Canine & Feline Coagulopathy

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Profile

Definition
- Coagulopathy is a condition in which the blood's ability to clot is impaired, leading to hemorrhage or thrombosis.
- The following focuses on hemorrhagic presentations.
- Any of these areas can be affected:
  - Failure of primary hemostasis, or formation of the initial platelet plug
  - Decreased platelet numbers or function or reduced von Willebrand factor (vWF) can lead to mucosal bleeding and bruising.
  - Failure of secondary hemostasis, or formation of a stable fibrin clot via a cascade of enzymes that ultimately convert fibrinogen to fibrin
  - Defects can lead to severe bleeding diatheses.
  - Excessive fibrinolysis, or plasmin breakdown of a fibrin clot
  - Excessive clot breakdown can result in prolonged bleeding or delayed rebleeding.

Systems
- Bone marrow: Production of platelets by megakaryocytes
- Liver: Production of all clotting factors and carboxylation of factors II, VII, IX, and X via a vitamin K–dependent enzyme
- GI tract: Absorption of vitamin K in the presence of fat and bile
- Endothelium: Production of vWF
- Site of hemorrhage: Exposure of tissue factor initiates platelet activation and coagulation cascade.
- Platelets: Provide the membrane surface for coagulation cascade and secrete granules that contain ingredients for clotting (ie, vWF, factor VIII)

Genetic Implications
- Numerous inherited bleeding disorders exist in dogs and cats (see handout Inherited Coagulopathy: Commonly Affected Breeds, page 85).
  - vWD is most common in dogs.
    - It is often seen with unexplained bleeding in young dogs with or without trauma.
    - There may also be suspicion with excessive bleeding after planned trauma (eg, neutering).

Geographic Distribution
- Infectious causes may vary by region (Table 1, next page).

Signalment

Breed Predilection
- Seen with inherited coagulopathy
- Cocker spaniels, poodles, and Old English sheepdogs are overrepresented in patients with immune-mediated thrombocytopenia.

vWD = von Willebrand disease, vWF = von Willebrand factor

For More

See the companion staff handout Inherited Coagulopathy: Commonly Affected Breeds on page 85 of this issue.
Age & Range
- Any age, but differentials may change based on age (see Coagulopathy in Juvenile Patients)

Causes
Disorders of Primary Hemostasis
- Thrombocytopenia (Table 1)
  - Decreased production, increased destruction or consumption, and sequestration
    - Platelet count must fall below ~50,000/µL for spontaneous bleeding to occur.
- Thrombocytopenia
  - Inherited
  - Acquired
    - Caused by certain drugs (see handout, page 85 of this issue), uremia, hepatic failure, and myeloproliferative disorders
    - vWD is caused by inherited structural and quantitative deficiencies of vWF

Disorders of Secondary Hemostasis
- Anticoagulant rodenticide toxicity
  - Brodifacoum is most common.
  - Inhibits vitamin K1 epoxide reductase resulting in dysfunction of factors II, VII, IX, and X and proteins C and S
- Hepatic disease
  - Decreased or abnormal coagulation factor synthesis
- Cholestatic disease
  - Decreased absorption of vitamin K can cause dysfunctional forms of factors II, VII, IX, and X.
- Inherited factor deficiencies
  - Factor VIII deficiency (ie, hemophilia) is most common.

Disorders of Fibrinolysis
- Postoperative bleeding in greyhounds

Disorders Affecting All Aspects of Coagulation
- Disseminated intravascular coagulation (DIC)
  - Early stage is characterized by thrombosis; late stages result in hemorrhage.
  - Bleeding after excessive consumption of endogenous platelets/clotting factors
  - DIC is secondary to an underlying issue (eg, severe trauma, neoplasia, sepsis, overwhelming inflammation).

