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Feline anaesthetic complications

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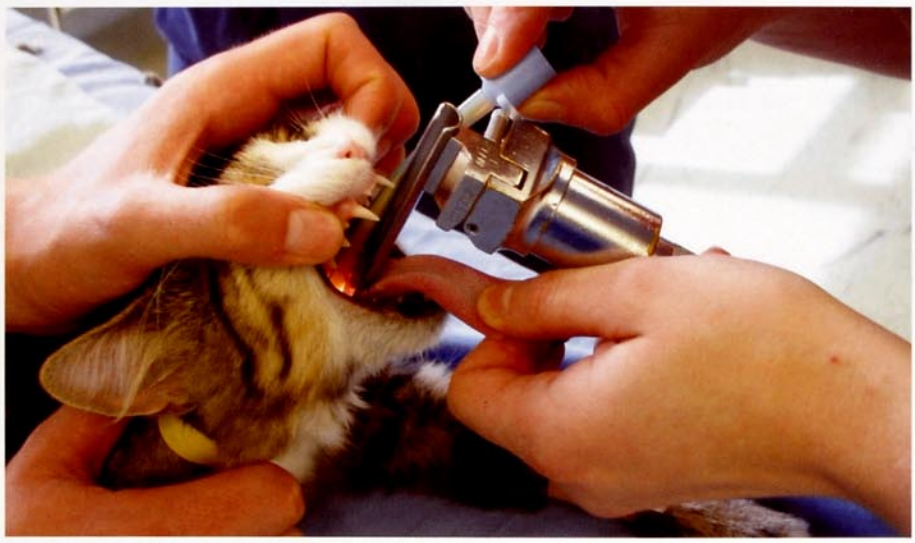

Figure 1: Miller's laryngoscope blade.

Some worrying statistics

A survey of small animal anaesthesia was conducted in 53 practices in the 1980s and revealed some worrying statistics. One in 552 (0.18%) healthy cats (ASA I or II) and 1 in 30 (3.33%) sick cats (ASA III-V) died during or immediately after anaesthesia *(Clarke & Hall 1990)*. A more recent confidential enquiry into perioperative small animal fatalities (CEPSAF), in which 117 practices took part, revealed a decreased incidence of anaesthetic related deaths in healthy cats (0.11%) and sick cats (1.4%) *(Brodbelt et al. 2008)*. However, the same study revealed the risk of death in dogs overall to be much lower (0.17%) than cats (0.24%). This raises some important questions about why the risk of death is greater in feline patients and what can be done to reduce the incidence of anaesthetic related complications.

Risk factors

A nested case-control study within CEPSAF found an association between certain factors and increased odds of sedation and anaesthetic related death. These included: increasing ASA status, procedural urgency, major v.s. minor intended procedures, increasing age, extremes of weight, endotracheal intubation and the use of intravenous fluid therapy. Pulse monitoring and use of pulse oximetry were associated with decreased odds *(Brodbelt et al. 2007)*.

Cats are not small dogs

Many common anaesthetic related complications in cats are also found in small dogs and are attributable to their small size. Examples include hypothermia due to high surface area to volume ratio, risk of overdose of injectable agents, difficulty in obtaining venous access and high breathing system dead space (Fig.2). Hypothermia increases recovery time, inhibits wound healing and promotes wound infection *(Kurz et al. 1996)*. Importance is placed on the need to weigh all cats to allow accurate dosing of anaesthetic agents. However, a great many differences exist which put cats at an increased risk of anaesthetic complications if a clinician treats them as if they are small dogs.

Anatomical and Physiological considerations

Renal system

Many environmental toxins have been identified which may increase the incidence of renal failure in cats. Chronic renal failure is known to be a common disease of older cats but biochemical evidence does not manifest until approximately a 75% loss of functional nephrons has occurred. The kidney is also extremely sensitive to reduced oxygen delivery resulting from hypoxia or hypotension which may cause further loss of renal function. Combine this with the frequent presentation of somewhat anorexic elderly cats for dental procedures which often exhibit hypotension under anaesthesia and add the indiscriminate use of non-steroidal anti-inflammatory drugs and there is a recipe for precipitation of renal failure.

