Anemia in dogs and cats – guidelines for the veterinary practice

Increased travelling with pets and the import of rescued animals from all over the world create new challenges for the veterinary practitioner. A frequently found clinical and laboratory diagnosis in these patients is anaemia. Sometimes the exact classification of anaemia can be difficult. Anaemia is a decrease of the erythrocyte content of blood. The typical clinical signs are pale mucous membranes, the laboratory characteristics of anaemia are decreased values of the erythrogramm.

There are different classification systems of anaemia, each with its advantages and limitations. The classification used in this article is based on bone marrow responsiveness, assessed by the number of reticulocytes in the peripheral blood. The major advantage of this method is its practicability. By means of a stained blood smear and a microscope the presence of reticulocytosis can easily be estimated in every in-house lab.

Fig. 1: Pale mucous membranes of an anaemic dog
Diagnosis

After determining the severity of the anaemia by assessing the erythrocyte count, the hematocrit and hemoglobin, the regenerative capability of the bone marrow is evaluated. For this purpose the enumeration of reticulocytes is gold standard. A regenerative anaemia is characterized by reticulocytosis (dog > 60,000 /nl and cat > 30,000 /nl). It may take up to 96 hours until reticulocytosis becomes detectable in peripheral blood.

The estimation of bone marrow responsiveness by examination of a blood smear is easily performed in the in-house lab. Polychromasia of erythrocytes (Fig. 2) is evidence of regeneration in properly stained smears. Polychromasia is less pronounced in cats than in dogs.

In chronic cases of blood loss bone marrow responsiveness decreases because iron deficiency develops over time. The hemoglobin concentration of reticulocytes (CHR) is a newly available parameter that detects iron deficiency earlier and more sensitive than microcytosis and hypochromasia, which develop at a later stage of iron deficiency anaemia. Determination of CHR is included in the reticulocyte count at LABOKLIN.

Highly regenerative anaemias – > 100,000 /nl in cats and > 120,000 /nl in dogs – are normally caused by hemolytic anaemia or acute blood loss. If bleeding is ruled out, the list of differential diagnosis of hemolyses has to be reviewed.

Etiology of hemolytic anaemia:

- Reduced membrane stability
  - e.g. PK deficiency, PFK deficiency
- Mechanic destruction
  - In capillaries e.g. glomerulonephritis, DIC, neoplasia...
  - Turbulences in large vessels e.g. in massive dirofilariosis
- Toxic lysis
  - (e.g. Heinz body anaemia, hypophosphatemia)
- Blood parasites (lysis by infectious agent directly) frequently in combination with
- IMHA (=immunmediated haemolytic anaemia)
  - infectious (blood parasites but also othcr infectious disease)
  - drug- or toxin-induced
  - neoplastic (e.g. lymphoma)
  - idiopathic (autoimmune)

Immunemediated hemolysis is confirmed if the coombs-test gives a positive result. The coombs-test detects antibodies against erythrocytes. In vivo these are recognized on the erythrocyte surface by cells of the mononuclear phagocytic system that subsequently phagocytize affected erythrocytes. The direct coombs test detects antibodies on the erythrocyte surface, the indirect one circulating antibodies in serum.

In the course of hemolytic anaemia occasionally very small, spherical erythrocytes may be found on blood smears, so called spherocytes. A high number of spherocytes is considered diagnostic for IMHA.

Regenerative Anaemia

Regenerative anaemia is caused by blood loss or a shortened life span of the erythrocytes (hemolysis).

A low total protein is suggestive rather of blood loss anaemia than of hemolysis, because bleeding patients loose erythrocytes together with plasma proteins.

When blood loss anaemia is suspected it is advisable to assess furthermore the platelet concentration and the coagulation times (thromboplastin time, partial thromboplastin time, thrombin time). The determination of the buccal mucosal bleeding time (BMBT) is an easily performed test of platelet function in practice.
CAVE: sometimes there is immunmediated hemolytic anaemia that does not show signs of regeneration!

Non Regenerative Anaemia

The etiology of non regenerative anaemia is much more divers. In various chronic diseases there is a reactive decrease of erythropoesis. (Table 2).

