Disseminated Intravascular Coagulation in Cats

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The purpose of this study was to describe the clinical characteristics of cats with disseminated intravascular coagulation (DIC), including associated diseases and hemostatic abnormalities, and to identify risk factors for death and treatments that potentially altered outcome. Medical records for cats with DIC from 1990–2004 were evaluated retrospectively. Inclusion criteria were the presence of an underlying disorder associated with DIC and either postmortem examination findings of intravascular fibrin deposition or thrombosis, or both of 2 or more organs or coagulation profiles that meet 3 of 5 criteria: prolonged prothrombin time (PT), activated partial thromboplastin time (aPTT), presence of fibrin degradation products (FDP), low plasma fibrinogen (FIB) concentration, and thrombocytopenia ($<$160,000 platelets/μL). Signalment, historical data, clinical findings, clinicopathologic data, underlying disorders, management, and outcome were recorded. Forty-six cats fulfilled the criteria for DIC. Cats ranged in age from 7 weeks to 17 years (median, 9 years). Hemorrhage was noted in 7 of 46 cats (15%). Three of 46 cats (7%) survived, whereas 43 of 46 (93%) died or were euthanized. The most common underlying disorders were lymphoma, other forms of neoplasia, pancreatitis, and sepsis. There was no association detected between outcome and signalment; underlying disease; hemorrhage; abnormalities in aPTT, FIB, FDPs, platelet count; transfusion of blood products; and heparin therapy. However, the median PT of nonsurvivors was more prolonged than in survivors ($P <$ .005). DIC in cats can result from a variety of neoplastic, infectious, and inflammatory disorders, and is associated with a high case fatality rate.

Key words: Coagulopathy; Heparin; Prothrombin; Thrombocytopenia; Thrombosis.

Disseminated intravascular coagulation (DIC) is an acquired disorder of hemostasis characterized by activation and perpetuation of the coagulation and fibrinolytic pathways and is secondary to inciting illness.[1] Conditions that have been associated with the development of DIC in dogs and cats include sepsis, neoplasia, trauma, heatstroke, liver disease, pancreatitis, gastric dilatation-volvulus, and immune-mediated disease.[2,3] Endothelial damage and tissue-factor expression result in generalized activation of coagulation, causing widespread thrombosis and fibrinolysis.[4] The characteristic clinical sign of hemorrhage is caused by consumption of platelets and coagulation factors. However, microvascular and large-vessel thrombosis are of more clinical importance but are less-often detected consequences of DIC, leading to tissue hypoxia and often irreversible organ damage.[5] As a result, DIC is associated with high mortality rates in humans and dogs, and is an important complication of underlying disease.[6] Mortality rates in dogs with DIC range from 50 to 77%.[6,a]

Proposed criteria for a diagnosis of DIC in humans include both physical findings and laboratory components. Clinical findings consistent with DIC include the presence of an underlying disorder known to be associated with DIC and evidence of hemorrhage,

thrombosis, or both in the appropriate clinical setting.[5] Laboratory findings should include evidence of procoagulant activation, fibrinolytic activation, inhibitor consumption, and organ damage or failure.[1,5] The presence of all these criteria is a reasonable standard for the diagnosis of DIC. Although a comprehensive review of laboratory tests that evaluate each of these 4 laboratory criteria is beyond the scope of this article, such tests are not routinely available in the clinical setting, and many have not been validated in veterinary patients. In dogs and cats, the lack of universal criteria based on clinicopathologic data has made it more difficult to establish guidelines for the diagnosis of DIC.

There have been many studies that evaluated aspects of the initiation, perpetuation, and therapeutic intervention of DIC in humans, but limited studies are available in veterinary medicine. Although studies of dogs on aspects of DIC have been performed, there is paucity in the literature on DIC in cats.[7–11,a] At the authors' institution, DIC in cats has been recognized for many years, and this condition is thought to be associated with a high case-fatality rate. Therefore, the purpose of this study was to describe clinical characteristics of a group of cats with DIC and their underlying diseases and hemostatic abnormalities, to identify treatments that potentially altered outcome, and to identify risk factors for death.

