

The Need to Assess Patients with Comprehensive In-House Blood Work

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Case Example

General and emergency practitioners have all faced the enigma of the anorexic, listless patient. For example, Chance Murphy, a 6-year-old 66-pound female spayed black lab mix, walks in the practice door.

The owners are faithful clients and are concerned because Chance is suddenly depressed, weak, lethargic, and has not eaten for the last two days. There has been no overall change in her history, no known toxins or poisons that she could have gotten into, and the other pets in the household are fine.

The veterinarian evaluates Chance and finds that her body temperature is 102.3°F (39°C). She has a strong 120 pulse rate,

40 respiration rate, light pink mucous membranes, a two-second capillary refill time, and normal hydration. She appears weak and possibly slightly painful in her caudal abdomen; no palpable abnormalities can be detected. All other elements of her physical examination are within normal limits.

The veterinarian discusses the concerns with the owners and outlines the diagnostic recommendations, which include a complete

blood count, chemistry profile, urinalysis and chest and abdominal radiographs. The owners agree to the initial diagnostic plan, and the medical team takes Chance to the back for radiographs and lab work.

Thoracic films show a possible microcardia with no significant changes in the lungs, diaphragm and trachea. Abdominal films suggest a slight loss of contrast in the ventral abdomen. Blood is collected and mild bruising is noted on Chance's hind limb venipuncture site. In-house lab work is completed, and except for the following changes in the blood work; all other parameters are unremarkable.

Test	Finding	Normal
HCT	26% (l)	35-55%
WBC	19,250 (h)	6,000-17,000
Platelet	125,000 (l)	200,000-500,000
Albumin	2.5 mg/dL	2.5-3.5 mg/dL



The medical team evaluates a blood film and a wet slide prep of Chance's blood. The technician team member finds no obvious agglutination on the wet prep, and a blood film that shows normal red and white blood cell morphology. The medical team agrees that the platelet number appears slightly decreased and sees no overall sign of a regenerative red blood cell response.

The differential list for this patient includes Disseminated Intravascular Coagulopathy (DIC) / Atraumatic Bleed of the Abdomen, Intestinal Disease / Chronic GI Ulceration, Liver Disease, Infectious Disease (i.e., Ehrlichiosis), Toxin / Poison, and Neoplasia.

The primary concern for this patient is whether Chance has a nonregenerative anemia such as anemia of chronic disease, has a chronic bleeding issue (i.e., gastrointestinal ulceration), or has an acute blood loss anemia. At this point, an in-house coagulation profile is necessary to help determine if there is a coagulation concern suggesting a life-threatening problem. The clotting profile shows:

Test	Canine	Normal
PT	25 s	12-17 s
aPTT	180 s	90-110 s

With the observed prolonged clotting times and evidence of anemia and thrombocytopenia, acute internal bleeding must be a primary concern. Ultrasound evaluation showed a moderate amount of free fluid in the abdomen which when tapped produced nonclotting blood with a packed cell volume of 32%. An emergency exploratory laparotomy revealed a small, irregular spleen with multiple nodules. The spleen was successfully removed and the bleeding resolved.

A Review of Coagulation

In this case, as with many other cases, the need to evaluate the clotting ability of the patient is essential. There are several principal events that are involved in coagulation:

- Constriction of the injured vessel
- Formation of the “primary platelet plug”
- Stabilization of the primary platelet plug by deposits of fibrin through activation of clotting factors

The three primary elements of hemostasis are the endothelial cells that line the wall of the blood vessels, platelets and clotting factors (see **Figure 1**). Each of these elements must function appropriately for normal hemostasis. Defects in any of these three participants can result in abnormal bleeding or inappropriate clot formation.

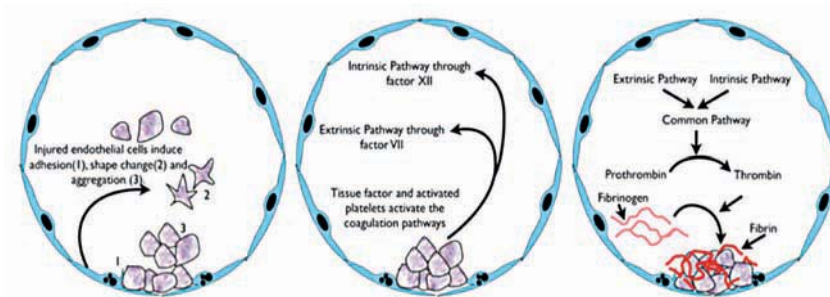


Figure 1

Damage to the endothelial cells exposes receptors (von Willebrand factor), and platelets adhere to the wall of the vessel covering the defect. The platelets become activated, undergo a shape change and begin to aggregate to form a plug at the injury. The platelets secrete substances and provide tissue factor for activation of the clotting factors. Once the coagulation pathways are activated, prothrombin is converted to thrombin; thrombin converts fibrinogen to fibrin and the fibrin “glues” the platelets together into a stable clot sealing off the injury.¹

Endothelial cells line all blood vessels. When injured, the endothelial cell retracts to expose proteins present in the tissue deep to the vessel wall or interstitium that interact with platelets to promote their adhesion. Further, these sites release molecules that promote activation of the clotting factors. The blood vessel wall plays a major role in both coagulation and fibrinolysis.