Cardiovascular system

Hypovolaemia, hypotension, depression by anaesthetic agents and electrolyte imbalances contribute to poor cardiac function and arrhythmias under anaesthesia. The cat has a relatively small circulating blood volume of approximately 66ml/kg compared to the dog at 88ml/kg. The significance

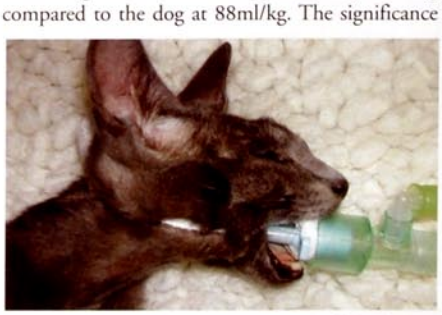

Figure 2: Intubated cat, minimisation of deadspace.

Figure 3: Lignocaine syringe arrangement.

of intra-operative fluid losses including haemorrhage, respiratory and abdominal evaporative losses may be overlooked. Fluid therapy should be used with care to restore volume and resolve electrolyte derangements before and during sedation and anaesthesia.

Interestingly the use of intravenous fluid therapy was associated with an increased risk of death in the CEPSAF study, although this figure may be biased by more frequent use of fluid therapy in cats which are already at high risk. However, due to their small size it is easy to dangerously overload the vascular system with fluids if appropriate preventative measures are not followed. Such measures would include the use of accurate infusion pumps or paediatric burette giving sets and close monitoring of patients receiving intravenous fluid therapy. Cats are especially sensitive to volume overload caused by colloid infusions, particularly haemoglobin replacement solutions *('Oxyglobin', Dechra)* which may be used off-licence. Signs of volume overload may include tachypnoea, pulmonary oedema, serous nasal discharge, and neurological signs.

Diseases with cardiovascular complications such as hyperthyroidism and hypertrophic cardiomyopathy are associated with an increased risk of anaesthetic death and treatment measures to stabilise the disease process should be undertaken as far as possible before anaesthesia.

Respiratory system

Cats are reported to be prone to laryngeal spasm *(Hall & Taylor 1994)*. Local anaesthetic sprays should be used with care as those designed for mucosal use are necessarily of higher concentration compared with solutions used for tissue infiltration and overdose can occur with relatively small volumes. Laryngeal and tracheal trauma can occur with rough intubation technique and the use of intraluminal stylets to support the ET tube during placement.

Tracheal rupture after the use of cuffed endotracheal (ET) tubes has been reported as a cause of anaesthetic morbidity and mortality in cats. This is largely due to the tapering or narrowing of the trachea so that an overestimation of tracheal diameter is made following inspection of the larynx. Some authors recommend that only non-cuffed endotracheal (ET) tubes should be used in cats *(Mitchell et al. 2000)*. However, the use of an inappropriately small non-cuffed ET tube can result in a poor seal, significant entrainment of room air, reduction of the inspired fraction of oxygen, difficulty in performing positive pressure ventilation, and potential for aspiration of fluids from the oropharynx. Adequate anaesthetic depth and use of the techniques below should allow tracheal intubation of most adult cats with a 5mm non-cuffed ET tube.

Intubation tips:

- The application of a drop of local anaesthetic (lidocaine 4%) to each arytenoid cartilage under direct visualisation using a syringe and 20 gauge catheter (stylet removed) allows for accurate desensitisation with minimum risk of overdose (fig.3).

Many aids to intubation are available to reduce the risk of trauma to the larynx.

- Use a laryngoscope with Miller (straight) blade and a good bright light. With the scope handle in the right hand place the tip of the blade on the tongue directly rostral to the epiglottis and apply firm ventral pressure to provide an excellent view of the larynx in most cases. Proceed with intubation using the left hand (fig.1).
- A 90° clockwise rotation of the tube will prevent the bevel of the ET tube tip catching on the left arytenoid cartilage as it passes through the larynx.
- The use of an introducer may aid passage of the ET tube through the larynx. Purpose made gum-elastic boogies and polythene coated malleable aluminium intubation stylets are available (fig.4).
- Alternatively a 6 french gauge dog urinary catheter makes a good atraumatic intubation guide. The luer connection of the urinary catheter fits a size 3.5 ET tube adaptor. This allows connection to an Ayre's T-piece to provide oxygen during a difficult intubation.

