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Hot Topics in Canine Medicine Mini Series

Session Three: Anaemia and Transfusion Medicine

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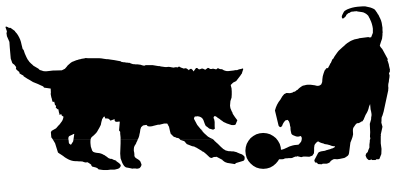

Session 3: Anaemia and Transfusion Medicine

Anaemia is a relatively common finding in canine patients. A logical diagnostic approach to the anaemic patient is essential to ensure the correct diagnosis is reached expediently. In this session, we will discuss the practical approach to the patient with anaemia and also the rational use of blood products in the anaemic dog.

- A practical approach to the dog with anaemia
- Is it regenerative or non-regenerative? Understanding haematology
- Blood typing and cross match- is it really necessary?
- Transfusion medicine- rational use of blood products

Anaemia & Transfusion Medicine

Animals with anaemia present with pallor; however, pallor can also be the result of hypoperfusion. The differentiation between anaemia and pallor is easily made by evaluating the PCV. Anaemia can be *relative* or *absolute.* Absolute anaemia is characterised by decreased red cell count in a normally hydrated animal. Relative anaemia occurs in animals which have expanded plasma volume with a normal red cell mass e.g. haemodilution.

Red cell indices that can be measured include MCV, MCH and MCHC. These parameters evaluate the size of the red cell and the haemoglobin concentration. Most anaemias are normocytic normochromic. Very regenerative anaemias may become macrocytic hypochromic. Macrocytic anaemia (increased MCV) is also found in cats with FeLV, toy poodles and in animals with myelodysplasia. Microcytic anaemias are typically associated with iron deficiency.

Anaemia is a clinical sign, NOT a diagnosis. Therefore, the most important step in the investigation of the anaemic patient is to examine a well-prepared blood smear in order to determine whether or not the anaemia is regenerative or not. The differential diagnoses for each category is outlined below. In addition, the severity of the anaemia and the presence/absence of icterus in the plasma should be considered.

Classification of Anaemia

Regenerative

- Haemolysis
- Haemorrhage

Non-regenerative Anaemia

- Chronic disease
- Hypoproliferative anaemia
- Iron deficiency anaemia
- Chronic renal disease
- Peracute haemorrhage/haemolysis (pre-regenerative)

Collect ALL blood samples before initiating any therapy.

A blood smear should be prepared for examination in-house and also sent to an external laboratory. Blood smears can be stained with Diff-quik in-house. The area just behind the feathered edge should be examined in detail (this area should have a monolayer of cells). Plasma proteins should be evaluated concurrently to help confirm/exclude haemorrhage as a possible cause of anaemia.

Examine blood smear for:

- Polychromasia/anisocytosis which provide evidence of regeneration
- Red blood cell parasites e.g. Babesia
- Spherocytes (lack area of central pallor)
- Platelet numbers (should be approx 8-12 plts/hpf)
- Check other cell lines e.g. neutrophils are present
- Atypical cells

In-house haematology analysers CANNOT be trusted to provide an accurate platelet count! Examination of a blood smear is essential.

If immune mediated red cell destruction is suspected, then also perform an in-saline agglutination test.

Regenerative Anaemia

Typically, this type of anaemia is associated with haemorrhage or haemolysis.

NB. It takes the bone marrow 3-5 days to respond to acute haemorrhage/haemolysis, therefore in the peracute case the anaemia may appear non-regenerative (pre-regenerative)!

A well-prepared blood smear should be evaluated for cytological evidence of a regenerative response (reticulocytosis):

- Polychromasia (variation in colour of rbcs)
- Anisocytosis (variation in rbc size)
- Spherocytes (small rbcs which lack an area of central pallor)
- Neutrophilia

However, although all polychromatophilic cells are reticulocytes, not all reticulocytes are polychromatophilic. This means that standard staining techniques may underestimate the regenerative response. New Methylene Blue stains can be used to more accurately identify reticulocytes.

Reticulocytes:
A regenerative response will be associated with an absolute reticulocyte count (ARC) of:
> 60 x 10^9/l in dogs

Haemorrhagic Anaemia:

- Trauma
- Parasites e.g. fleas, hookworms
- Clotting factor disorders e.g. thrombocytopenia, coumarin toxicity
- Ruptured neoplasms e.g. haemangiosarcoma

External blood loss will result in concurrent loss of plasma proteins and iron. Increased hepatic protein production will return protein levels to normal within 5-7 days.
Iron and rbcs can be reabsorbed in cases of internal haemorrhage.