Materials and Methods

A search of medical records for cats with DIC at the University of Minnesota Veterinary Medical Center (VMC) was performed by using the hospital coding system and diagnostic laboratory postmortem examination databases for the period January 1990 to April 2004. The animals identified from the diagnostic clinopathologic database were selected based on inclusion of DIC as a diagnosis in the final postmortem examination report. In addition, all coagulation profiles of cats performed between August 2002 and April 2004 were reviewed. Cats were included in this study if they had an underlying disorder known to be associated with DIC[1,7,11] and either (1) evidence of intravascular fibrin deposition or thrombosis in more than 1 organ on postmortem

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histopathologic evaluation,[12] or (2) 3 or more of the following abnormalities of their coagulation profiles: prolonged prothrombin time (PT > 12.8 seconds), prolonged activated partial thromboplastin time (aPTT > 16.4 seconds), high fibrin degradation products (FDP > 5 μg/mL), thrombocytopenia (<160,000/μL), and low plasma fibrinogen concentration (FIB < 0.2 g/dL). Cats with cardiac or hepatic disease were included in this study only if they had a concomitant disease process, such as neoplasia, pancreatitis, or sepsis, that was associated with DIC. For those cases in which a full coagulation profile was not performed, a prolonged activated clotting time (ACT > 120 seconds) was used as a positive criterion in place of a prolonged aPTT. Because of subjectivity of interpretation, red blood cell fragmentation was noted if identified but was not considered one of the criteria for the diagnosis of DIC.

All coagulation profiles were performed at the VMC clinical laboratory. The fibrinogen concentration was determined on ethylenediamine-tetraacetic acid (EDTA) whole blood samples by the heat precipitation method and was measured via refractometer. The PT, aPTT, and FDP values were determined from samples of citrated plasma by using automated coagulation equipment and standard laboratory methods and reagents.[b] Reference ranges were determined by calculating the mean ± 2 standard deviations of values obtained in 20 healthy control cats. The coagulation analyzer and reagents were evaluated twice daily Monday–Friday and once daily on weekends by using control plasma provided by the manufacturer.

The medical records were reviewed, and signalment, historical data, clinical findings, clinicopathologic data, imaging findings, management, and outcome were recorded. In addition, abnormalities detected on physical examination were recorded, including the presence or the absence of hemorrhage (defined as one of the following: petechiae, ecchymoses, epistaxis, hemothorax, hemoabdomen, rectal bleeding, or hematuria), bradycardia (heart rate < 150 beats per minute [bpm]), tachycardia (heart rate > 200 bpm), pulse quality, hypothermia (rectal temperature < 99.5°F [37.5°C]), or hyperthermia (rectal temperature > 102.5°F [39.2°C]). Other data collected included results of hematologic and biochemical examinations, urinalysis, postmortem examination findings, underlying diseases, use of blood products (including the use of whole blood, fresh frozen plasma [FFP], packed red blood cells [pRBC], or Oxyglobin [OXY][c]), and the use of heparin or vitamin K_1 therapy.

To best characterize which disease processes resulted in the underlying stimulus for DIC, underlying disorders were evaluated and separated into the following general categories: neoplasia; sepsis; infectious disease; pancreatic disease; urinary disease; trauma, tissue necrosis, or both; and other. In addition, the number of disorders was recorded for each cat. For example, if a cat was diagnosed with lymphoma and pancreatitis, then it would be categorized under both neoplasia and pancreatic disease, with a total of 2 disorders recorded.

For purposes of this study, survivors were defined as cats who were alive at the time of discharge, with no recorded death or euthanasia within 14 days of discharge. Nonsurvivors were defined as those cats who died or were euthanized while in the hospital, as well as cats who died or were euthanized within 14 days of discharge.

