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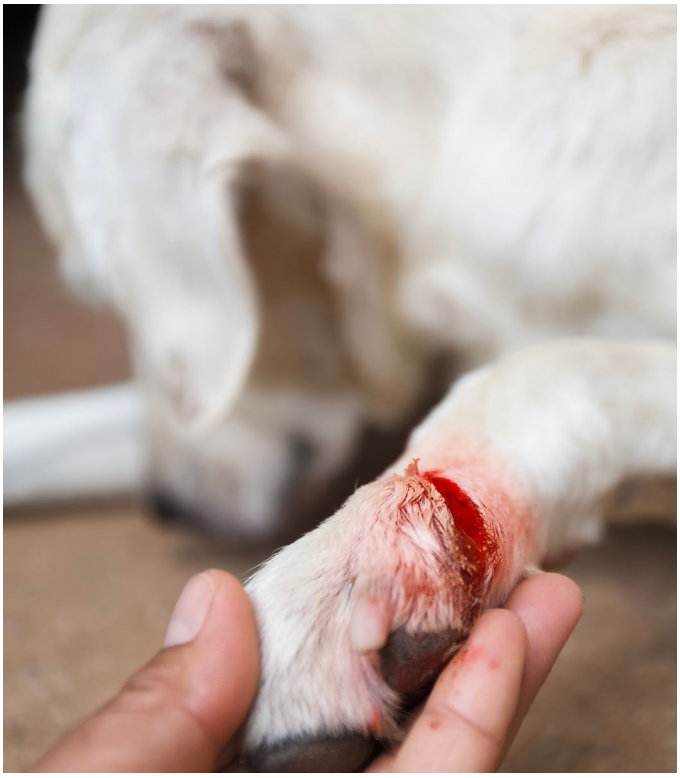
Coagulation Disorders in Dogs



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Have you experienced any of these situation whilst in veterinary practice: an eight-week-old puppy suddenly developing a large haematoma after a microchip has been inserted, a female dog experiencing increased bleeding during her oestrus cycle, unusual post-operative bleeding after a routine neutering, a Labrador with a history of eating something in the park a a few days ago and is now presenting with signs of apathy, haematomas and coughing, a patient presented to the emergency room with severe thrombocytopenia?
These are not uncommon scenarios, however they can seriously disrupt the daily routine of a veterinary practice or clinic.
As a veterinarian you will be faced frequently with both congenital and acquired coagulation disorders. In daily practice, we encounter congenital and acquired coagulation disorders. After a (micro) trauma, clot/thrombi formation occurs physiologically in the blood vessels to limit blood loss.
The interaction between coagulation promoting and coagulation-inhibiting factors is important in this process. If these processes are disrupted, serious bleeding or thrombus formation can occur.
Coagulation disorders are potentially life-threatening, especially if they remain undetected. A detailed case history, clinical examination and the right diagnosis are therefore extremely valuable so that early changes can be detected and the appropriate treatment regimes initiated.

Diagnostic Work-up

Pre-report and Clinical Examination

The work-up of a patient with a suspected coagulation disorder can be complex, as it is not always clear from the outset that there is a coagulation disorder. A detailed case history is therefore fundamental. The general case history for a patient with a suspected coagulation disorder includes the following:

- Breed, age and gender of the patient
- Regular tick prophylaxis?
- Any history of travel
- Previous illnesses
- Has the patient ever been diagnosed with a blood clotting disorder or thrombosis?
- Family history: Are there any cases of coagulation disorders in littermates or parents?
- Have unusually long bleeding times or increased bleeding been observed after injuries or procedures?
  - Dental treatment/teething
  - Castration
  - Births
  - Oestrus
  - Other surgical procedures or traumas
- Is the patient receiving medication that can affect blood clotting?
  - Painkillers
  - Blood-thinning medication
  - Other medication (antibiotics, dietary supplements, vitamins, etc.)
- Could the patient have ingested anything?
  - Rodenticides
  - Medication from the owner

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In addition to the preliminary patient history, a thorough clinical examination is important.