History & Examination
- A thorough history is essential and can guide diagnostics:
  - Signalment
  - Duration and progression of signs
  - Recent trauma or surgery
  - Bleeding events (eg, teething, vaccination, elective surgery)
  - Evidence of bleeding at multiple sites
  - Previous transfusions
  - Medication history
  - Toxin exposure
  - Travel history

Table 1 Causes of Thrombocytopenia

<table>
<thead>
<tr>
<th>Decreased Production</th>
<th>Causative Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug induced</td>
<td>Actinomycin D, bleomycin, chloramphenicol, cytosine arabinoside, doxorubicin, estrogen, lomustine, melphalan, methotrexate, platinum</td>
</tr>
<tr>
<td>Primary</td>
<td>Fibrosis, immune mediated, myelophthisic anemia, neoplasia</td>
</tr>
<tr>
<td>Secondary</td>
<td>Ehrlichiosis, FeLV, hypothyroidism</td>
</tr>
<tr>
<td>Consumption &amp; sequestration</td>
<td>DIC, significant hemorrhage, sepsis, splenomegaly, vasculitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Destruction</th>
<th>Causative Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug induced</td>
<td>Cephalosporins, furosemide, H2-receptor antagonists, many cardiac medications, penicillins, phenylbutazone, quinines, trimethoprim–sulfamethoxazole</td>
</tr>
<tr>
<td>Primary</td>
<td>Antibodies directed against normal platelet antigens</td>
</tr>
<tr>
<td>Secondary</td>
<td>Inflammation, neoplasia</td>
</tr>
<tr>
<td>Infectious</td>
<td>Adenovirus, anaplasmosis, babesiosis, borreliosis, candidiasis, cytiauxzoonosis, dirofilariosis, distemper, ehrlichiosis, FeLV, FIP, FIIV, hemotropic mycoplasmosis, herpesvirus, histoplasmosis, leishmaniasis, leptospriosis, panleukopenia, parvovirus, Rocky Mountain spotted fever, septicemia</td>
</tr>
</tbody>
</table>

aPTT = activated partial thromboplastin time, BMBT = buccal mucosal bleeding time, DIC = disseminated intravascular coagulation, PT = prothrombin time, vWD = von Willebrand disease, vWF = von Willebrand factor
Clinical Signs

- Clinical signs related to sites of bleeding or systemic signs of blood loss
- Primary hemostasis
  - Capillary or small vessel hemorrhage
  - Petechiae (Figure 1, next page) or ecchymosis
  - Mucosal hemorrhage (ie, epistaxis, hematuria, gingival bleeding, hematemesis, melena, and hemoptyisis)
- Secondary hemostasis
  - SC or cavitary bleeding
  - Single or multiple hematomas
  - Dyspnea
  - Dull lung or heart sounds
  - Abdominal distention
  - Lameness
- Fibrinolysis
  - Excessive bruising 12–24 hours after surgery or injury
- General blood loss
  - Lethargy, inappetence, collapse, pale mucous membranes, tachycardia, and bounding or weak pulses

Diagnosis

**Definitive**

- Results of laboratory coagulation testing are essential for disease classification (Table 2, page 81).

**Differentials**

- Unwitnessed trauma, neoplasia, postsurgical complications (eg, ligature slippage)

**Laboratory Findings & Imaging**

- CBC and blood smear
  - Platelet estimate, presence of anemia/leukopenia, intracellular organisms, and RBC morphology
- Chemistry panel
  - Evaluation of total protein concentration and liver function studies
- Buccal mucosal bleeding time (BMBT)
  - Prolongation
    - Abnormal platelet function

Coagulopathy in Juvenile Patients

<1 year of age

- Hemorrhage from mucosal surfaces
  - Epistaxis
  - Hematuria
  - Melena

- Excessive hemorrhage after surgery or trauma

- Hemorrhage (ie, hemathorax, hemarthroses, hematomas)

- Excessive hemorrhage with teething

- ↑ BMBT
- ↑ PT/aPTT
- ↑ aPTT

- WVF
- Anticoagulant rodenticide
- Hemophilia

vWF activity

- To diagnose and characterize type of vWD

Prothrombin time (PT)

- Evaluates extrinsic (factor VII and tissue factor) and common pathways
- Can be measured 48–72 hours after known exposure to anticoagulant rodenticides (without vitamin K administration)
- If results are within reference ranges, vitamin K therapy is not required.

