical signs of DIC (bleeding or multiorgan failure forms) is very high, the most effective preventative in any patient at risk for DIC is to initiate administration of heparin as soon as the underlying disease is detected, together with therapy for the specific underlying disease (Box 1). Early clinical management of these patients is paramount to reducing the severity of hypercoagulation and coagulation consumption, DIC, and related fibrin deposition and the associated mortality rate.

REFERENCES