Statistical Analysis

Statistical analysis was performed to identify significant risk factors associated with survival or death. Normally distributed data were represented as the mean and standard deviation, whereas non-normally distributed data were reported as median and range. Analysis was completed by using t-tests and one-way analysis of variance. Nonparametric statistical methods were used to analyze the data that were not normally distributed. The Wilcoxon rank sum test and the Mann-Whitney test were used to evaluate the probability that selected median values were unequal. The chi-square test for homogeneity was also used on count data. Signalment, body weight, physical variables, concurrent diseases, clinicopathologic variables, underlying disease processes, and treatment modalities were compared between survivors and nonsurvivors. Chi-square tests that compared use of blood products, underlying disorders, number of underlying disorders, use of heparin or vitamin K therapy, hemorrhage, and magnitude of hemostatic abnormalities were evaluated for their association with outcome. The Mann-Whitney test was used to compare survivors and nonsurvivors with respect to coagulation parameters. For all comparisons, $P < .05$ was considered statistically significant. All analyses were performed with a commercially available statistical software package.[d]

Results

Clinical Characteristics

Forty-six cats with DIC based on the diagnostic criteria described above had medical records available for analysis at the VMC. The median age of the affected cats was 9 years (n = 46; range, 7 weeks to 17 years). Twenty-one of the 46 cats (46%) were neutered males, 1 of 46 was an intact male (2%), and 24 of 46 were spayed females (52%). The median body weight was 4.5 kg (n = 44; range, 0.76–8.2 kg). Thirty-two of the 46 cats (70%) were Domestic Shorthair, whereas the remaining were Domestic Longhair (8), Siamese (2), and one of each of the following breeds: Abyssinian, Himalayan, Ragdoll, and Domestic Mediumhair. Of those cats for whom data were available, 30 of 39 cats (77%) lived exclusively indoors and 9 of 39 (23%) lived both indoors and outdoors; no cats lived exclusively outdoors. There was no statistically significant relation among age, sex, weight, breed, and outcome.

Historical findings were nonspecific and are reported by frequency (n, %) (Table 1). In the 46 cats who presented with DIC, depression and anorexia were the most frequent primary complaints recorded (38 cats, 83%), followed by weakness (28, 61%), vomiting (17, 37%), dyspnea (14, 30%), and diarrhea (4, 9%). Common abnormalities on physical examination in this group included hypothermia (13, 28%), hyperthermia (11, 24%), weak femoral pulses (10, 22%), tachycardia (10, 22%), a cardiac murmur (8, 17%), a palpable abdominal mass (7, 15%), and bradycardia (5, 11%). Of cats with cardiac murmurs, 6 of 8 had severe anemia (hematocrit ≤ 15%). The remaining 2 of 8 cats had neoplasia and tissue necrosis, respectively, as the underlying cause of DIC, with no cardiac disease identified at postmortem examination.

Petechiae or ecchymoses were recorded in 5 cats (11%). Hemorrhage of any type was recorded in 7 cats (15%). Sources of hemorrhage consisted of hemothorax (3, 7%), hemoabdomen (2, 4%), rectal bleeding (2, 4%), epistaxis (1, 2%), and hematuria (1, 2%). One cat had both rectal bleeding and epistaxis, whereas another cat had both a hemothorax and hemoabdomen. In cats with profound prolongation of their coagulation time (aPTT, PT, or both), hemorrhage was noted in 2 of 4 cats, with

Table 1. History and physical examination findings in cats with DIC.

Abnormality	No. Affected	% Affected
Depression or lethargy	38	83
Anorexia	38	83
Weakness	28	61
Vomiting	17	37
Dyspnea	14	30
Hypothermia	13	28
Hyperthermia	11	24
Weak femoral pulses	10	22
Tachycardia	10	22
Cardiac murmur	8	17
Palpable abdominal mass	7	15
Bradycardia	5	11
Diarrhea	4	9

a PT of ≥120 seconds (reference range, 7.4–12.8 seconds) and in 3 of 5 cats with an aPTT of ≥120 seconds (reference range, 11.1–16.4 seconds). There was no statistically significant relation detected between hemorrhage and outcome.

Thirty-five cats (76%) had one underlying disorder associated with DIC. Nine cats (20%) had 2 disorders, and 2 (4%) had 3 disorders. The most common underlying disorders associated with DIC were neoplasia, sepsis, and pancreatitis (Table 2). All surviving cats had only 1 underlying disorder. Underlying disorders diagnosed in surviving cats were lymphoma, pancreatitis, and immune-mediated hemolytic anemia. There was no statistically significant relation between any individual disorder or the total number of disorders (≥2) and outcome.