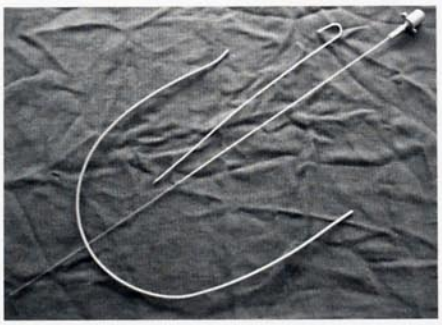

Figure 4: Intubation aids.

Other respiratory system complications such as blocked or kinked ET tubes (more common with narrow ET tubes), disconnection of breathing system, weight of surgical instruments over thorax and abdomen can have fatal consequences. These are easily overlooked in a small patient entirely covered in surgical drapes and the need for a dedicated nurse to observe and maintain anaesthesia cannot be overemphasised.

Many volatile and injectable anaesthetic agents cause respiratory depression and this may become clinically significant, particularly if the plane of anaesthesia is inappropriately deep. Pathologies such as diaphragmatic rupture (congenital or acquired) and traumatic tracheal avulsion may not present with clinical signs and may only be detected for the first time when cats are anaesthetised for other reasons. This highlights the necessity for an accurate clinical history and a thorough clinical examination to be carried out before induction of anaesthesia

Age

Increasing age is associated with an increased risk of peri-operative death in cats. This may be related to increased susceptibility to depressive effects of volatile anaesthetic agents, impaired thermoregulation resulting in hypothermia, prolonged recovery and slower metabolism of drugs *(Brodbelt et al. 2008)*. Older cats should be evaluated carefully before anaesthesia and this may include appropriate haematology, biochemistry and urinalysis. A balanced anaesthesia technique combined with careful monitoring should always be employed.

Obesity

Obesity may result in respiratory compromise, poor cardio-vascular reserve and prolonged recovery due to redistribution of lipid soluble drugs to the tissues. Drug doses should be calculated based on estimated normal body weight and care should be taken to avoid injecting into fat. Injecting drugs intended for subcutaneous or intramuscular injection into fat may have a slower onset of action. This may be interpreted as an inadequate dose and further doses given may then lead to overdosing. Ventilation may need to be assisted artificially and anaesthetic time should be minimised where possible.

Behavioural considerations

The feline temperament is not always conducive to handling and stressful restraint can cause release of catecholamines which may predispose to myocardial arrhythmias especially under volatile anaesthesia. Use of sedative agents should be tailored to the health status of the patient and applied with careful monitoring. Dyspnoeic cats resent handling and present a particular challenge. The clinician must weigh up the advantages of oxygen supplementation over the risks of handling and make every effort to stabilise the condition where possible. In some cases an inhalation induction technique in a suitable chamber where a high inspired fraction of oxygen can be provided may be preferable. However, induction of anaesthesia tends to be slower with this technique than when rapid acting injectable agents are used and it may be prolonged further by the presence of lung pathology or changes in cardiac output. Intubation and control of the airway is also delayed. Cats are particularly prone to poor recovery from anaesthesia if they are in pain or are stimulated by noise, barking dogs etc. Careful application of adequate analgesia will help to prevent a stormy recovery and this may be of paramount importance after orthopaedic surgery. Pain behaviours in cats are poorly interpreted by many clinicians as they tend to be very different from those seen in dogs and are often similar to those behaviours exhibited in fearful and stressed cats. As a result cats are frequently allowed to suffer pain unnecessarily and this affects many aspects of recovery from surgery and illness. Nursing staff should be trained in feline pain assessment and will become a most valuable asset to the practice.

Anaesthetic agents

Although selection of anaesthetic drugs is determined by many factors, recent studies have provided data about the relative risks associated with some anaesthetic agents.