There is no laboratory testing that can evaluate the function of endothelial cells.

There are diseases that can interfere with the function of the endothelial cells. In most cases, abnormal endothelial cells result in abnormal clot formation because

they do not maintain their anticoagulant nature. ***Sepsis and metabolic diseases such as diabetes can result in pro-coagulant changes in endothelial cells throughout the body.***

Platelets are essential for primary hemostasis; the formation of the initial primary platelet plug. The injured endothelial cells promote the adhesion, aggregation, swelling and secretion by platelets (activation). Activated platelets also promote the activation of other platelets. When platelets are activated, they release factors that promote activation of the coagulation cascade. In addition to the secreted factors, platelets provide

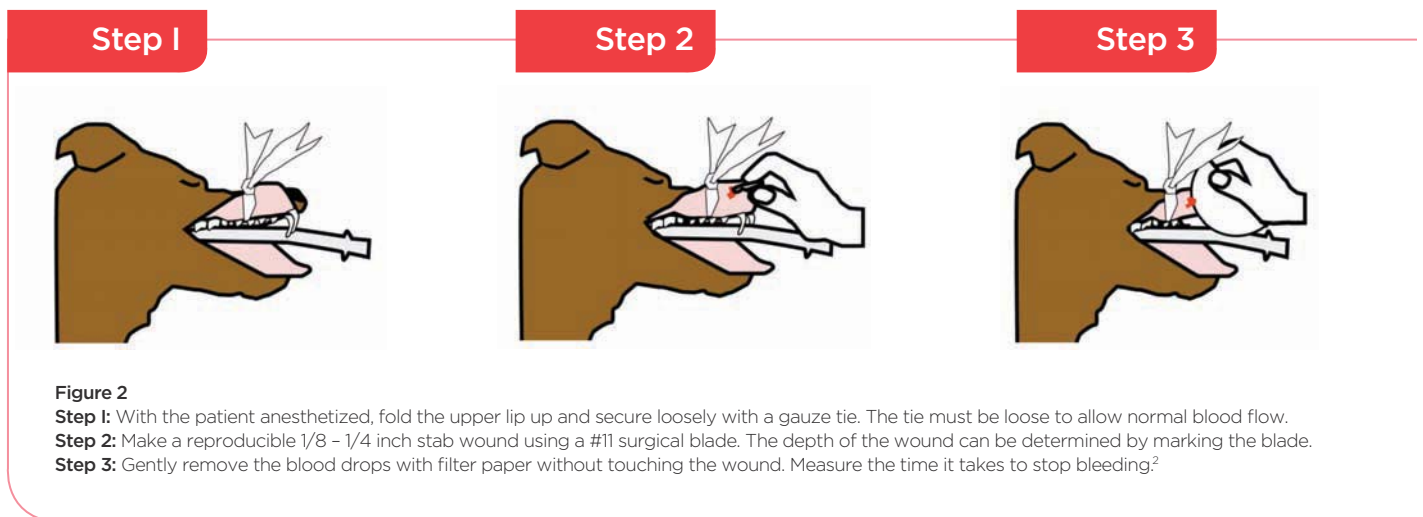
1. Image courtesy of Clinical Pathology for the Veterinary Team, Rosenfeld, A & Dial, S. Wiley, Ames, IA, 2010.

a surface for the clotting process and the cellular mass that will form the clot. Defects in primary hemostasis can occur due to decreased numbers of circulating platelets (**thrombocytopenia**) or **platelet dysfunction**.

Thrombocytopenia is the most common defect in primary hemostasis. The platelet count is the most common test to evaluate platelet number. **In general an animal will not begin to spontaneously bleed until platelet number is less than 40,000/ μ L.**

Platelet function tests should be performed in the bleeding patient with normal platelet numbers and coagulation times. There are sensitive tests for platelet function that require submission of a sample to a specialty laboratory. However, there are in-house

tests that can be done to identify patients with possible defects in platelet function; the most reliable is the buccal mucosal bleeding time. The **buccal mucosal bleeding time** is commonly done to screen dogs for von Willebrand's disease. A small shallow cut is made in the mucosal surface of the upper lip and the time from the initial cut to cessation of bleeding is recorded. It is very important to perform this test in a standard and consistent manner. A standard procedure for this test is outlined in **Figure 2**. Normal buccal bleeding times are 1.7 to 4.2 minutes with a mean of 2.6 minutes. If there is a prolonged buccal mucosal bleeding time, further laboratory tests are required to determine the cause of the platelet dysfunction.



