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Disseminated intravascular coagulation (DIC), previously referred to as consumptive coagulopathy or defibrination syndrome, refers to a complex syndrome in which excessive intravascular coagulation leads to multiple-organ microthrombosis and paradoxical bleeding caused by inactivation or excessive consumption of platelets and clotting factors secondary to enhanced fibrinolysis. DIC is not a specific disorder, but rather a common pathway in a variety of clinical situations. Moreover, DIC constitutes a dynamic phenomenon in which marked changes in the patient's status and in the results of coagulation tests occur rapidly and repeatedly during the course of treatment. This syndrome is relatively common in dogs and cats.

Pathogenesis.

Several mechanisms can lead to activation of intravascular coagulation. Endothelial damage commonly results from electrocution and heat stroke, although it may play a role in sepsis-associated DIC. Platelet activation can occur as a consequence of viral infections (e.g., feline infectious peritonitis – FIP - in cats). Release of tissue procoagulants occurs in several common clinical conditions, including trauma, hemolysis, pancreatitis, bacterial infections, acute hepatitis, and possibly some neoplasms (e.g., HSA).

The best way to understand the pathophysiology of DIC is to think about the whole vascular system as a single, giant blood vessel, and to think about its pathogenesis as an exaggeration of the normal hemostatic mechanisms. Once the coagulation cascade has been activated in this “giant vessel” (i.e., widespread within the microvasculature in the body), several events take place. Although they are listed sequentially, most of them occur simultaneously, and the intensity of each individual process varies with time, thus leading to an extremely dynamic process. First, the primary and secondary hemostatic plugs are formed; because this is happening in multiple small vessels simultaneously, multiple thrombi are formed in the microcirculation, which, if left unchecked, eventually lead to ischemia. During this excessive intravascular coagulation, platelets are consumed in large quantities, leading to thrombocytopenia. Second, the fibrinolytic system is activated, resulting in clot lysis and inactivation (or lysis) of clotting factors and impaired platelet function (fibrin degradation products – FDPs - are strong inhibitors of platelet function). Third, AT and possibly also proteins C and S are consumed in attempts to halt intravascular coagulation, thus leading to “exhaustion” of the normal anticoagulants. Fourth, the formation of fibrin within the microcirculation leads to hemolytic anemia as the RBCs are sheared by these fibrin strands (i.e., fragmented RBCs or schistocytes).

When all this is taken into consideration, it is easy to understand (1) why a patient with multiple-organ thrombosis (caused by excessive intravascular coagulation and depletion of natural anticoagulants) is bleeding spontaneously (as a result of thrombocytopenia, impaired platelet function, and inactivation of clotting factors), and (2) why one of the therapeutic approaches that appears to be beneficial in dogs and cats with DIC is to paradoxically halt the bleeding by administering heparin (i.e., heparin, if sufficient AT is available, halts intravascular coagulation, which in turn decreases the activity of the fibrinolytic system, thus releasing its inhibitory effect on the clotting factors and platelet function).

A variety of disorders have been associated with DIC in dogs and cats. Neoplasia (primarily hemangiosarcoma – HSA), liver disease, and immune-mediated blood diseases are the most common disorders associated with DIC in dogs; liver disease (primarily hepatic lipidosis), neoplasia (mainly lymphoma), and feline infectious peritonitis are the disorders most frequently associated with DIC in cats in our clinic.

Clinical features.
There are several clinical presentations in dogs with DIC; the two common forms are chronic silent (subclinical) and acute (fulminant) DIC. As discussed above, in most cats DIC is subclinical. In the chronic (silent) form, the patient does not experience spontaneous bleeding, but clinicopathologic evaluation of the hemostatic system reveals abnormalities compatible with this syndrome (see following paragraphs). This form of DIC appears to be common in dogs with malignancy and, possibly, other chronic disorders. The acute (fulminant) form may represent a true acute phenomenon (e.g., after heatstroke, electrocution, or acute pancreatitis), or, more commonly, it represents acute decompensation of a chronic silent process (e.g., HSA, liver disease). Regardless of the pathogenesis, dogs with acute DIC often present for evaluation of profuse spontaneous bleeding, in combination with signs secondary to anemia or to parenchymal organ thrombosis (i.e., end-organ failure). The clinical signs of bleeding suggest both primary (i.e., petechiae, ecchymoses, mucosal bleeding) and secondary (i.e., blood in body cavities) bleeding. In addition, clinical and clinicopathologic evidence of organ dysfunction is present (see following paragraphs).

In a recent retrospective study of 50 dogs with DIC conducted in our clinic, only 26% had evidence of spontaneous bleeding; only 1 of 21 cats with DIC retrospectively evaluated in our clinic had evidence of spontaneous bleeding (Couto CG: Unpublished data, 1998). Most patients were presented for evaluation of their primary problem and were not bleeding spontaneously; DIC was diagnosed as part of the routine clinical evaluation.

**Diagnosis.**

Several hematologic findings help support a presumptive clinical diagnosis of DIC, including hemolytic anemia, hemoglobinemia (caused by intravascular hemolysis), hemoglobinuria, presence of RBC fragments or schistocytes, thrombocytopenia, neutrophilia with left shift, and, rarely, neutropenia. Most of these features are evident after evaluating a spun hematocrit and a blood smear.