Disorders of **primary haemostasis** are often characterised by diffuse mucocutaneous colour changes due to vascular defects.
Petechiae (punctiform bleeding), ecchymoses (small-area skin or mucous membrane bleeding), mucocutaneous haemorrhages, and epistaxis may also occur. In disorders of **secondary haemostasis**, haematomas, body cavity effusions, and bleeding into large joints are more likely to be found.
Note: The initial patient history and the clinical examination of the patient are important for the initial assessment of whether there is an increased tendency to bleed and whether the disorder is one of primary or secondary haemostasis.

Laboratory Diagnostics

The selection of appropriate laboratory diagnostic tests are essential for further evaluation.
Global tests are not always reliable. Activated partial thromboplastin time (aPTT) and prothrombin time (PT) can remain unchanged even when the patient has a coagulation disorder.
Depending on the clinical picture, a full blood count focusing on the platelet count and organ screening should also be conducted. Based on these results and clinical suspicion, further diagnostic work-up may be indicated.

Preanalytics

Preanalytics includes all the steps prior to the actual analysis and significantly contributes to the reliability of laboratory diagnostic findings, particularly for coagulation values.
Poor blood collection technique, severe stasis, or incorrect tube order can lead to inaccurate laboratory results. Citrate tubes should always be filled first when coagulation disorders are suspected. The reason for this is simple: serum tubes are often coated with procoagulants, which can contaminate the citrate tube and distort the measurement results. Citrate tubes may vary in colour depending on the manufacturer (usually blue or green) and come in different sizes.
The correct mixing ratio is crucial (9 parts blood, 1 part sodium citrate). Unlike other anticoagulants, coagulation in blood treated with sodium citrate can be restarted by adding activators. The amount of activator is precisely calibrated to the mixing ratio in the tube, so it is essential that the tube be filled exactly to the specified fill line. Any deviation in fill level can lead to inaccurate laboratory results and thus invalid values for the patient. Since these tubes are rarely used, it is advisable to check the expiry date before use. Even the formation of small or large clots can invalidate the analysis or render it impossible.
Tip: Regularly check your tube inventory for completeness and expiration dates, and ensure proper filling quantities.

Coagulation Tests

An overview of the various coagulation tests can be found in Table 1.

Disorders of Primary Haemostasis

Various conditions can lead to disorders in primary haemostasis, including thrombocytopenia and platelet dysfunction.

Thrombocytopenia

In most cases, **thrombocytopenia** in small animals is an incidental finding. Thrombocytopenia refers to the reduction in platelet count to below the species-specific norm. It usually indicates a pathological process, which can lead to a coagulation disorder with significantly reduced platelet levels.
Often, more than one cause can contribute to thrombocytopenia. A distinction should be made between pseudothrombocytopenia and true thrombocytopenia. Pseudothrombocytopenia occurs when not all the platelets present are counted during platelet analysis.
Therefore, a manual microscopic assessment is always recommended before proceeding with further investigation. Possible causes of true thrombocytopenia include reduced production in the bone marrow, increased consumption, destruction of thrombocytes, or increased sequestration.

Test	Description	Interpretation	Material
Platelet Concentration	Automated platelet count or microscopic platelet estimation	Thrombocytopenia: decreased production, increased consumption, or increased destruction/loss	EDTA Blood
PT (Prothrombin Time)	(Quick Test) extrinsic and common pathway	Decreased amount or reduced activity of Factor VII, X, V, II, I (e.g., in poisoning with rodenticide)	Citrate Plasma
aPTT	(Activated Partial Thromboplastin Time) intrinsic and common pathway	Decreased amount or reduced activity of Prekallikrein, HMWK, Factor XII, XI, IX, VIII, X, V, II, I	Citrate Plasma
TCT	(Thrombin Time) extrinsic and common pathway	Conversion of fibrinogen to fibrin; therapy control (Heparin); fibrinogen decreased with increased consumption	Citrate Plasma
D-Dimers	Breakdown product of fibrin lysis	Increased fibrinolysis may indicate a hypercoagulable state or increased clot formation	Citrate Plasma
Fibrinogen	Converted to fibrin	Inflammation (increase), consumption with hypercoagulability	Citrate Plasma
ACT	(Activated Clotting Time) intrinsic and common pathway	Decreased amount or reduced activity of Factor IX, VIII, II, I (lower sensitivity than aPTT)	Whole Blood
Factor VIII	Intrinsic and common pathway	Decreased amount or reduced activity of Factor VIII; Haemophilia A	Citrate Plasma
Factor IX	Intrinsic and common pathway	Decreased amount or reduced activity of Factor IX; Haemophilia B	Citrate Plasma
vWF	(Von Willebrand Factor) Activity level in percentage	Decrease affects primary haemostasis	Citrate Plasma
TEG	(Thromboelastography) Platelet function test	Important: Timely execution is mandatory!; Hyper- or hypocoagulability	Citrate Whole Blood

