ALL BLEEDING STOPS EVENTUALLY

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All bleeding stops eventually, right?

In a typical veterinary practice, we see patients bleeding everyday whether it be in surgery or during an emergency. Most of us would think that the bleeding would stop on its own, but what if it doesn't? The goals of this presentation are to go over the physiology of hemostasis, diseases of the hematology system, and products that may help with coagulation.

Physiology of clot formation

Hemostasis is defined as the stoppage of bleeding. It is divided into primary hemostasis and secondary hemostasis. Coagulation is defined as the process of forming a clot. Naturally there is a balance between clot formation and clot breakdown within the body. It is a balance between procoagulant and anti-coagulant forces within the walls of the vessels.

In order for a clot to form and coagulation to start, the first step involves damage to the vessel wall. After it is damaged, the first response of the vessel is to vasoconstrict. This can help to hold blood, inflammatory mediators, and coagulation factors at the site of injury. Vasoconstriction also causes the blood to go to different areas of the body. Collagen is exposed when the vessel wall is damaged, leading to activation of the hemostatic system. There are two steps to hemostasis, primary hemostasis and secondary hemostasis.

Primary hemostasis has three components: platelet adhesion, platelet activation and platelet aggregation. During platelet adhesion, platelets in the blood stream adhere to the exposed collagen. Von Willebrand factor helps to create a junction between exposed collagen and the platelets. As the platelets adhere to the collagen, they become activated. Activated platelets release calcium, thromboxane A_2, and platelet aggregation factor. Calcium binds to phospholipids and eventually aids in the creation of thrombin. The last step, platelet aggregation, is when the platelets layer on the injured area, resulting in a "clump" of platelets.

Secondary hemostasis is the formation and completion of a platelet plug. Tissue factor plays a major role in secondary hemostasis. Clotting factors are primarily made in the liver and remain inactive in the blood stream until they become activated. There are three main pathways in the classic coagulation cascade. These pathways are the intrinsic pathway, the extrinsic pathway, and the common pathway (See Figure 1). The extrinsic pathway is initiated by TF binding to factor VII and then continues to the common pathway. The intrinsic pathway is initiated by factor XII. The intrinsic pathway includes factor XI, IX, VIII and then goes into the common pathway. The common pathway consists of factor X, factor , factor II (thrombin), and factor I (fibrin).

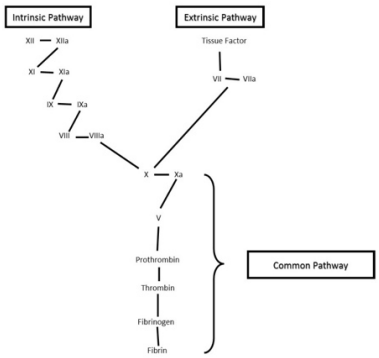

Figure 1: The coagulation cascade

There are multiple diseases of the coagulation system. During this presentation, I will only be going over a few of the multiple diseases. There are disorders of the primary hemostasis system and the secondary hemostasis system.

- **Disorders of Primary Hemostasis**

  Thrombocytopathias are primary hemostasis disorders where the platelets are non-functional. Thrombocytopathias can be inherited or acquired. A common acquired thrombocytopathy can occur secondary to medications that have an adverse effect on platelets. Some medications that can have adverse effects on platelets are aspirin, ibuprofen, naproxen, aminophylline, diltiazem, and NSAIDS. Petechia or purpura can be seen with thrombocytopathies.

  Von Willebrand disease is a deficiency of von Willebrand factor (vWF). Von Willebrand factor allows platelets to aggregate together. It is common to diagnose von Willebrand disease after the patient has had surgery. The patient's signs can range from mild petechia to severe bleeding. Once von Willebrand disease is diagnosed and a patient is bleeding, fresh frozen plasma would be the best option in a general practice setting. Dobermans, Burmese mountain dogs, Chesapeake Bay retrievers, and Scottish terriers are among the most common breeds with von Willebrand's disease.

  Thrombocytopenias occur when platelet numbers are low. The most common thrombocytopenic condition -- immune mediated thrombocytopenia (ITP) -- can be idiopathic (primary) or a secondary disorder in patients with another illness such as neoplasia. Primary ITP occurs when the body's immune system recognizes the platelet as a foreign substance and destroys the platelets for no good detectable reason.

- **Disorders of secondary hemostasis**

  Liver failure is a secondary hemostasis disorder because the liver is where most of the clotting factors are produced. If the liver is not functioning properly, the clotting factors are unable to be utilized in the rest of the body.
  Hemophilias are a common secondary hemostasis disorder. Hemophilia A is caused by a factor VIII deficiency. Hemophilia B is caused by a factor IX deficiency. These hemophilia's are only expressed in male animals and are usually only found if a patient is bleeding after it has undergone surgery or trauma.
  A common toxicity we see that causes bleeding is *anticoagulant rodenticide toxicity*. This can present as "coughing up blood" or having some kind of internal bleeding. When anticoagulant rodenticide is eaten by a pet, the enzyme that recycles vitamin K from "old" clotting factors is inhibited. Without the ability to

recycle the vitamin K, clotting factors II, VII, IX, and X cannot be activated. This leads to widespread bleeding in the body.

- **Disseminated intravascular coagulopathy**

  Disseminated intravascular coagulopathy (DIC) is where coagulation is activated in the body in response to another illness. This can lead to thrombi in the vasculature. The most common diseases associated with DIC are sepsis, pancreatitis, and neoplasia. Once clots form in the vasculature it causes ischemia, decreased perfusion, and possible hypoxia. The body eventually depletes all coagulation factors which then causes hemorrhage.