One of 23 and 0 of 15 cats tested were seropositive for feline leukemia virus infection or feline immunodeficiency virus, respectively. The median hematocrit (HCT) was 24% (n = 41; range, 3–47%), and anemia (HCT ≤ 26%) was identified in 21 of 41 cats (51%). The median total white blood cell count was 12,900/µL (n = 41; range, 100–75,200/µL), and leukopenia (<3,400/µL) was

identified in 4 of 41 cats (10%), and leukocytosis (>15,700/µL) was present in 29 of 41 cats (71%).

Thirty-two cats had coagulation profiles that met the criteria for DIC. The PT was prolonged (>12.8 seconds) in 26 of 34 cats (77%) (median, 15.6 seconds; range, 8.9 to >120 seconds). The aPTT was prolonged (>16.4 seconds) in 100% of cats (33/33) for whom data were available (median, 35 seconds; range, 16.8 to >120 seconds). A numerical platelet count was available for 24 cats, of whom 12 of 24 (50%) had thrombocytopenia (median, 98,500/µL; range, 4,000–479,000/µL). Fibrin degradation products were high (>5 µg/mL) in 10 of 33 cases (30%). Fibrinogen was low (<0.2 g/dL; median, 0.1 g/dL; range, <0.1–0.7 g/dL) in 22 of 33 cats (67%). An activated clotting time was measured in 14 cats and was prolonged (>120 seconds) in all cases (median, 300 seconds; range, 195 to >720 seconds). Three of 38 blood smears (7.9%) evaluated had evidence of red blood cell fragmentation based on the presence of either keratocytes or schistocytes. The median PT of nonsurvivors (18.4 seconds) was significantly more prolonged than the median PT of survivors (9.9 seconds, $P < .005$). No other statistically significant differences were identified between survivors and nonsurvivors with respect to coagulation parameters. D-dimer concentration or antithrombin (AT) activity was not measured in any cat.

Therapy

Cats received specific and supportive therapy for their underlying disease when possible. Therapy directed toward the management of DIC included supportive care and administration of blood products, unfractionated heparin, or both. Vitamin K_1 was administered to 13 cats.

Thirty of 46 cats (65%) were transfused with some type of blood product. Eleven of 30 cats (37%) received 1 unit of FFP alone, 10 of 30 (33%) received both 1 unit of FFP and pRBCs, and 2 of 30 cats (7%) received pRBCs alone. OXY was administered to 7 of 30 cats (23%); all of these cats received OXY in addition to ≥1 transfusion

Table 2. Final diagnoses in cats with DIC.

System or Category	No. Affected	Disorder (No. cats)
Neoplasia	19	Lymphoma (8), biliary adenocarcinoma (2), hepatocellular carcinoma (1) mastocytosis in spleen and bone marrow (1), metastatic pulmonary adenocarcinoma (1), multiple myeloma (1), metastatic carcinoma (1), pancreatic adenocarcinoma (1), myeloproliferative disease (not further characterized) with secondary IMHA[a] (1) intrascapular fibrosarcoma (1), metastatic anaplastic neoplasia (not further characterized) (1)
Pancreatic disease	12	Pancreatitis (12)
Sepsis	9	Cutaneous abscess/cellulitis (4), bacterial peritonitis (3), peritonitis secondary to intra-abdominal neoplasia (2)
Infectious disease	6	Toxoplasmosis (2), yeast septicemia (1), feline panleukopenia virus (1), feline infectious peritonitis (1), feline leukemia virus (1)
Urinary system	4	Pyelonephritis (2), glomerular and renal medullary amyloidosis (1), uroabdomen (1)
Trauma/tissue necrosis	2	Trauma (fell 4 stories) (1), tissue necrosis secondary to biliary cystadenoma (1)
Other	3	IMHA[a] (2), vaccine reaction (1)

[a] IMHA, immune mediated hemolytic anemia.

product (3 cats also received FFP and pRBCs, 2 cats also received FFP, and 2 cats also received pRBCs). There were no statistically significant relations between transfusions of FFP, pRBCs, or OXY, and the outcome.