Secondary hemostasis is the process of stabilizing the platelet plug by formation of **fibrin**, the mortar that holds the platelets together. The processes of primary and secondary hemostasis occur simultaneously. The formation of stable fibrin is the result of activation of numerous circulating clotting factors and enzymes or enzyme complexes that form the coagulation cascade. The coagulation cascade depends on many

cofactors such as calcium and multiple feedback loops that accelerate and inhibit the process. If there is a deficiency in the coagulation cascade, the primary plug will degrade prematurely and bleeding will resume. The common tests for defects in secondary hemostasis are the **Prothrombin Time (PT)** and the **activated Partial Thromboplastin Time (aPTT)**.

2. Image courtesy of Clinical Pathology for the Veterinary Team, Rosenfeld, A & Dial, S. Wiley, Ames, IA, 2010.

A prolonged PT and normal aPTT indicate a defect in the extrinsic pathway, while a prolonged aPTT with a normal PT indicates a defect in the intrinsic pathway. If both tests are prolonged, there may be a combined pathway disorder, such as Vitamin K

antagonism due to warfarin toxicity or liver disease, or DIC, or there may be a common pathway disorder such as an inherited coagulation factor defect such as Factor X or Factor II (Prothrombin).

Indications for Clotting Times

There are many congenital and acquired disease entities that can produce a coagulopathy, either from dysfunctional endothelial cells, decreased platelet number, platelet dysfunction or decreased clotting factors (see **Table 1**). Recommendations to establish baseline clotting times include:

- **Presurgical Blood Work Evaluation:**

Evaluating clotting times as part of a first-time presurgical (i.e., kitten/puppy) blood screen can help identify patients with hereditary disorders such as Hemophilia A or B. Identification of these patients prior to surgery is a necessity to prevent prolonged surgical bleeding. Although these diseases can affect any pure or mixed-breed canine or feline, veterinarians should screen the following breeds closely for hereditary coagulation disorders:

- **Hemophilia A:** Beagles, Alaskan Malamutes, Boxers, Miniature Schnauzers, Bulldogs
- **Hemophilia B:** Cairn Terriers, Airedales, Coonhounds, St. Bernards, American Cocker Spaniels, French Bulldogs, Alaskan Malamutes, Scottish Terriers, Shetland Sheepdogs, Labrador Retrievers, Bichon Frise, Old English Sheepdogs, British Short-Haired Cat

- **Hospitalized and Ill Patients:**

Syndromes that increase clotting times can include diseases that affect liver

function, ingestion of toxins which affect Vitamin K metabolism, and diseases that promote Disseminated Intravascular Coagulopathy. These entities can present subtly in an ill patient and develop into a severe acute life-threatening syndrome. Baseline clotting times are recommended for the following disease conditions:

- Sepsis/Infectious (Parvo Viral Infection, Pneumonia, Pyometra...)
- Liver Disease
- Heat Stroke
- Anemia/Hemorrhage
- Toxins or Poisonings
- Severe Metabolic Disease (Diabetic Ketoacidosis (DKA), Amyloidosis...)
- Neoplasia

Patients requiring surgical procedure or surgical biopsy should always have a thorough coagulation profile completed prior to the procedure.

Conclusion

The ability to evaluate and treat the at-risk patients with coagulopathy is becoming a practical and necessary solution to save patients' lives.



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From an emergency and general practice perspective, the use of in-house clotting analyzers or coagulation tests is an important aspect of the standard of care. With the tightening economy, clients are expecting more from the general practitioner and are less responsive to referring cases out to larger

secondary and tertiary care centers. The ability to evaluate in-hospital clotting factors and complete blood counts in ill patients allows the veterinarian to treat the patient effectively before severe bleeding occurs, and can save lives and help maintain the patient's quality of life.

Table 1

Pathology that disrupt the clotting process	Cause (Not intended to be a complete list)	In-house clinical diagnostics
Endothelial Dysfunction	<ul style="list-style-type: none"> • Hereditary Disease • Sepsis (i.e., Parvo, Pyometra, Pneumonia) • Endocrine Disease: Diabetes Mellitus 	There are no specific tests for endothelial dysfunction. Diagnosis of this process is seen through elevation of clotting times based on prolonged bleeding.
Decreased platelet number	<ul style="list-style-type: none"> • Immune Mediated Disease • Infectious Disease (i.e., Ehrlichia) • Consumption • Production Disorder (i.e., Bone Marrow) 	Platelet Count
Decreased platelet function	<ul style="list-style-type: none"> • Congenital Disease (i.e., von Willebrand's disease) • Toxins / Drugs (i.e., Aspirin) 	Buccal Mucosal Bleeding Time
Decreased Clotting Factors	<ul style="list-style-type: none"> • Congenital Disease (i.e., Hemophilia A [deficiency of Factor VIII] & Hemophilia B [deficiency of Factor IX and deficiency of Factor X]) • Hepatic Dysfunction: Infectious, Inflammatory, Toxin, Metabolic, Neoplastic • Toxin – Coumadin / Anti-Vitamin K Poisons (Rodenticides) • DIC: Sepsis, Heat Stroke, Neoplasia, Immune Mediated Disease, Shock, GDV, Advanced Heartworm Disease • Neoplasia: Atraumatic Abdominal Bleeding • Chronic Bleeding Disorder 	Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT)

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