In this case an organ screening especially of the kidneys and liver is recommended. Chronic renal insufficiency decreases erythropoesis in bone marrow via decreased erythropoetin production.

Increased activity of liver enzymes and elevated liver function tests may indicate a decreased synthesis of proteins, in particular globulins, that are essential for hemoglobin synthesis in bone marrow.

Increased unconjugated Bilirubin can also be suggestive of hemolytic anaemia and may be recognized by yellow colouration of plasma.

Nutrient deficiency

With conventional feeding malnutrition is a rare condition nowadays, nevertheless it should be considered as differential diagnosis, if other causes of anaemia have been ruled out.

In iron deficiency there is not enough iron to be incorporated into hemoglobin and a hypochromic, in later stages even microcytic anaemia develops.

This can be verified by determining the CHR, which is consistent with the hemoglobin content in reticulocytes.

A shortage in copper also causes defective hemoglobin synthesis. Evaluation of copper status in serum is the method of choice to confirm copper deficiency.

Indication for bone marrow aspiration

In non regenerative anaemia without detectable systemic cause a bone marrow examination is the best way to find a diagnosis.

Especially when pancytopenia is present and for the diagnosis and staging of hematopoetic neoplasia, but also to provide samples for PCR of infectious agents (leishmania, ehrlichia,...) a biopsy of bone marrow is indicated.

Infectious causes of anaemia

In this etiologic group regenerative as well as non regenerative anaemias are comprised.

For quite some time the terminus feline/canine infectious anaemia is encountered in literature frequently. The infectious agents in this case are hemotropic mycoplasma species (formerly hemobartonalla spp.). But there are far more infectious causes of anaemia in dogs and cats.

Infectious disease in general

In every febrile disease a temporary, often mild anaemia may be caused by the elevated body temperature. In other cases the infectious agent itself is able to induce anaemia e.g. by suppression of the bone marrow. In this context the FeLV and FIV induced anaemia in the cat has to be mentioned above all.

Blood parasites

The term „blood parasites“ covers a heterogeneous group of microorganisms, e.g. babesia and hepatozoon are eucariotic protozoa, while ricettisia or hemotropic mycoplasma species are
Anemia in dogs and cats – guidelines for the veterinary practice

Increased travelling with pets and the import of rescued animals from all over the world create new challenges for the veterinary practitioner. Frequently found clinical and laboratory diagnosis in these patients is anaemia. Sometimes the exact classification of anaemia can be difficult. Anaemia is a decrease of the erythrocyte content of blood. The typical clinical signs are pale mucous membranes, the laboratory characteristics of anaemia are decreased values of the erythrograph.

There are different classification systems of anaemia, each with its advantages and limitations. The classification used in this article is based on bone marrow responsiveness, assessed by the number of reticulocytes in the peripheral blood. The major advantage of this method is its practicability. By means of a stained blood smear and a microscope the presence of reticulocytes can easily be estimated in every in-house lab.

Fig. 4: Hemotropic mycoplasms

Fig. 5: Anaplasma phagozytophilum (morula)

Intoxication

A variety of toxins can provoke regenerative or non-regenerative anaemia. Intoxications by zinc or other heavy metals induce regenerative, hemolytic anaemia. The causative mechanism is the integration of the metal into the hemoglobin instead of iron. As a consequence of this erythrocytes are destroyed. The bone marrow however is capable of maintaining erythropoiesis, even though an incomplete one. Concerning non-regenerative anaemia lead intoxication and estrogen toxicosis have to be mentioned. High serum levels of estrogen induced e.g. by sertoli cell tumour or granulosa cell tumour sometimes cause severe bone marrow hypoplasia in dogs.

Final remark

This article makes no claim to be complete, because it is not always possible to „press“ the pathogenesis of anaemia into certain schemes. It is supposed to provide a quick guide for the veterinary practitioner and support the reader in achieving a precise and efficient diagnostic process. In case of doubt however further medical procedures like imaging techniques are necessary to make a diagnosis.

Diagrams adapted from Willard, Tvedten, Turnwald: Small Animal Clinical Diagnosis by Laboratory Methods 2nd Edition