Q: Is vitamin K always indicated in bleeding disorders?
A: Vitamin K is only indicated in cases of vitamin K deficiency or antagonism. This includes Coumadin (warfarin) overdose, anticoagulant rodenticide, gastrointestinal malabsorption, liver failure, and hereditary vitamin K dependent coagulopathy in Devon Rex and Sphinx cats.

Q: Can you please discuss indications/contraindications/use of the IDEXX analyzer?
A: The IDEXX Coag Dx™ analyzer is a point-of-care instrument that permits determination of PT and aPTT on citrated blood within an hour from collection without separation and chilling, and thus is most helpful to determine any coagulopathies such as rodenticide poisoning, hereditary coagulopathies, coagulopathy due to hepatic failure or DIC. By the way, the IDEXX Coag Dx analyzer is replacing the SCA2000. Additionally, it offers software integration with the IDEXX VetLab Station.

Q: Because my clinic does not regularly store blood products, is there any condition where fresh whole blood is actually contraindicated?
A: Indeed fresh whole blood can be used in many circumstances when an animal is bleeding. However, some animals are not anemic and thus do not need the red cell component; too much may cause them to become polycythemic. Moreover, patients are going to be more likely sensitized with whole blood than with plasma products (which are free of red cells). It might be advisable to store fresh frozen plasma from a commercial blood bank with a storage period of one year. Thereby, animals with bleeding due to a coagulopathy or von Willebrand disease can be more specifically treated. Finally, it is often difficult to find a suitable donor when presented with a bleeding dog.

Q: How frequently do you monitor the PT when you have diagnosed a coagulopathy?
A: It depends on the cause and degree of the coagulopathy, the severity and site of hemorrhage, the degree of PT and aPTT prolongations observed, and the treatment instituted. Transfusions generally can produce an immediate response. Therefore, measuring PT, aPTT, platelets, and/or PCV one hour following transfusion is ideal. For instance, the PT and PTT normalizes shortly after FFP or within 2–3 days after vitamin K administration. However, the platelet count may not rise in ITP following transfusion of fresh whole blood or platelet concentrate but may provide some life-saving short-term hemostasis. Also, the clinical signs should be evaluated.

Q: If you have a PT or an aPTT that is elevated (i.e., >100), what is the treatment before an elective surgery?
A: An elective surgery should not be done when the PT and aPTT are massively prolonged. Whenever possible, a diagnosis for the massive PT and aPTT prolongations should be investigated. Rodenticide poisoning should be suspected when both PT and aPTT are massively prolonged. However, if the animal is not bleeding, this may be due to an in-house testing or laboratory error, or an error with blood collection, separation, and shipment.

Q: At what PCV do you recommend a blood transfusion?
A: This very much depends on the clinical signs, the rapidity of the PCV drop, hydration status, and underlying disease. Generally we are considering transfusions when the PCV falls below 20–15% in a normovolemic animal.

Q: How do you store/transport whole blood?
A: Fewer than a dozen commercial blood banks have established shipping procedures that assure arrival within 24 hours; these banks also provide instructions for the storage of blood products. Whole blood and packed red blood cells can be typically stored in the refrigerator at 4°C for up to 35 days. Fresh frozen plasma and other plasma products can be stored frozen at <-20°C for one year.

Q: I've had a dog get IMT from Trimeth-sulfa drug. How long does it take for the platelet count return to normal once off the drug?
A: No formal studies are available. In my experience the platelet count returns into the safe >40,000/µL range within days upon drug withdrawal. I found the thrombocytopenia always reversible within a couple of weeks. However, there are other drugs where the effects may be irreversible or longer lasting.
Q: If you have a dog that needs to be transfused with fresh whole blood and you don’t have the capabilities to blood type the blood, what’s your recommendation? We do not have plasma.
A: There are typing cards and typing cartridges for in-clinic use. You will also want to submit a pre-transfusion sample for typing—results are available within a day. You always want to type your donors ahead and, if you do not know the type of the patient, transfuse DEA 1.1 negative blood.