Haemolytic Anaemia:

- Immune-mediated (primary vs secondary)
- Mechanical injury e.g. vascular neoplasms, heartworm
- Oxidative injury e.g. Heinz bodies
- Parasitic e.g. Babesia

In addition to the aforementioned signs of regeneration, haemolytic anaemias may have specific characteristics which indicate the underlying cause e.g. spherocytes or autoagglutination in immune-mediated haemolytic anaemia.

Immune-mediated Haemolytic Anaemia (IMHA)

IMHA may be primary or secondary. In dogs, the majority of cases will be primary, whereas in cats the opposite is true, with most having an underlying condition.

Dogs:

- Most are primary (secondary causes more likely in elderly animals)
- Young adults (4-7 years)
- Entire females overrepresented
- Cocker spaniels, springer spaniels, collies

Pathophysiology:
Red blood cells coated with IgG or IgM which results in their early destruction and removal by the mononuclear phagocytic system in the spleen and liver. A small piece of membrane is removed from the rbc resulting in formation of spherocytes.

The presence of large numbers of spherocytes and agglutination is pathognomonic for IMHA. Intravascular haemolysis may occur in severe cases. Red cells are destroyed in the circulation resulting in free haemoglobin and resultant haemoglobinuria.

Clinical Signs:
Moderate to severe anaemia with resultant tachycardia, tachpnoea and a haemic murmur. Splenomegaly and/or hepatomegaly may be identified. Many cases may be pyrexic and some may be icteric.

Diagnosis:
- Regenerative anaemia (unless directed against red cell precursors in bone marrow)
- Spherocytes
- Agglutination (N.B. distinguish from rouleaux using in-saline agglutination test)
- Positive Coombs test is supportive
- Rule out secondary causes (survey radiographs, Babesia PCR)

Coombs Test
Up to a third of cases with IMHA may have a negative Coombs test. This may be due to insufficient antibody in these cases or previous steroid administration. Alternatively, low positive Coombs titres can be associated with inflammatory, infectious or neoplastic causes. In patients with autoagglutination, a Coombs test is not necessary.

Treatment:
- Oxygen
- Cage rest
- Corticosteroids
- Azathioprine?
- Transfusion
- Splenectomy?
- Human immunoglobulin?
- Cyclosporine?
- Heparin?
- Treat underlying cause if identified

Poor prognostic indicators:
- Severe anaemia
- Poorly regenerative anaemia
- Autoagglutination
- Intravascular haemolysis
- Hyperbilirubinaemia

Mortality associated with IMHA is high (approx 50%) and management is usually expensive in initial stages. Death may result from thromboembolism, which has a higher risk in animals which are jaundiced and in which IV catheters are in place. Prophylactic use of heparin may help reduce the risk of thromboembolism.

Monitoring:
Monitor PCV daily/every other day until improvement noted.
Once stable check PCV weekly then every 2-4 weeks
If azathioprine is used, haematology should be checked every 2-4 weeks to assess white cell and platelet counts. In addition, sporadic monitoring of liver parameters is advisable and this drug should be avoided in dogs prone to pancreatitis or with previous history of pancreatitis.

Once PCV is stable, aim to reduce the dose of one of the drugs (usually the drug with most side effects i.e. prednisolone) by 25% every 2-4 weeks. Never reduce the dose of more than one drug at a time. Some patients will require lifelong treatment.

Non-regenerative Anaemia

There are several categories of non-regenerative anaemia:

- Chronic disease
- Hypoproliferative disease
- Iron deficiency
- Chronic renal disease
- Acute blood loss/haemolysis (pre-regenerative)

Chronic disease
Any chronic disease (neoplastic, inflammatory, degenerative) can result in a mild normocytic, normochromic anaemia. Sequestration of iron in macrophages and bone marrow results in it being unavailable for normal red cell production.

Hypoproliferative Anaemia
This type of anaemia occurs secondary to bone marrow disease (neoplasia, dysplasia, hypoplasia). Usually affects several/all cell lines and so pancytopenia may be noted. Bone marrow biopsy required for definitive diagnosis.

Iron Deficiency Anaemia
May be mildly regenerative and often microcytic hypochromic. Iron is unavailable for normal red cell production often due to chronic blood loss.

Chronic Renal Disease
The kidney is the source of erythropoietin production, the hormone responsible for stimulating production of red cells. In chronic kidney disease, erythropoietin production is reduced. Uraemia may also shorten the lifespan of rbcs.