Unfractionated heparin therapy was administered at varying doses (9.8, 10, and 118 U/kg) to 3 patients. One of 3 survived. There was not a detectable statistically significant relation between heparin therapy and the outcome.

Vitamin K_1 was administered orally or subcutaneously at varying doses (median dose, 2.3 mg/kg/d; range, 0.86–5.56 mg/kg/d) to 13 cats with DIC. Six of these cats (46%) had hepatic disease in addition to one or more disorders associated with DIC. No cats treated with vitamin K_1 survived.

Outcome

Three cats (7%) survived, whereas 43 of 46 cats (93%) died or were euthanized. The majority of nonsurvivors (38/43, 88%) died or were euthanized during hospitalization, whereas 5 of 43 (12%) died or were euthanized within 2 weeks of discharge. Of the nonsurvivors, 29 of 43 (67%) were euthanized, whereas 14 of 43 (33%) died of natural causes. Two cats were euthanized primarily because of financial reasons. Of the 3 surviving cats, one lived for 230 days after DIC was diagnosed, one lived for 335 days, and one was lost to follow-up after 50 days.

Postmortem Examination Findings

A postmortem examination was performed in 24 of 46 cats (52%), and DIC was identified in 19 of 24 cats (79%) based on histopathologic examination. Of these 19 cats who had documentation of DIC on postmortem examination, a coagulation profile was available in only 8 cases. Five of these 8 cats (62.5%) had coagulation profiles that met the criteria for DIC. Three of these 8 cats (37.5%) had coagulation profiles that did not meet the criteria for DIC, despite having histopathologic evidence of DIC on postmortem examination.

Discussion

This study evaluated and described clinical features, case fatality rate, associated underlying diseases, hemostatic abnormalities, and treatments used in cats with DIC. Despite progressive improvement in the quality of veterinary critical care medicine, the death rate of cats with DIC was high in this study. This may be because of the poor prognosis associated with the specific underlying diseases, including neoplasia or sepsis, which resulted in a high incidence of euthanasia. Regardless, because of the low number of survivors and the retrospective nature of this study, further studies are needed to more accurately assess the efficacy of different methods of therapeutic intervention on survival and to assess risk factors for mortality.

Cats with liver disease, including, eg, hepatic lipidosis, cholangitis, might develop prolonged coagulation times (specifically PT and aPTT) because of decreased clotting factor synthesis.[13,14] Fibrinogen concentration can be low because of decreased hepatic synthesis. In addition, FDPs may be high in hepatic disease because of decreased clearance from blood.[14] Thus, differentiation among cats with hepatic disease alone, DIC, and hepatic disease plus concomitant DIC is difficult. Cats with underlying liver disease alone can have concomitant DIC; however, the authors elected not to include these cats because of confounding factors.[13] None of the cats treated with vitamin K_1 in this study survived. This may be because of their coagulopathies being associated with DIC rather than vitamin K_1-dependent factor deficiencies.

Cats with underlying cardiac disease can similarly develop thromboembolic complications secondary to local disease factors, such as left atrial blood stasis and endomyocardial damage. While a murmur was ausculted in 8 cats, no cats in this study were diagnosed with any form of cardiomyopathy by echocardiography or postmortem examination. Six of 8 cats with murmurs had severe anemia, which can cause turbulent blood flow. Therefore, primary cardiac disease was unlikely to be associated with thromboembolic phenomena in the cats described in this study. For this reason, cats with hepatic or cardiac disease were included in this study only if they had a concomitant disease process, such as neoplasia, pancreatitis, or sepsis, that was associated with DIC.

The aPTT in this study of cats was a significant marker of DIC, because it was prolonged in all cats with DIC in which this variable was measured. In addition, the median PT of nonsurvivors was significantly longer than the median PT of surviving cats. Because of the high case-fatality rate of cats in this study, differences in coagulation variables between survivors and nonsurvivors were difficult to detect.