Von Willebrand Factor Deficiency

Von Willebrand disease (vWD) is the most common genetic bleeding disorder and varies in severity. It results from a defective or missing Von Willebrand factor (vWF) in the blood, which plays a role in blood clotting. A defective or absent vWF causes affected animals to bleed for extended periods when injured and, in severe cases, can lead to fatal haemorrhage. The bleeding primarily affects mucous membranes and can be exacerbated by additional illnesses or stress. Typical signs include recurrent bleeding in the gastrointestinal tract (with or without diarrhoea), epistaxis, bleeding gums, prolonged bleeding during oestrus, lameness due to joint haemorrhage, bruising, excessive bleeding after surgery, or from nails that have been cut too short. vWD is classified into three types (Type 1, 2, and 3), with Type 1 being the mildest form. Laboratory findings show no prolongation of PT, aPTT, and TCT.

Disorders of Secondary Haemostasis

Various diseases can cause disorders of secondary haemostasis, which may be either congenital or acquired.

Haemophilia A and B

These congenital coagulation disorders follow an X-linked recessive inheritance pattern.
Male animals are either clinically affected or healthy, while females are usually clinically asymptomatic carriers. **Haemophilia A** is caused by a deficiency or reduced activity of **factor VIII**, whereas **Haemophilia B** results from a deficiency of **factor IX**. Mild to severe bleeding disorders are possible. Clinically noticeable signs in affected animals often include large haematomas, epistaxis, and bleeding in the skin, muscles, and joints. Severe cases following major injuries or surgeries can be fatal. Haemophilia often occurs in certain families or breeds.

Haemophilia A is one of the most important inherited blood clotting disorders in Havanese dogs, while Haemophilia B is significant in the Rhodesian Ridgeback breed.

Liver Disease

Liver disease can result in defective production of both procoagulant and anticoagulant factors. PT, aPTT, ACT, or TCT may be increased.
Bleeding is uncommon but can occur in severe liver failure or in the setting of disseminated intravascular coagulation (DIC).

Vitamin K Antagonists and Vitamin K Deficiency

Vitamin K antagonists, such as coumarin derivatives (e.g. from rat poison), sweet clover, or certain medications, can cause internal and/or external bleeding, which usually occurs within 3 to 7 days of ingestion. Since these substances affect the vitamin K cycle, a possible increase in **vitamin K epoxide concentration** can be measured (coumarin activity). Coagulation tests typically show an increase in PT first (Quick value), with aPTT and TCT usually also increasing over the course of the test.

Consumption Coagulopathy

Consumption coagulopathy, or disseminated intravascular coagulopathy (DIC), is a coagulation disorder caused by the intravascular activation of blood coagulation. This leads to a significantly increased consumption of plasma coagulation factors and thrombocytes, resulting in a deficiency of these factors and thrombocytopenia.
The outcome can be bleeding. DIC always develops secondarily as a result of diseases that trigger excessive coagulation, such as tissue necrosis, heat stroke, infection with Angiostrongylus vasorum, neoplasia, endotoxaemia, sepsis, liver disease, poisoning, and pancreatitis.
Laboratory findings include thrombocytopenia, prolonged PT, aPTT, and TCT, along with increased D-dimers.

Conclusion

Blood coagulation is a complex topic,
and diagnosing patients with coagulation disorders is often challenging. However, a thorough medical history and targeted tests can help make the correct diagnosis and thus rectify the problem.

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Translation: Laboklin

Further reading

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