Blood and Blood Products

Blood transfusions are indicated in many situations including severe haemorrhage, haemolytic anaemia, decreased red cell production and sometimes in shock.

Blood volume in dogs	90ml/kg
Blood volume in cats	60ml/kg

Canine Blood Types

There are several canine blood groups, but the most important include:

- DEA 1.1
- DEA 1.2
- DEA 7

Canine blood donors should preferably be DEA 1.1 negative, DEA 1.2 negative and DEA 7 negative (Blood typing cards test for DEA 1.1)

Canine Blood Donors

- In good health
- >25kg
- 1-8 years old
- Preferably male dogs or neutered females that have not had a litter
- High PCV (greyhounds have higher PCVs than other breeds)
- Quiet temperament
- Not travelled abroad

It is wise to perform a cross-match before transfusing a dog, but in an emergency situation the first blood transfusion is unlikely to cause a severe reaction. All dogs that have had a previous transfusion should be cross-matched before further blood is administered.

Blood Collection

Blood collection bags are available containing anticoagulant. Double bags are available which can be used to separate plasma from red blood cells following centrifugation where facilities exist. The donor should be examined by a veterinary surgeon prior to collection of blood. Three people are required: one to restrain the animal, one to collect the blood and a third to mix the blood and provide additional restraint. Lateral recumbency is most often used, but some dogs can be bled in a standing position.

- Sedate patient if necessary (most cats require sedation)
- Place IV catheter in donor to administer fluids if required
- Clip a large area of hair over the jugular vein
- Surgically prepare the area using chlorhexidine or equivalent
- EMLA cream can be used as a topical anaesthetic
- Raise the jugular vein
- Kink the tubing before removing the needle cover to prevent anticoagulant emptying into the bag
- Direct needle into the jugular vein
- If venipuncture is successful, then a flash of blood will be seen in the tubing
- During collection, the blood should be gently rocked to ensure adequate mixing with the anticoagulant
- The needle is removed when approx 450ml (450g) of blood has been collected
- The tubing is sealed (can be clamped or tied in a knot)
- The remaining blood in the tubing can be used to measure PCV
- Pressure should be applied to the donor's neck for 5 minutes
- 1 litre of crystalloid is usually given to the donor dog during or after collection

Blood is an excellent medium for bacterial growth and should be handled as aseptically as possible!

Blood Administration

If the blood has been stored in the fridge prior to use, then warm to room temperature (Do not use a microwave!)

- An in-line filter is **essential** to remove microthrombi
- Hartmanns and Ringers cannot be given via the same line as blood as they contain calcium
- Record baseline vital signs from the recipient before starting the transfusion
- See blood transfusion record on next page for further instructions

Transfusion Reactions

- Anaphylaxis
- Volume overload
- Citrate intoxication
- Microbial contamination
- Hyperammonaemia
- Hyperkalaemia

Signs of transfusion reactions

- Increased HR & RR
- Increased rectal temperature
- Vomiting
- Angioedema & urticaria
- Salivation
- Seizures

The patient should be monitored closely for any reactions especially during the first 15mins. If a possible reaction occurs- STOP THE TRANSFUSION!

Blood Banks

Canine blood banking facilities now exist in the UK and can provide packed red cells and other component therapies including fresh frozen plasma. Consider asking clients to bring their dogs to one of the Pet Blood banks regular blood drives.

www.petbloodbankuk.org

Record of Blood Transfusion

Patients Name: Date:
Owner's Name: Weight:
Case Number: Breed:
Age: Sex:

Reason for transfusion:
Donor Animal:
Crossmatch performed?: Previous transfusion?:

Volume to be transfused = k x wt(kg) x $\frac{\text{(Required PCV – recipient PCV}}{\text{Donor PCV}}$ =

Where k = 90 for dogs, 60 for cats

Time	Rate	HR	RR	Temp.	Other findings

Rate: Start at 1ml/kg/hr & monitor q15mins for 30 mins
Increase to 5-10 mls/kg/hr in normovolaemic patients if no reaction
Increase to 20 mls/kg/hr in hypovolaemic patients if no reaction
Absolute max transfusion rate for whole blood:
Normovolaemic 22ml/kg/24hrs
Hypovolaemic 22ml/kg/hr
Maximum of half of this for packed red cells!

Signs of Transfusion Reaction:

- Urticaria/erythema/vomiting/pyrexia
- Dyspnoea/tachypnoea/coughing/tachycardia/bradycardia

IF THESE SYMPTOMS OCCUR STOP TRANSFUSION!