In the survey in the 1980s, use of xylazine was associated with the highest frequency of deaths *(Clarke & Hall 1990)*, although the number of animals that received xylazine was low compared to other premedication agents such as acepromazine. However in the more recent study *(Brodbelt et al. 2007)* another alpha-2-adrenoreceptor agonist, medetomidine, did not alter odds ratio for anaesthetic death in cats *(Brodbelt et al. 2007)*. This suggests that in healthy animals medetomidine is an equally safe drug to use compared to other drugs used in premedication protocols.

Alphaxalone/alphadolone *(Saffan, GlaxoVet Ltd)* was found to be the safest anaesthetic agent with just 1 death in 986 feline anaesthetics despite being associated with the highest incidence (17-26%) of

non-lethal complications of swollen ears and paws *(Clarke & Hall 1990)*. A new formulation of alphaxalone in cyclodextrin which does not cause histamine release *(Alfaxan, Vetoquinol UK Ltd)* has recently gained marketing authorisation for induction and maintenance of anaesthesia in dogs and cats in the UK. Acute tolerance to overdose has been demonstrated up to 5 times the recommended dose in the cat. Such doses cause apnoea and a temporary decrease in mean arterial blood pressure which is compensated for by changes in heart rate. However, there are currently limited published data from the use of alphaxalone in clinical cases.

No significant difference in odds ratio was found between sedation and anaesthesia and no drug associations were observed in the more recent CEPSAF study *(Brodbelt et al. 2008)*. Non-statistically significant tendencies to reduced odds were associated with acepromazine, benzodiazepine and opioid combinations for pre-medication compared with no pre-medication *(Brodbelt et al. 2007)*.

The use of propofol on repeated occasions within a few days has been associated with Heinz body anaemia and signs of toxicity in cats *(Andress et al. 1995)*. If cats are to be anaesthetised on several occasions in a short space of time other anaesthetic agents should be employed.

Opioids or benzodiazepines used alone may cause excitement in cats and should be used with care. Combination of opioids with sedative agents may avoid this complication. Cats in pain are less likely to respond to appropriate doses of opioids with excitement.

Monitoring

The use of monitoring equipment may reduce the incidence of anaesthetic complications by alerting the clinician to physiological derangements at an early stage.

Pulse oximetry is now commonly available in veterinary practice but it must be kept in mind that it only provides information of saturation of haemoglobin with oxygen and pulse rate. It does not indicate adequate delivery of oxygen to the tissues and significant tissue hypoxia may be present in a markedly anaemic patient with a reading of 100% on the pulse oximeter. Cats may present more of a challenge in obtaining a pulse oximeter reading due to the small size of the tongue and extremities resulting in compression of tissue by the probe and a reduction in peripheral blood flow through the tissue at the site of probe placement. Judicious use of a small probe can minimise the risk of this complication.

Capnometry or capnography alerts the clinician to apnoea, airway obstruction, hypo and hyperventilation and severe cardiac dysfunction. Development of smaller capnometers at reduced cost have made these valuable tools available to general practice.

Pulse pressure and quality is more difficult to detect by digital palpation in cats than dogs and hypotension under anaesthesia may go unnoticed due to a lack of monitoring equipment. Many practices have a Doppler monitor which is used with sphygmomanometry in the clinical arena to measure arterial blood pressure in conscious hypertensive cats. These work equally well in the anaesthetised patient and their use can alert the clinician to hypotension early so treatment can be instituted and further complications prevented. Maintaining the Doppler probe secured with tape over a radial artery provides a constant audible signal of pulse rate, rhythm and quality. Oscillometric devices have been developed for small animals but frequently give poor results when used in cats.

Any number of monitoring tools cannot replace the value of constant observation by a dedicated and trained nurse. Equipment failure is not a problem if a regular checks of pulse rate, rhythm and quality, mucous membrane colour, capillary refill time, respiratory rate and character are made.

Post-operative period

The CEPSAF study highlighted that 61% of peri-operative deaths in cats occurred during the post-operative period and the majority of these were within the first 3 hours of recovery. Respiratory obstruction, cardiovascular compromise, hypothermia and prolonged recoveries may be resolved and treated provided they are noticed. Poor observation of post-operative patients in busy and understaffed clinics may contribute to these figures. Close observation during this period is necessary.

In summary

Cats have become increasingly popular as pets and present particular challenges in anaesthesia. They should not be treated as small dogs for they differ in a number of important ways which influence anaesthetic considerations. Familiarisation with these differences and experience will result in fewer complications when anaesthetising cats.