Q: Pre-op in-house labs often show low platelets. It is best to follow with blood smear or buccal mucosal bleeding time or both?
A: Artificially low automated platelet counts are a problem for both in-house and lab instruments. Reference labs and in-house instruments generally flag their low platelet counts. The review of a blood smear for the presence of platelet aggregates (not counted) and a morphologic evaluation (macroplatelets are often not counted) is typically part of a lab report. A brief microscopic blood smear evaluation should always be done except for the most routine pre-op evaluation of a healthy animal. A BMBT is not indicated unless the platelet count is normal or at least >100,000/µL.

Q: Do you see clinical thrombocytopathia with other NSAIDs aside from aspirin (i.e., Rimadyl, Derrammaxx, Previcox, etc.)?
A: Clinically, the platelet inhibition of aspirin and other NSAIDs is relatively mild except when combined with another underlying bleeding tendency, such as vWD, or when associated with gastrointestinal ulcers.

Q: Can the PT, aPTT, ACT be performed in a human laboratory?
A: Human labs do not generally have their instruments and assays validated for animals. The times of the PT and aPTT are much shorter in small animals than in humans, thus instruments for humans may not be able to accurately measure the PT. The normal ranges in humans are actually in the range of coagulopathic in animals. Finally, an ACT requires very fresh non-anticoagulated blood.

Q: Does PRBC transfusion help with D-con poisoning at all?
A: In anticoagulant rodenticide poisoning, animals may become anemic and, if the anemia is severe, transfusion with PRBCs is indicated. This will not only provide the oxygen carrier support needed, but the higher PCV also helps with hemostasis as RBCs are part of the clot.

Q: If you have a normal BMBT, ACT, PT and aPTT and normal vWF but still have a dog that bleeds abnormally, is there anything else that would be causing this?
A: Your normal ranges may be too large or for a different species to detect the cause of bleeding. You may wish to repeat testing through a different lab, such as an established veterinary reference lab. You want to also make sure you have a normal platelet count and normal platelet morphology. Finally, it should be noted these tests are screening tests that may not detect every abnormality. There is a Scott syndrome in German shepherds as well as some thrombopathias that may not or only slightly prolong one or the other screening test. Special factor and platelet studies may be required.

Q: What is IVIG?
A: Intravenous immunoglobulin G is a product generated from human plasma and is enriched in IgG. It is extremely expensive. It may be indicated in some serious immune diseases known to not respond to any other agents, such as serious allergic drug-induced skin, joint and systemic reactions, and possibly in immune-mediated hemolytic anemia and thrombocytopenia. No trials have documented its efficacy, but generally it has been found to be safe when given once over a 2–3 day period.

Q: In treating anticoagulant rodenticide poisoning with plasma support, are you trying to replace all coagulation factors or increase the vitamin K dependent ones?
A: Fresh frozen plasma contains all coagulation factors while cryo-poor plasma (the preferred product) has equal amounts of these factors except less fibrinogen, FVIII and vWF. Plasma is indicated whenever there is life-threatening bleeding.

Q: If an owner is not sure if their pet was exposed to second generation rodenticides, how often do you check PT/aPTT times to rule out exposure?
A: Due to the short survival of vitamin K-dependent coagulation factors and the lack of any appreciable amount of stored factors in tissues, coagulation factor depletion is seen within 1–3 days, and PT and aPTT will become massively prolonged. If just ingested and the PT is normal, emesis should be induced. Assuming the PT was normal, screening at 1 and 3 days after ingestion will be appropriate to discover any intoxication.

Q: Does abnormal platelet number/function effect aPTT, ACT, PT?
A: PT and aPTT are not affected by thrombocytopenia and thrombopathia. However, the ACT relies on the presence of some platelets as a phospholipid source, and in severe thrombocytopenia of <20,000/µL the ACT can be slightly prolonged.
Q: Why is plasma yellow?
A: The yellow color is caused by an increased amount of bilirubin. Occasionally other products (vitamin supplements) may also cause some yellow coloration.

