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[1]
    - 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[1]
    - Defects can lead to severe bleeding diatheses.
  - Excessive *fibrinolysis*, or plasmin breakdown of a fibrin clot[1]
    - 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[2-5] (see handout **Inherited Coagulopathy: Commonly Affected Breeds**, page 85).
  - vWD is most common in dogs.[1,2,5]
    - 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.[5]

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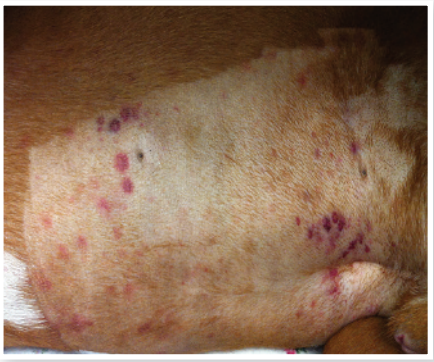


For More

See the companion staff handout **Inherited Coagulopathy: Commonly Affected Breeds** on page 85 of this issue.

vWD = von Willebrand disease, vWF = von Willebrand factor

Age & Range

- Any age, but differentials may change based on age (see **Coagulopathy in Juvenile Patients**)

Causes

Disorders of Primary Hemostasis

- Thrombocytopenia (**Table 1**)[1,5]
  - Decreased production, increased destruction or consumption, and sequestration
    - Platelet count must fall below ~50,000/µL for spontaneous bleeding to occur.
- Thrombocytopathia
  - Inherited
  - Acquired
    - Caused by certain drugs[5] (see handout, page 85 of this issue), uremia, hepatic failure, and myeloproliferative disorders
    - vWD is caused by inherited structural and quantitative deficiencies of vWF.[2]

Disorders of Secondary Hemostasis

- Anticoagulant rodenticide toxicity
  - Brodifacoum is most common.[6]
  - Inhibits vitamin K1 epoxide reductase resulting in dysfunction of factors II, VII, IX, and X and proteins C and S[6-8]
- 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.[2,4]

Disorders of Fibrinolysis

- Postoperative bleeding in greyhounds[9]

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[1]
  - DIC is secondary to an underlying issue (eg, severe trauma, neoplasia, sepsis, overwhelming inflammation).