Hemostatic abnormalities in dogs with DIC may include the following: thrombocytopenia, prolongation of the one-stage prothrombin time (OSPT) and/or activated partial thromboplastin time (APTT) (more than 25% of the concurrent control), hypofibrinogenemia, positive FDP test, and decreased AT concentration. If evaluated, enhanced fibrinolysis can also be documented in these patients (e.g., decreased plasminogen activity, enhanced clot lysis test). In our clinic, a diagnosis of DIC is made if the patient exhibits four or more of the above hemostatic abnormalities and/or schistocytosis. Recently, thromboelastography has become a novel diagnostic and monitoring tool for patients in DIC.

In dogs, thrombocytopenia, prolongation of the APTT, anemia, and schistocytosis are common; in contrast with previous descriptions of the syndrome in dogs, regenerative anemia, prolongation of the OSPT, and hypofibrinogenemia are not. In cats, prolongation of the APTT and/or OSPT, schistocytosis, and thrombocytopenia are common, while the presence of FDPs and hypofibrinogenemia are rare.

**Treatment.**

Once a diagnosis of DIC has been established (or even if there is a high degree of suspicion that DIC is present), treatment should be instituted without delay. Unfortunately there are no controlled clinical trials evaluating the effects of different treatment modalities in dogs or cats with DIC. Therefore the following discussion reveals my own personal beliefs in the management of dogs with DIC; our experience in treating cats with DIC is limited, but the same basic principles apply. It is unquestionable that removing or eliminating the precipitating cause constitutes the main therapeutic option in patients with DIC. However, this is rarely possible. Situations in which the precipitating causes can be eliminated include surgical excision of a primary HSA or chemotherapy for disseminated or metastatic HSA, appropriate antimicrobial treatment for dogs with sepsis, and immunosuppressive treatment for dogs with IHA. In most other situations (e.g., electrocution, heatstroke, pancreatitis) the cause can rarely be eliminated within a short period of time. Therefore the treatment of dogs with DIC is aimed at:

- **Halting intravascular coagulation**
- **Maintaining good parenchymal organ perfusion**
- **Preventing secondary complications**
It should be remembered that, if blood and blood products were to be available in an unlimited supply (such as occurs in most hospitals for human beings), dogs and cats with DIC would not die from hypovolemic shock. Most dogs with DIC die of pulmonary or renal dysfunction. In our clinic, “DIC lungs” (i.e., intrapulmonary hemorrhages with alveolar septal microthrombi) appear to be a common cause of death in these patients.

*Halting intravascular coagulation.*

This is accomplished by a dual approach: administration of heparin and of blood or blood products. As mentioned previously, heparin is a cofactor for AT and therefore is not effective in preventing activation of coagulation unless sufficient AT activity is present in the plasma. Because AT activity in patients with DIC is usually low (as a result of consumption and, possibly, inactivation), sufficient quantities of this anticoagulant should be provided to the patient. The most cost-efficient way of achieving this is through administration of whole fresh blood or fresh frozen plasma (or cryoprecipitate). The old adage that administering blood or blood products to a dog with DIC is analogous to adding “logs to a fire” has not been true in my experience. Therefore blood or blood products should never be withheld solely on this premise.

Heparin has been used historically to treat DIC in humans and dogs. However, there is still controversy as to whether it is beneficial. In our clinic the survival rate of dogs with DIC appears to have increased markedly since we routinely use heparin and blood products (Couto CG: Unpublished data, 1998). Although this result can also be attributed to improvement in patient care, it is my belief that heparin is beneficial in such patients and indeed may be responsible for the increased survival rate. In my experience, low molecular weight heparin does not provide any advantages over unfractionated heparin in dogs and cats.

Sodium heparin can be used at a wide dose-range. Traditionally, there are four dose-ranges for this anticoagulant:

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mini-dose</td>
<td>5 to 10 IU/kg SQ q8h</td>
</tr>
<tr>
<td>Low-dose</td>
<td>100 to 200 IU/kg SQ q8h</td>
</tr>
<tr>
<td>Intermediate-dose</td>
<td>300 to 500 IU/kg SQ or IV q8h</td>
</tr>
<tr>
<td>High-dose</td>
<td>750 to 1000 IU/kg SQ or IV q8h</td>
</tr>
</tbody>
</table>

If evidence of severe microthrombosis is present (e.g., marked azotemia with isosthenuric urine, increase in liver enzyme activity), dyspnea or hypoxemia, intermediate- or high-dose heparin can be used; the target is to prolong the ACT to 2 to 2.5 times the baseline (or normal if the baseline was already prolonged). Once improvement in the clinical and clinicopathologic parameters has been achieved, the heparin dose should be tapered off gradually (over 3 to 4 days).

*Maintaining good parenchymal organ perfusion.*

This is best achieved by using aggressive fluid therapy with crystalloids or plasma expanders such as dextran. The purpose of this is to dilute out the clotting and fibrinolytic factors in circulation, to flush out microthrombi from the microcirculation, and to maintain the precapillary arterioles patent, so that blood is shunted to areas in which oxygen exchange is not efficient.

*Preventing secondary complications.*

Attention should be directed to maintaining oxygenation (i.e., by oxygen mask, cage, or nasopharyngeal catheter), correcting acidosis, correcting cardiac arrhythmias, and preventing secondary bacterial infections (i.e., the ischemic gastrointestinal mucosa no longer functions as an effective barrier for microorganisms, bacteria are absorbed and cannot be cleared by the hepatic MPS, and sepsis occurs). Central IV lines should be used with caution (or not at all) since dogs in DIC appear to be prone to catheter-associated thrombosis; thrombosis of the anterior vena cava usually results in secondary chylothorax.

The prognosis of dogs and cats with DIC is not as dismal as originally thought. In our clinic, over 60% of patients with DIC are managed successfully using the approach discussed above.