Q: What are lyophilized platelets?
A: As indicated, platelets are made dysfunctional whenever blood is chilled. Storage of platelets is difficult and practically limited to a few hours at room temperature (unless you have a platelet rocker at a defined temperature). Thus, experiments are being conducted with other storage methods. Lyophilizing refers to freeze-drying; the material is rapidly frozen and dehydrated under high vacuum. The advantage is the product can be stored for months and/or years at room temperature or 4°C without losing activity. For instance, some vaccines and human IV Ig are lyophilized. Clinical studies are in progress to evaluate the safety and efficacy of lyophilized platelets.

Q: I have an 8-year-old Doberman with vWF normal, PT and aPTT normal, bruising and petechia in the past but normal now. Platelets have been declining from 93k to 42k, now 11k. Mast cell tumor was removed 3 weeks ago with clean margins; lungs and abdomen are clear on US.
A: A thrombocytopathia, vasculopathy, and the paraneoplastic effects of a metastatic mast cell tumor may have to be considered.

Q: Do you recommend prescreening breeds other than Dobermans before elective surgery?
A: Besides vWD in Doberman pinschers, vWD is seen in many other breeds and may be prevalent in a certain breed. Hence screening vWF concentration in plasma may be indicated in those breeds, particularly those with a family history of bleeding. Moreover, there are a few coagulopathies such as FVII deficiency in Beagles, Klee Kais and Scottish Deerhounds, and FXI deficiency in Kerry Blue terriers for which screening may be indicated. Fortunately those coagulopathies and vWD cause mild to moderate bleeding tendencies and are readily controlled with appropriate plasma therapy.

Q: Can frozen plasma be stored in a regular freezer?
A: It depends on what you consider a regular freezer. A small open compartment in a refrigerator, which may also be used for food, is inadequate. However, a freezer chest or freezer combined with refrigerator with separate doors can be adequate as long as the material stays deep frozen (<20°C). Ideally the freezer should be dedicated for plasma products, rarely opened (to avoid temp fluctuations) and not used for food items (safety). There are fading indentations in the bag or actual markers that tell if the product has been thawed. After thawing, the product may have lost its efficacy for hemostasis.

Q: Does oral prednisone dose for ITP typically need to stay at high daily dose for life or can it usually be dropped down to eod lower dose once under control?
A: A high prednisone dose is needed until a response is observed and is typically given for a week or more. However, if an underlying cause has been identified to trigger ITP and when the platelet count rises above 40,000–80,000, tapering can be started. Tapering is more rapidly done in secondary (a couple of weeks) versus primary thrombocytopenias (several weeks to months). It is uncommon to have to give prednisone life-long and, when indicated, is generally at a very low dose.

Q: How long can whole blood be stored in the refrigerator (citrated)?
A: Blood collected into CPDA via a closed blood-collection system can be stored for 4 weeks (some commercial blood banks may have a system to store for longer). However, if you are using only citrate and are not providing the nutrients of CPDA or Adsol or other red cell preservative, you are also likely using an open collection system and the unit should be used fresh or within 24 hours.

Q: Will ITP, as IMHA is, be refractory to response to treatment if treatment is discontinued and then restarted due to recurrence of signs?
A: In my experience few ITP cases remain refractory after a relapse to prednisone and vincristine. If they are refractory, the underlying cause should be investigated. In one case a small skin lesion was the culprit and the dog had no relapses after removal of this small abscess.

Q: You mentioned aspin therapy for IMHA—is that the protocol you currently recommend?
A: Thromboembolic disease is the major complication in cases of IMHA and is still poorly understood. Vascular abnormalities, hyperactive platelets and hypercoagulability may contribute as well. Unfortunately, no preventive and therapeutic interventions have been shown to be really successful. Furthermore, some of the anticoagulant agents such as heparin may be associated with increased hemorrhage. An ultralow dose of aspirin may help prevent thrombus formation and will not lead to a bleeding tendency.

Q: Aspirin only effects platelets?
A: Correct—aspirin inhibits the thromboxane synthetase in platelets and thus inhibits platelet aggregation. Of course, aspirin may also cause GI ulcerations, which can result in serious bleeding by itself.
Q: Why is oral vitamin K so expensive?
A: Oral vitamin K at a therapeutic dose for a large dog is expensive, but parenteral products are even more expensive. The drug company sets the price.