There are multiple signs of a possible bleeding problem that can be diagnosed on a physical exam. The signs that any technician should watch out for are petechia, ecchymosis, purpura, and continuous bleeding.

Petechia are small pinpoint red spots that are commonly found on ears, gingival surfaces, and possibly the ventral abdominal wall. Petechia is sometimes caused by low platelets. When a patient is thrombocytopenic and a capillary ruptures, there are not enough platelets to adhere to the injured vessel wall and stop all bleeding. However, coagulation factors are still produced which will eventually create a clot after there has been some bleeding resulting in the site of petechia.

Purpura is slightly larger area than petechia and indicates bleeding under the skin. Ecchymosis is a larger red area and is more commonly known as a bruise. This can be due to thrombocytopathies.

Melena is an indicator of bleeding into the GI tract. It often occurs with platelet function abnormalities or thrombocytopenia's. The gastrointestinal tract should be examined if melena is apparent. A rectal exam should be performed on all patients to look for melena.

Bleeding into the thorax or abdomen can occur. This can present as pale mucous membranes, respiratory distress, distended abdomen, lack of hind limb pulses, tachycardia, ataxia, and overall lethargy. Radiographs and ultrasound may confirm suspected cavity bleeding. A thoracic and abdominal tap can be done to confirm the presence of an effusion. If the effusion looks like blood, a PCV/TP should be tested on both the effusion and from a peripheral vein. If the PCV/TP are similar in both locations, this indicates that there is active bleeding within the cavity; this should be further explored to find the source of the bleeding. Surgery may be indicated with these patients.

There are different types of diagnostic testing depending on the type of clotting disorder is suspected.

- **Testing primary hemostasis**

  A platelet count can estimate if the patient has adequate platelets. This is done by drawing a blood sample in an EDTA (purple top) tube and making a blood smear.

  Blood mucosal bleeding time (BMBT) is an easy test that examines the amount of time a 1mm incision that is made with a spring-loaded device stops bleeding. Filter paper is used to blot the blood, but the incision must not be disturbed. Normal BMBT is < 3-5 minutes. This test should only be done when the platelet count is normal. It tests platelet function.

- **Testing secondary hemostasis**

  A *prothrombin time (PT) and partial thromboplastin time test (PTT)* are blood tests that measures the extrinsic/common and intrinsic/common pathways respectively. These tests are performed on blood collected into a citrate (blue top) tube. These tests will be prolonged if there is a deficiency of one of more clotting factors.

  Activated clotting time (ACT) can also test for coagulation factor deficiency. This test can be done bedside in-house. Blood is drawn and placed in a grey top (diatomaceous earth) tube. It tests the same clotting factors as

the PTT test (ie. the intrinsic and common pathways). To have prolongation of the PTT test, 75% of at least one clotting factor need to be deficient. To have prolongation of the ACT test, at least 90% of one or more clotting factors need to be deficient.

At some point in your veterinary career, you will see a bleeding patient either due to trauma or maybe during surgery or a dental. If a hemorrhaging patient comes into your veterinary clinic, the first thing any veterinary professional should do is apply pressure or a quick bandage. This will help with the vasoconstriction and help slow down the bleeding. It will also give more of a surface for a clot to form. At the same time or right after pressure is applied, an intravenous catheter should be placed. You may need it to administer fluids or blood to replace the blood volume that is lost. A chemistry panel, complete blood count, and any other coagulation tests should be drawn to distinguish an underlying cause for the bleeding. If the bleeding still hasn't stopped, there are multiple other options to make the bleeding stop.

If the blood is coming from an extremity, a tourniquet can be used to cause the blood to stop flowing to that particular part of the body. A tourniquet should not be used for an extended period of time because it can damage the tissues and cause ischemic damage. Icing is another way to help slow down bleeding. Ice will vasoconstrict vessels and slow down blood flow to help create a clot. If cautery is available, it can be used to quickly cauterize the vessels and make blood flow in a different direction.

If the bleeding is on a toe or in the mouth, a product called Quik Stop®, can help. It may not taste very good, so be prepared for possible drooling or resistance. Yunnan Baiyao is a Chinese herb supplement that is has been used all over the world. There are limited studies on the product and the manufacturer has never told anyone what is actually in it. It comes in blister packed capsules with one red capsule. The red capsule is supposed to be only taken with severe hemorrhage. There have been a few cases in the ICU that have been on this Chinese herb.

Greyhounds have been known to bleed after surgery. They have enhanced fibrinolysis (ie. enhanced clot breakdown) which may be the cause of post-operative bleeding. Aminocaproic acid, or EACA, and transexamic acid are drugs that are used to inhibit fibrinolysis. It is can be given orally or intravenously.

Other medications that can be used are sedation medication like acepromazine. Acepromazine lowers blood pressure by dilating the vessels and causing the heart rate to decrease. This creates more time for a clot to form as the blood flow slows through the vessels.

There are also a few other products that are on the market that are specifically to help stop hemorrhage. They are labeled as Vetigel® and Bleed-X-Vet®. It is unknown how these products work, but they are believed to activate the intrinsic part of the cascade and provide a surface on which a clot can form.

A blood transfusion of whole blood or plasma should be given if the bleeding has not stopped and the patient has lost a significant amount of blood. If blood products are not available in your hospital, an auto-transfusion may be warranted. This is the process of taking blood that is pooling in a body cavity and giving it back intravenously.

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