History & Examination

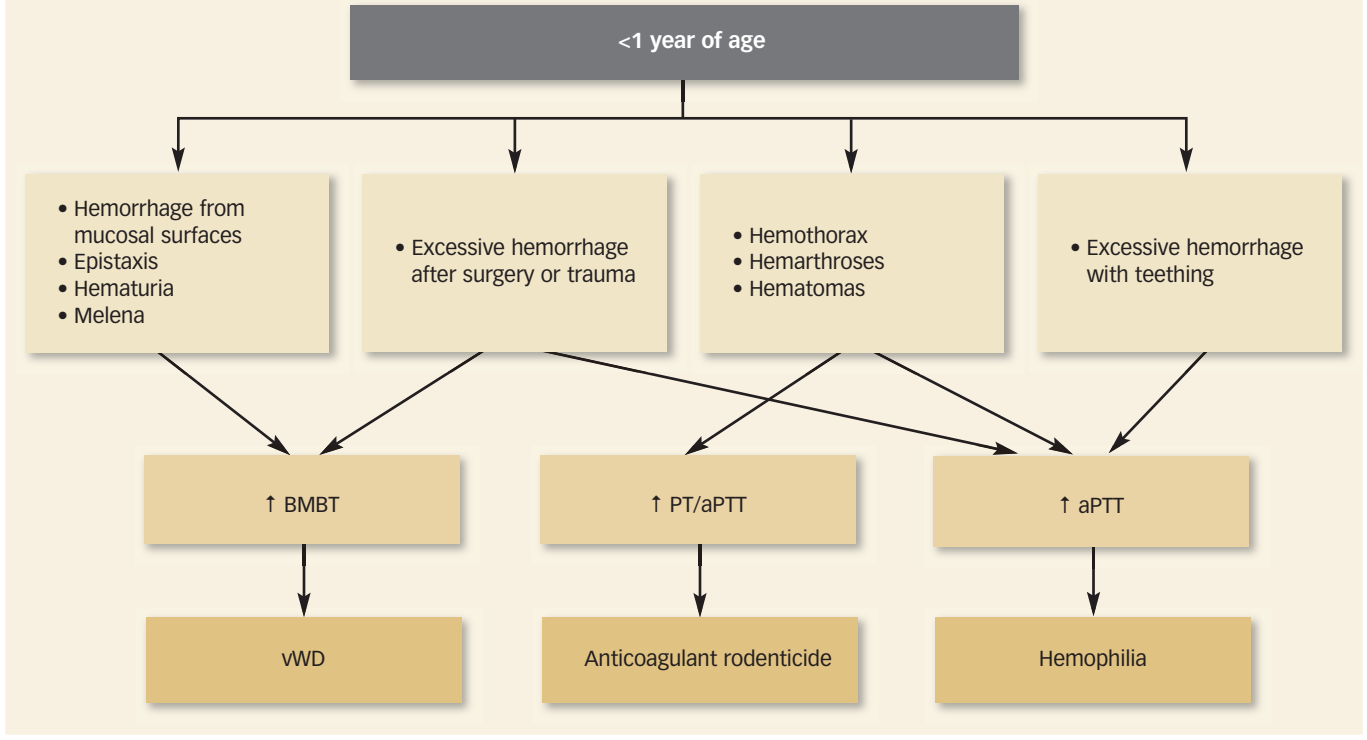
- A thorough history is essential and can guide diagnostics[10]:
  - Signalment
  - Duration and progression of signs
  - Recent trauma or surgery
  - Bleeding events (eg, teething, vaccination, elective surgery)
  - Evidence of bleeding at multiple sites
  - Previous transfusions
  - Medication history
  - Toxin exposure
  - Travel history

Table 1 Causes of Thrombocytopenia[1,5]

Decreased Production	*Causative Factor*
Drug induced	Actinomycin D, bleomycin, chloramphenicol, cytosine arabinoside, doxorubicin, estrogen, lomustine, melphalan, methotrexate, platinum
Primary	Fibrosis, immune mediated, myelophthisic anemia, neoplasia
Secondary	Ehrlichiosis, FeLV, hypothyroidism
Consumption & sequestration	DIC, significant hemorrhage, sepsis, splenomegaly, vasculitis
Destruction	***Causative Factor***
Drug induced	Cephalosporins, furosemide, H_2-receptor antagonists, many cardiac medications, penicillins, phenylbutazone, quinines, trimethoprim–sulfamethoxazole
Primary	Antibodies directed against normal platelet antigens
Secondary	Inflammation, neoplasia
Infectious	Adenovirus, anaplasmosis, babesiosis, borreliosis, candidiasis, cytauxzoonosis, dirofilariasis, distemper, ehrlichiosis, FeLV, FIP, FIV, hemotropic mycoplasmosis, herpesvirus, histoplasmosis, leishmaniasis, leptospirosis, panleukopenia, parvovirus, Rocky Mountain spotted fever, septicemia

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

Coagulopathy in Juvenile Patients



Clinical Signs

- Clinical signs related to sites of bleeding or systemic signs of blood loss
- Primary hemostasis
  - Capillary or small vessel hemorrhage[1,5,10]
  - Petechiae (**Figure 1**, next page) or ecchymosis
  - Mucosal hemorrhage (ie, epistaxis, hematuria, gingival bleeding, hematemesis, melena, and hemoptysis)
- Secondary hemostasis
  - SC or cavitary bleeding[1,5,10]
  - 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)[1,10,11]
  - Prolongation
    - Abnormal platelet function or vasculitis
    - Should be performed with a normal platelet count as thrombocytopenia alone may result in a prolonged or abnormal test result.
- vWF activity[5,10]
  - To diagnose and characterize type of vWD
- Prothrombin time (PT)[1,10]
  - 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)[1,10]
  - Evaluates intrinsic (ie, factors VIII, IX, XI, XII) and common (ie,