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CLASSIFYING FELINE ANAEMIA

Generally anaemias can be divided into regenerative (blood loss or haemolytic) and non-regenerative types. In cats, most anaemias are non-regenerative in type, in contrast to the dog. However, multiple causes of anaemia can be present concurrently, leading to difficulties in classification of the anaemia and a diagnostic challenge.

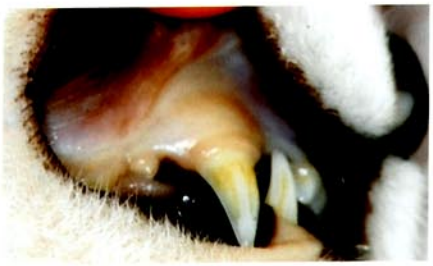


Figure 1: Pallor of the oral mucous membranes visible in a severely anaemic cat.

DIFFERENTIATING REGENERATIVE AND NON-REGENERATIVE ANAEMIAS

Haematology Findings

The mean cell volume (MCV) indicates the average size of red blood cells (RBCs). Regenerative anaemias are usually macrocytic (increased MCV) because reticulocytes (immature RBCs) have higher MCVs than mature RBCs. But it is important to recognise that macrocytosis is not exclusively a feature of regenerative anaemias since non-regenerative anaemias associated with FeLV infection or myelodysplasia can also be associated with an increased MCV (*Shimoda et al 2000, Weiss 2006b*).

The mean cell haemoglobin concentration (MCHC) indicates the average concentration of haemoglobin per RBC. A reduced MCHC is termed hypochromic. Regenerative anaemias are usually hypochromic because reticulocytes have higher MCVs and lower haemoglobin content than mature RBCs.

The red cell distribution width (RDW) represents the degree of anisocytosis in a patient and is available on some haematology analysers. A high RDW may indicate the presence of increased number of macrocytes, microcytes (RBCs with reduced MCV) or both.

Nucleated RBCs (NRBCs) are immature RBCs and can indicate active regeneration but may also be seen with splenic dysfunction, shock, heavy metal toxicity and bone marrow disorders.

The presence of polychromasia, anisocytosis and NRBCs on blood smears are all features that may indicate regeneration.

Reticulocyte Counts

Counting the number of reticulocytes in a patient allows the RBC regenerative response to be quantified. Vital stains such as new methylene blue (NMB) allow the reticulocytes to be identified by clumping the ribonuclear material present within them. Reticulocytes correspond to polychromatic cells on a Romanowsky-stained blood smear.

Cats differ to dogs in having two types of reticulocytes: punctate and aggregate. Feline aggregate reticulocytes are identical in appearance to canine reticulocytes, with multiple basophilic granules, and these only last in the circulation for about 24 hours before maturing into punctate reticulocytes. Punctate reticulocytes have only a few basophilic granules and are the more mature reticulocytes that survive in the circulation for up to 10 days. Since only aggregate reticulocytes reflect recent bone marrow RBC production, these should be the main type of reticulocyte counted to evaluate for regeneration, when evaluating moderate to marked anaemia. However with mild anaemias, it may be beneficial to count punctate reticulocytes too, as mild anaemias may fail to induce production of significant numbers of aggregate reticulocytes but have significantly increased punctate reticulocytes if the anaemia is of sufficient duration (>7 days). Calculation of the absolute reticulocyte count allows assessment of the degree of regeneration for the anaemia present by taking into account the cat's RBC count, as shown in the equation below:

$$\text{Absolute reticulocyte count } (\times 10^9/l) = \%\ \text{reticulocytes} \times \text{RBC count } (\times 10^{12}/l) \times 10$$

Regenerative response	Absolute aggregate reticulocyte count ($\times 10^9/l$)
Negligible	< 50
Mild	50-100
Moderate	100-200
Substantial	>200