Activated partial thromboplastin time (aPTT)

- Evaluates intrinsic (ie, factors VIII, IX, XI, XII) and common (ie,
factors I (fibrinogen), II, V, X) pathways

- Prolonged aPTT with normal PT suggests specific intrinsic factor abnormalities.
- Activated clotting time (ACT)\(^1\)
  - Evaluates intrinsic and common pathways
  - Less sensitive than aPTT
- High-performance liquid chromatography (HPLC)\(^6\)
  - Recommended if exposure to anticoagulant rodenticides is suspected but not confirmed, especially when other differentials are likely (e.g., hemangiosarcoma)
- Individual factor analysis\(^{10}\)
  - Performed to identify inherited factor deficiencies
- Tests of fibrinolysis\(^{10}\)
  - Include fibrinogen assays, thrombin time, fibrin degradation products, and D-dimers
- Infectious disease screening
  - Cases with primary hemostatic defects, fever, and/or generalized illness should be screened for *Ehrlichia canis, Anaplasma phagocytophilum, A platys, and Rickettsia ricketsii* by measuring antibody titers or conducting a PCR assay as indicated by geographic location.
- Bone marrow aspiration/biopsy\(^5\)
  - Indicated with thrombocytopenia if other cell lines (RBC or WBC) are unusually increased or decreased
- Radiography and abdominal ultrasonography
  - Survey radiography is indicated for pulmonary, pleural, or abdominal hemorrhage (Figures 2A and B).
  - For primary disease processes in patients with DIC (e.g., masses, pneumonia)
- Advanced imaging
  - CT scan or MRI in cases of CNS hemorrhage

### Treatment

#### Inpatient
- Shock
- Intravascular volume support
- Transfusion as indicated

#### Outpatient
- Within 24 hours following ingestion of anticoagulant rodenticides and if patient is systemically normal
- Can be performed in a thrombocytopenic patient if it is eating and drinking well and not severely anemic

#### Medical (see Medications)

**Primary Goals**
- Stabilizing shock patients with IV fluids
- Packed RBCs or fresh whole blood may be necessary.
Secondary Goals

- Arresting bleeding, if possible
  - Transfusing missing clotting factors (fresh-frozen plasma or cryoprecipitate)
  - Encouraging platelet formation if thrombocytopenic (e.g., administration of vincristine)
  - Managing local bleeding if possible (e.g., wrap distensible areas, excising bleeding masses as soon as is safe)

Tertiary Goals

- Treating underlying cause
  - Treatments will be diagnosis-specific and may include immunosuppressive medication, vitamin K1, or antibiotics.

Client Education

- Clients should be advised to restrict activity if patient is at risk for spontaneous bleeding or is weak from previous bleeding.
- Inherited coagulopathy
  - Clients should be informed that the patient may require numerous transfusions throughout its life and should not be bred.
- Immune-mediated thrombocytopenia
  - Clients should be educated about the risk for relapse and to avoid future antigenic stimulation (e.g., vaccines).

### Coagulation Testing for Hemostatic Defect Type

<table>
<thead>
<tr>
<th>Defect Type</th>
<th>Platelet Count &lt;50,000/µL?</th>
<th>PT</th>
<th>aPTT</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIC</td>
<td>Typically</td>
<td></td>
<td></td>
<td>Increased D-dimers</td>
</tr>
<tr>
<td>Hemophilia A+B</td>
<td>No (except extreme hemorrhage)</td>
<td>Normal</td>
<td>Prolonged</td>
<td>Factor analysis</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>No (except extreme hemorrhage)</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Abnormal liver values</td>
</tr>
<tr>
<td>Rodenticide</td>
<td>No (except extreme hemorrhage)</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Yes</td>
<td>Normal</td>
<td>Normal</td>
<td>Increased BMBT</td>
</tr>
</tbody>
</table>

### Medications

#### Drugs & Fluids

| IV isotonic crystalloids    | Boluses should be administered in increments of 20–30 mL/kg of lactated Ringer’s solution or 0.9% saline solution until heart rate, blood pressure, mucous membrane color, and mental status are normal. | Bolus infusion of acetate-containing fluids (e.g., P-lyte) is not recommended; rapid infusions of acetate can cause vasodilation and hypotension. | Hypertonic saline (7.2%–7.5% NaCl) | Effective only if the patient is not already dehydrated or hyponatremic | 2–4 mL/kg administered no faster than over 15 minutes, followed by isotonic crystalloids | Blood transfusion | Indicated if the patient still shows signs (e.g., tachycardia, abnormal pulses) or weakness after fluid resuscitation | PCV of <20% after an episode of acute bleeding warrants transfusion |