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factors I [fibrinogen], II, V, X) pathways
  - ❏ Prolonged aPTT with normal PT suggests specific intrinsic factor abnormalities.
- Activated clotting time (ACT)[1,10]
  - ❏ 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 (eg, 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 rickettsii* 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 (eg, masses, pneumonia)
- Advanced imaging
  - ❏ CT scan or MRI in cases of CNS hemorrhage

Tx Treatment

Inpatient

- Shock
- Intravascular volume support
- Transfusion as indicated

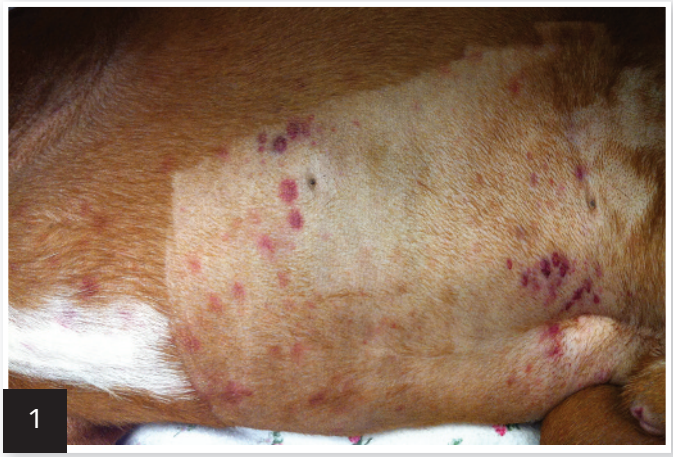
Outpatient

- 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

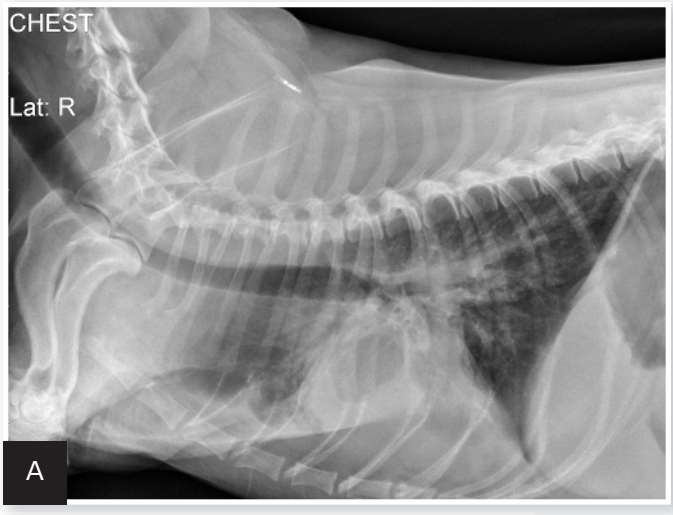
Medical (see Medications)

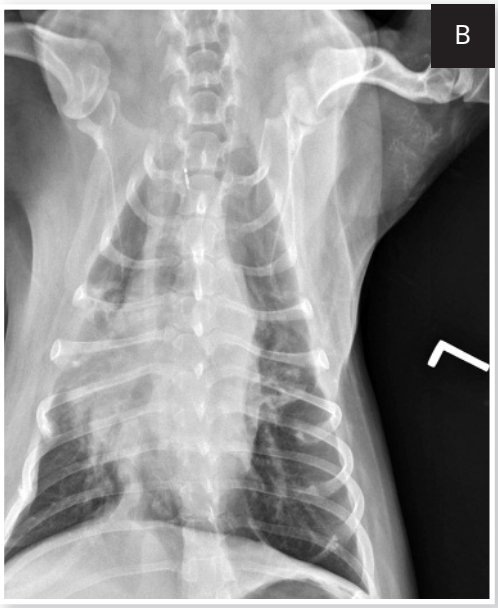
Primary Goals

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



Petechiation in a boxer (4 years of age) with immune-mediated thrombocytopenia. Note bruising in the unclipped region.