REGENERATIVE ANAEMIAS: HAEMORRHAGE

Causes

In one study, haemorrhage was reported as the most common indication for cats to receive a blood transfusion *(Weingart et al 2004)*. Acute haemorrhage is relatively common in cats, particularly after trauma (including surgery). Haemostatic disorders may develop due to liver disease or inherited coagulopathies. Systemic amyloidosis is a condition associated with the build up of amyloid in body tissues, and this can be associated with spontaneous liver rupture and sometimes a fatal abdominal haemorrhage in Siamese and related cats. Chronic haemorrhage is said to be uncommon in cats but can result from severe ectoparasitism in kittens or urogenital/GI tract bleeding. Gastroduodenal ulceration/bleeding can be associated with neoplasia, NSAID toxicity and inflammatory bowel disease. Cats with gastroduodenal ulceration/bleeding sometimes can present as an emergency due to shock and severe anaemia rather than chronic haemorrhage. If external haemorrhage is chronic, the loss of iron within the RBCs from the body can eventually lead to iron deficiency.

Diagnostic Features

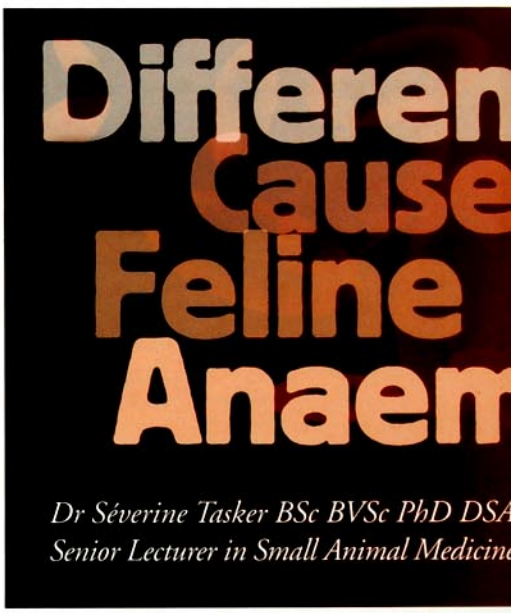
After haemorrhage, reticulocytes appear in the circulation 3-5 days later and peak at 5-7 days, although the PCV may take up to 2-3 weeks to return to normal. Regeneration is evidenced by the presence of anisocytosis, polychromasia and maybe NRBCs on blood smear examination. Hypoproteinaemia may occur in the first week after bleeding due to loss of protein. Persistent anaemia and hypoproteinemia suggest ongoing blood loss. Iron deficiency anaemia is a non- or poorly regenerative microcytic hypochromic anaemia.

REGENERATIVE ANAEMIAS: HAEMOLYSIS

The destruction of RBCs in haemolysis may be extravascular or intravascular in nature. Extravascular haemolysis usually occurs by macrophage phagocytosis in the spleen, liver and bone marrow. Intravascular haemolysis is less common and occurs within the vascular system itself. Both intravascular and extravascular haemolysis may be mediated by antibodies bound to the surface of RBCs in a process known as immune-mediated haemolysis.

Causes

- **Infections** which may result in direct haemolysis e.g. haemoplasmosis, Babesia, Cytauxzoonosis.
- **Oxidant injury** due to exposure to chemicals or toxins (e.g. onions, present in some babyfoods etc.) or the existence of some disease states such as diabetic ketoacidosis, hyperthyroidism and lymphoma. Here oxidant injury can result in a Heinz body haemolytic anaemia. Feline haemoglobin is particularly sensitive to oxidation so the feline species tends to be prone to this sort of anaemia compared to other species. Anaemia is more likely to result if the Heinz bodies



are large and affect a large number (>30%) of RBCs.

- **Secondary immune-mediated haemolytic anaemia (IMHA)** can arise secondary to infectious agents such as FeLV, haemoplasma and feline coronavirus (in feline infectious peritonitis [FIP]), drugs (e.g. methimazole, trimethoprim-sulphonamides), neoplasia (e.g. lymphoma).
- **Primary IMHA** is suspected in cases of IMHA where no underlying cause can be identified. This is common in the dog and was thought to be rare in the cat, but recent reports *(Husbands et al 2002; Kohn et al 2006)* suggest it may be more common than previously believed.