Therapeutic management for DIC included supportive care, heparin administration, and transfusion therapy; no particular therapy appeared to alter outcome. Heparin therapy did not appear to affect outcome, but its use was limited to 3 cats. In addition, the dose and the route of administration were not standardized, and the use of fractionated heparin was not assessed. There was also no effect on survival of transfusions in this group of cats. One limitation was that repeated coagulation profiles were not statistically evaluated after transfusions, so responses to transfusions were difficult to assess in this retrospective study. Because more than 1 transfusion product was used in several cats, it was not possible to assess individual response to 1 particular product alone.

The ability to determine the presence of DIC and thromboembolic disease on postmortem examination in conjunction with coagulation parameters may underrepresent the significance of the disease. DIC may be diagnosed based on postmortem examination findings of microthrombosis of multiple organs. However, there are several limitations to this method of diagnosis. Although multiple petechiae and ecchymoses may be identified, these are nonspecific findings that may be seen with a number of unrelated coagulopathies.[15] Microthrombi

or macrothrombi may be initially present at the time of death but postmortem fibrinolysis may result in their dissolution. Although the postmortem histopathologic finding of microvascular thrombosis in multiple organs represents supportive evidence for DIC, these changes might not be identified on postmortem examination in many cats in which DIC is strongly suspected to exist.[6] A possible explanation for this discrepancy is postmortem dissolution of microthrombi, which may occur within several hours.[6] Therefore, although it may be useful in identifying certain patients with diffuse thrombosis and hemorrhage, postmortem examination should not be relied upon as a "gold standard" for the diagnosis of DIC. In this study, 3 cats had evidence of DIC on postmortem examination, with coagulation profiles that did not meet the criteria for DIC. These cats might have been in a hypercoagulable state in an early stage of DIC before the consumption of coagulation factors and the prolongation of coagulation parameters. In addition, the presence of activated clotting factors in circulation, which occurs in the initial stages of DIC, may result in more rapid formation of fibrin, thus shortening the PT, aPTT, or both.[1]

As with retrospective studies, there are certainly limitations to this study. Coagulation panels, postmortem examination, or both were not available on all cats. With improvement in veterinary critical care medicine, the routine use of coagulation panels, D-dimer, AT, and other diagnostics allow for a more rapid diagnosis of coagulation disorders. The use of thromboelastography has recently been described to identify both hypo- and hypercoagulability in cats.[e] Although AT activity and D-dimer concentrations were not measured in this critically ill population of cats, the evaluation of these parameters may not have been very fruitful.[f] Whereas AT activity in cats can be detected with a chromogenic assay, its measurement was not helpful in the diagnosis of DIC in cats in a recent unpublished study in which only 2 of 7 cats who fulfilled criteria for DIC had low AT activity.[f] In addition, an accurate assay for the measurement of D-dimer has not yet been validated for the cat patient.[f]

Previous veterinary medical publications have used differing and sometimes divergent criteria for the diagnosis of DIC. In 1981, Feldman et al[9] published a retrospective study on coagulation abnormalities in dogs with DIC. Their diagnostic criteria included at least 3 abnormal laboratory findings (PT, aPTT, thrombin time, platelet count, fibrin-fibrinogen split products, fibrin monomers by protamine gel, evidence of red blood cell fragmentation, ATIII activity, fibrinogen, factor V activity, factor VIII:C activity, and plasminogen activity), evidence of abnormal bleeding, and a disease process known to be associated with DIC.[9] In 1999, Bateman et al[7] prospectively evaluated hemostatic function in dogs admitted to an intensive care unit. They diagnosed DIC in dogs who had underlying predisposing diseases and coagulation profiles that fulfilled 3 or more of the following criteria: (1) aPTT, PT, or thrombin clotting time outside the reference interval, (2) decreased plasma fibrinogen, (3) decreased