2 Lateral thoracic radiograph of a Welsh corgi (9 years of age) following ingestion of an anticoagulant rodenticide at least 3 days before presentation. Note the mixed pattern of alveolar infiltrates and scant pleural effusion (hemorrhage).

VD radiograph of the patient. Alveolar pattern in the right cranial and middle lung lobes represents one of the radiographic manifestations of pulmonary hemorrhage.

Table 2 **Coagulation Testing for Hemostatic Defect Type**

Defect Type	*Platelet Count <50,000/μL?*	*PT*	*aPTT*	*Other*
DIC	Typically	Prolonged	Prolonged	Increased D-dimers
Hemophilia A+B	No (except extreme hemorrhage)	Normal	Prolonged	Factor analysis
Hepatic failure	No (except extreme hemorrhage)	Prolonged	Prolonged	Abnormal liver values
Rodenticide	No (except extreme hemorrhage)	Prolonged	Prolonged	
Thrombocytopathia	No	Normal	Normal	Increased BMBT
Thrombocytopenia	Yes	Normal	Normal	

Secondary Goals

- Arresting bleeding, if possible
  - Transfusing missing clotting factors (fresh-frozen plasma or cryoprecipitate)
  - Encouraging platelet formation if thrombocytopenic (eg, administration of vincristine)
  - Managing local bleeding if possible (eg, 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 (eg, vaccines).

Rx 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.
  - After resuscitation, IV fluids should be continued at rates accounting for ongoing loss, dehydration, and maintenance needs (often 3–6 mL/kg/h but will vary).
  - Bolus infusion of acetate-containing fluids (eg, P-lyte) is not recommended; rapid infusions of acetate can cause vasodilation and hypotension.[12,13]
- Hypertonic saline (7.2%–7.5% NaCl)
  - Effective only if the patient is not already dehydrated or hypernatremic
  - 2–4 mL/kg administered no faster than over 15 minutes, followed by isotonic crystalloids
- Blood transfusion
  - Indicated if the patient still shows signs (eg, tachycardia, abnormal pulses) or weakness after fluid resuscitation
  - PCV of <20% after an episode of acute bleeding warrants transfusion consideration.
  - Whole blood: 10–22 mL/kg IV[14]
  - Packed RBCs: 6–10 mL/kg IV[14]
- Fresh-frozen plasma
  - Supplies clotting factors rapidly (XII, XI, X, IX, VIII, VII, V, II, vWF, fibrinogen)
  - Indicated for hemophilia, vWD, anticoagulant rodenticide ingestion with hemorrhage
  - 6–10 mL/kg IV[14]
- Cryoprecipitate
  - Indicated for vWD
  - 1 U/10 kg[14]
- Desmopressin acetate
  - Stimulates release of vWF
  - Indicated in patients with vWD
  - 1 μg/kg SC 1 hour before surgery[5]
- Vitamin K
  - Oral formulation is ideal for anticoagulant rodenticide.
  - May enhance absorption when given with a fatty meal
  - Injectable form is poorly absorbed but necessary for cases when malabsorption of vitamin K is suspected (ie, cholestasis, liver failure, shock).
  - Rodenticide
    - Vitamin K at 3–5 mg/kg PO (ideal) divided q12h for 4 weeks[7,15]

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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[16]
- ❑ Malabsorption
  - 0.5–1 mg/kg SC q12–24h for 3 doses
- Antifibrinolytic agents (eg, aminocaproic acid)
  - ❑ Used in greyhounds to prevent postsurgical bleeding[9]
- Doxycycline
  - ❑ Used in cases of infectious thrombocytopenia
  - ❑ 5–10 mg/kg PO q12h
- Immunosuppressive medications (eg, prednisone, azathioprine, cyclosporine, leflunomide)[17]
  - ❑ 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[18]

Precautions & Interactions

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

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.

Drugs Associated with Acquired Thrombocytopathia[5]

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

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
  - ❑ 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

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

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