Q: Are you aware that IDEXX does not have grey-top tubes anymore for ACT times? What are we supposed to use?
A: Since IDEXX has introduced its IDEXX Coag Dx™ Analyzer, which offers PT and aPTT, it is understandable that they cancelled the ACT tube distribution. The fresh, non-anticoagulated whole blood aPTT is more standardized and equal to the ACT in regard to factor analyses. In general—unless you are dealing with a very small animal and cannot collect the right amount of blood into a citrate tube (9 parts blood and 1 part citrate)—the PT and aPTT tests on fresh, whole citrated blood are preferred, as citrated plasma can be stored up to an hour at room temperature until run by the IDEXX Coag Dx Analyzer and still be separated for subsequent additional plasma studies.

Q: Where can we learn to give or get demos on giving transfusion products along with storage and collection?
A: Over the years, including this year, I have organized and presented workshops at the ACVIM Forum in Texas with others from Penn and other institutions where we show and allow limited practicing on blood donors, collection, separation and storage. There are also organizations that focus on blood banking, including the Association of Veterinary Hematology and Transfusion Medicine and the American Association of Veterinary Blood Banking.

Q: How often do you use ACT in the evaluation of your hemorrhagic patients?
A: This depends on the case, the severity of bleeding signs, and the PT and aPTT (or ACT) prolongations. Whenever possible we will do a PT and aPTT (or an ACT) for the diagnosis of a coagulopathy prior to treatment of a bleeding patient. When abnormal, we follow the abnormal test(s) within one hour with plasma products and then daily until healing and coagulation time normalization occurs.

Q: Where can we find the vWF ELISA?
A: In most reference laboratories (including IDEXX), the plasma vWF is generally determined by an ELISA assay.

Q: Have you seen an increase in DIC over the years and, if so, is there any reason why that may be?
A: Comparison of the frequency of DIC with the past is difficult. We certainly have better diagnostics to identify this syndrome. We are also treating more serious illnesses in companion animals for longer periods, which may end in a DIC situation.

Q: Is there a difference in the route of vitamin K (i.e., oral vs. injection in rat poisoning)?
A: Vitamin K is readily absorbed after oral administration and corrects the PT and aPTT within 1–3 days. The IV route is restricted to animals that are vomiting or cannot take anything orally and is not really substantially faster in action. In the past there was a major concern in giving vitamin K intravenously, but the company reformulated the product to be safe.

Q: Is cryo-poor plasma the same as cryoprecipitate?
A: No! Cryoprecipitate is the slurry that forms when fresh frozen plasma is slowly thawed in the refrigerator. Cryo is rich in large clotting factors, such as fibrinogen, factor VIII and von Willebrand factor. In contrast, cryo-poor plasma is the supernatant of the slow thawing process and contains the smaller coagulation factors including all the vitamin K-dependent coagulation factors (FII, VII, IX and X). Cryo-poor plasma is ideal for anticoagulant rodenticide poisoning as it preserves the other coagulation factors in the cryoprecipitate for other patients with hemophilia and von Willebrand disease.

Q: What is your thought on d-dimer testing?
A: D-dimer testing is indicated when excessive, intravascular coagulation and thrombotic tendencies are suspected. While a point-of-care test was once available, currently only laboratory methods are offered through some reference labs. Again, validation of their methods should be assured.