plasma ATIII, (4) serum fibrin-related antigen >10 mg/mL, and (5) platelet count <150,000/μL.[7] In 2000, Stokol et al[8] compared D-dimer assays with measurements of serum and plasma fibrin-fibrinogen degradation products in dogs with DIC and in healthy dogs. Dogs were diagnosed with DIC if they fulfilled criteria that consisted of an identifiable primary disease process associated with DIC, bleeding from ≥2 unrelated sites, thrombocytopenia, and ≥2 of the following abnormalities: prolonged PT, prolonged aPTT, decreased ATIII activity, and red-cell fragmentation.[8] In 1995, Peterson et al[16] retrospectively reviewed hemostatic disorders in cats, diagnosing DIC in cats with at least 3 of the following abnormalities: ≥25% prolongation of aPTT or PT, thrombocytopenia, hypofibrinogenemia, presence of fibrin-fibrinogen degradation products, and red-cell fragmentation. In a study of coagulation abnormalities in cats with naturally occurring liver disease, Lisciandro et al[13] classified cats with DIC if they had prolonged PT or aPTT, prolonged thrombin time, low factor VII activity, and marked thrombocytopenia (<100,000/μL).

Despite all the previously published literature, there is no single test or combination of tests that serves as a gold standard for the diagnosis of DIC in veterinary or human medicine. Instead of being viewed as a distinct clinical problem that is either present or absent, DIC may be more appropriately thought of as a continuum in degree of loss of control of activation of the intravascular coagulation cascade represented by compensated (nonovert) and decompensated (overt) phases.[17] The International Society of Thrombosis and Haemostasis recently developed an algorithm for the diagnosis of overt DIC in humans based on the use of widely available global coagulation tests (platelet count; PT; fibrinogen; and a fibrin-related marker, such as fibrin-fibrinogen degradation products or soluble fibrin monomer).[18] The presence of an underlying disorder known to be associated with DIC is necessary for use of this algorithm.[18] Such underlying disorders in humans include severe infection, trauma, organ destruction, neoplasia, obstetrical complications, vascular abnormalities, hepatic disease, intravascular hemolysis, burns, tissue necrosis, cardiovascular disorders, and severe toxic or immunologic reactions.[1] This scoring system has been validated (93% sensitivity and 97% specificity, on a per patient basis) in a prospective study that compared a positive DIC score with a gold standard based on expert opinion interpretation of an extensive series of coagulation tests.[19] Development of a diagnostic protocol by using routine coagulation tests and by comparing results of such tests to a gold standard based on rigorous criteria is urgently needed in veterinary medicine. Because a comprehensive list of underlying disorders known to be associated with the development of DIC in cats is not available, such a list should be established based on data from cats in this study and previous studies. An accurate classification system for DIC is a prerequisite for the design of clinical trials to evaluate the effect of interventional modalities on survival. One such promising treatment in human

patients is with recombinant human activated protein C (APC).[17,20] In a randomized, double-blind trial that compared APC and unfractionated heparin in 132 humans with DIC, 28-day mortality rate was significantly lower in the APC group compared with the heparin group (20.4 versus 40%, $P < .05$).[20] Studies evaluating the use of heparin and APC in cats with DIC are warranted.

In conclusion, this study confirms that the case fatality rate in cats with DIC is unacceptably high. Although in many cases DIC can be the result of an irreversible or end-stage fatal disease, there could be a population of patients for which early detection of DIC, appropriate and aggressive supportive care, and specific treatment aimed at underlying disease processes will favorably influence outcome. Further studies are needed to develop universally accepted diagnostic criteria for feline DIC and to evaluate treatments aimed at improving survival in this population of cats.

Footnotes

[a] Ross SJ, Smith SA, Lekcharoensuk C. Disseminated intravascular coagulation (DIC) in dogs: 252 cases (1999–2000). J Vet Intern Med 2002;16:350 (abstract 95)

[b] Roche/Stago STA Compact, Roche Diagnostics, Indianapolis, IN

[c] Oxyglobin, Biopure Corporation, Cambridge, MA

[d] SPSS VII.5, Chicago, IL

[e] Alwood AJ, Downend AB, Slensky KA, et al. Evaluation of thromboelastography (TEG) in normal cats. J Vet Emerg Crit Care 2004;14(S1):S1 (abstract)

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