#### Hypertonic saline

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#### Whole blood

| Whole blood: 10–22 mL/kg IV | Prolonged | Prolonged | Increased D-dimers |

#### Packed RBCs

| Packed RBCs: 6–10 mL/kg IV | Prolonged | Prolonged | Factor analysis |

#### Fresh-frozen plasma

| Fresh-frozen plasma | Supplies clotting factors rapidly (XI, X, IX, VIII, VII, V, II, vWF, fibrinogen) | Indicated for hemophilia, vWD, anticoagulant rodenticide ingestion with hemorrhage | 6–10 mL/kg IV |

#### Cryoprecipitate

| Cryoprecipitate | Indicated for vWD |

#### Desmopressin acetate

| Desmopressin acetate | Stimulates release of vWF |

#### Vitamin K

| Vitamin K | Oral formulation is ideal for anticoagulant rodenticide. |

#### Rodenticide

| Rodenticide | Vitamin K at 3–5 mg/kg PO (ideal) divided q12h for 4 weeks |

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Consultant on Call

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**Drugs Associated with Acquired Thrombocytopenia**

- Aminophylline
- Aspirin
- Carbenicillin
- Cephalosporins
- Dextran
- Diltiazem
- Ibuprofen
- Isoproterenol
- Naproxen
- Propranolol
- Verapamil

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**In General**

**Relative Cost**

- Recent anticoagulant exposure with immediate decontamination: $
- Inherited coagulopathy, if diagnosed before severe bleeding event: $$$
- Any coagulopathy with severe bleeding: $$$$$

**Cost Key**

- $ = up to $100
- $$ = $101–$250
- $$$ = $251–$500
- $$$$ = $501–$1000
- $$$$$ = more than $1000

**Prognosis**

- Prognosis varies based on coagulopathy type and underlying cause.
- Thrombocytopenia
  - Infectious: good
  - Immune mediated: fair
- Hereditary coagulopathy
  - Primary hemostatic defects (eg, vWd): normal lifespan possible, although multiple transfusions may be required

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**Follow-up**

**Patient Monitoring**

- For recurrence of clinical signs or further bleeding episodes
- Patient may need ongoing laboratory monitoring.

**At-Home Treatment**

- Strict rest with padded bedding to prevent rebleeding until risk has passed (ie, platelet count, PT, and/or aPTT have returned to normal as indicated)
- Clients should inform any veterinary providers about prior transfusions and history of coagulopathy.

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**Precautions & Interactions**

- Blood typing and crossmatching is indicated in patients receiving multiple transfusions.

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**PT should be rechecked 48 hours after last dose.**

- Not required after acute ingestion and decontamination if PT is normal 48–72 hours after exposure.

- Malabsorption
  - 0.5–1 mg/kg SC q12–24h for 3 doses

- Antifibrinolytic agents (eg, aminocaproic acid)
  - Used in greyhounds to prevent postsurgical bleeding

- Doxycycline
  - Used in cases of infectious thrombocytopenia
  - 5–10 mg/kg PO q12h

- Immunosuppressive medications (eg, prednisone, azathioprine, cyclosporine, leflunomide)
  - Used to treat immune-mediated thrombocytopenia

- Decontamination
  - Apomorphine administered at 0.03 mg/kg IV and activated charcoal at 1–4 g/kg PO for recent (ie, within 1–3 hour) rodenticide ingestion

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**Type III vWd and inherited factor: variable**

- Some live full lifespans while others have multiple bleeding events.

**Anticoagulant rodenticides**

- Recent exposure and decontamination: excellent
- 3–5 days postexposure with bleeding: good, but treatment more costly

**DIC**

- Guarded, unless the underlying cause can be rapidly corrected

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**Future Considerations**

- Point-of-care testing (eg, PFA-100, thromboelastography [TEG]) is not widely available but may become useful in future diagnosis and treatment.

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**cb**

See Aids & Resources, back page, for references & suggested reading.

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