Q: Where can you get the human IVIG? As so many of us can not save ITP dogs that present first with a GI fresh blood on stool—no petechia or any other signs. It first appears as a colitis with fresh blood and mucus, but then platelets are 40,000. We have not been able to save any of these.
A: I am sorry to hear about your experience with exclusive GI bleeding due to ITP and your lack of success with conventional treatment. In such cases, transfusion support and local hemostasis by endoscopy may be needed. Human IVIG is not approved for use in animals and has not been proven to be effective in canine ITP. It can be obtained at pharmacies of human hospitals or from the manufacturer; it is extremely expensive.
Q: My dog’s PT and aPTT are normal but my dogs PIVKA is high—what could this mean?
A: The normal ranges for PT, PIVKA and aPTT are different and may vary depending on the methods used. As the PT and PIVKA test are plasma coagulation assays initiated with slightly different tissue factors via the extrinsic cascade, they should either be both prolonged or both normal. As indicated, the PIVKA test does not confirm rodenticide poisoning, and rodenticide poisoned dogs with hemorrhage have very prolonged PT (as well as PIVKA) and aPTT tests. You may run a healthy control along with your patient for any coagulation test that you rarely perform. Sometimes the PT prolongation is not as well appreciated as it is normally shorter than the PIVKA time. If only the PIVKA and PT are prolonged, I suggest screening for FVII deficiency. We offer a DNA test for Beagles, Scottish Deerhounds and Alaskan Klee Kais (PennGen).

Q: My neighbor put out rodenticide and his dog died. I ran a PIVKA on my dog and it was at 21, PT was normal. I treated for 4 weeks with vitamin K and retested a month later and the PIVKA was at 40. I retreated again and it is now at 20. I cannot find the rodenticide; what should I do?
A: I am sorry to hear about your neighbor’s dog and you are facing a challenging situation. Surely your neighbor tried to remove everything. I suggest you rerun your dog’s PT, aPTT and PIVKA along with a control from a healthy dog. An isolated mild PIVKA prolongation does not really suggest rodenticide poisoning (see above).

Q: What is the normal range for the BMBT and is it accurate without the automated device?
A: The normal buccal mucosal bleeding time performed with a snapper and one or two blades that cut precisely 1 mm deep is less than 5 minutes—typically we observe times of 2.5–4 minutes. Incisions with a blade (but without the snapper) cannot be standardized and thus have very varied times.

Q: Has the IVIG been utilized in cats?
A: Yes, it has been used in a few cats. We published first a cat with serious dermatologic drug reaction (Byrne KP, Giger U. Severe erythema multiforme in a cat successfully treated with human intravenous immunoglobulin. J Am Vet Med Assoc. 2002; 220: 197-201.) and it worked as well as those we later observed in dogs. As for any non-approved and human protein products, there are concerns for allergic and other drug reactions, particularly if readministered.

Q: Do you prefer the plasma test or the newer DNA test for detecting von Willebrand disease?
A: As the plasma vWF is readily available and accurate, I always use the ELISA test in clinical cases of bleeding. I might use the DNA test to make breeding decisions for breeds where it is available.

Q: How can PT/aPTT be used as a parameter for monitoring post-op, septic or other critical patients (pancreatitis)?
A: Such seriously ill animals may be treated with heparin and FFP and, in order to determine their effects, it might be best to follow these parameters.

Q: 10 Month old Papillion that bleeds profusely after blood draws. Normal PT, aPTT, normal platelet count. Any suggestions?
A: Again it will be important that the platelet count, PT and aPTT are truly normal. A vWF assay can readily be added. When normal results are confirmed and vWD is excluded, a buccal mucosal bleeding time may be indicated to screen for a thromboctoypathia. There are specific platelet studies that may then be pursued in a few labs, such as platelet aggregation, secretion, and granule content studies.

Q: Could you repeat the test used for DIC? Which labs provide this test? Also, which type of sample do you need to submit?
A: Sorry to be too fast on these tests—they were presented previously in the webinar on “New Insight into the Diagnosis of Bleeding Disorders” offered by the IDEXX Learning Center and were meant here as review. Thrombocytopenia, schistocytes, variable coagulation test prolongations, low fibrinogen, decreased Antithrombin III, increased fibrin split products and increased d-dimer concentrations may all be observed.

Q: For LMW Heparin treatment, you mentioned monitoring tenase. What is that?
A: The Tenase assay is a specific coagulation function assay that is affected by LMWH. It is offered in a few laboratories including human hospitals, but the correlation to its antithrombotic effect and concern for excessive hemorrhage has not been well established. Frequently LMWH is used at a particular dose without monitoring by lab test.

Practice what’s possible

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