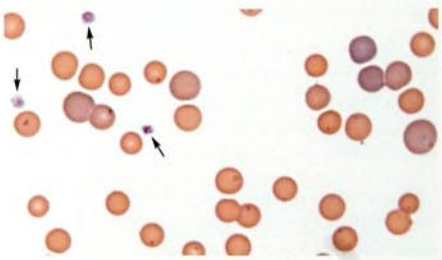
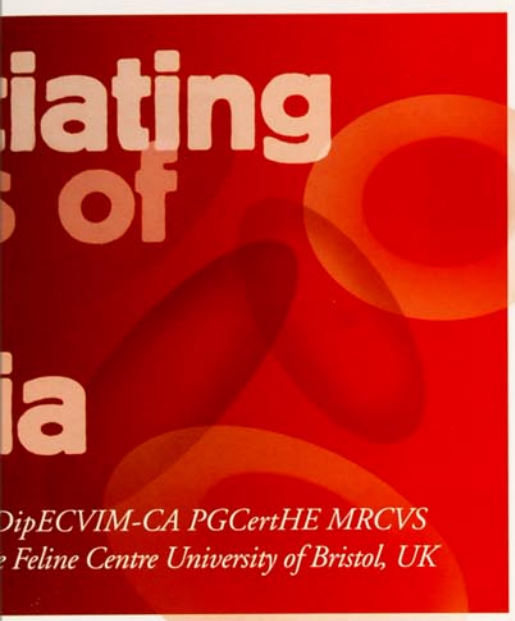


Figure 2: Romanowsky-stained blood smear from a cat with a regenerative anaemia due to haemoplasma infection. Note the variation in erythrocyte size (anisocytosis), polychromasia (polychromatic cells are larger and more purple in colour and indicate the presence of immature erythrocytes; reticulocytes). Platelets (arrowed) are smaller and granular in appearance compared to erythrocytes.

- **Haemolytic blood transfusion reactions and neonatal isoerythrolysis** are mediated by haemolysis of RBCs by antibodies that arise due to incompatibility of donor and recipient, or queen and kitten, blood types respectively.
- **Hypophosphataemia** *(phosphate levels <0.35 mmol/l)* can result in RBC haemolysis due to depletion of the energy supply to the RBCs and has been associated with diabetes mellitus, hepatic lipidosis, refeeding syndrome (refeeding a cat after a period of anorexia) and oral administration of phosphate-binding antacids.
- **Microangiopathic haemolytic anaemia** can arise due to disseminated intravascular coagulation or trauma.
- **Inherited RBC defects** are rare in cats but are occasionally seen. Osmotic fragility of RBCs is seen in Abyssinians and Somalis and pyruvate kinase (PK) deficiency in Abyssinians, Somalis and occasionally DSHs.



Diagnostic Features

Haemolytic anaemias are usually strongly regenerative after 3-5 days with anisocytosis, polychromasia, reticulocytosis and sometimes NRBCs visible. In IMHA, if the immune response is directed at RBC precursors in the bone marrow, as well as peripheral RBCs, the anaemia may appear to be non-regenerative despite being haemolytic in nature. Unlike anaemia due to external blood loss, serum protein concentrations remain normal with haemolysis as protein is not lost externally. The presence of hyperbilirubinaemia and bilirubinuria indicate the presence of severe acute haemolysis (intra- or extravascular), whilst the presence of haemoglobinaemia & haemoglobinuria specifically indicate intravascular haemolysis due to the release of free haemoglobin directly into the circulation from lysed RBCs. The presence of large numbers of Heinz bodies (precipitated haemoglobin) suggests exposure to oxidant damage. Heinz bodies are colourless with Romanowsky stains but blue-green with NMB staining. In cats Heinz bodies tend to be single and uniform in size but can be very large. IMHA cases may show autoagglutination on a blood smear, indicated by the presence of irregular clumps of RBCs. Positive slide agglutination (agglutination of RBCs visible on a smear following several washes of the RBCs in saline to remove the plasma) or positive Coombs' tests both indicate the presence of RBC-bound antibodies which can help in the diagnosis of IMHA cases.

Figure 3: Spun microhaematocrit tubes from a normal cat (right) and a cat with a severe haemolytic anaemia (left). Note the presence of a normal packed cell volume and clear serum in the normal cat whilst the anaemic cats shows a markedly reduced packed cell volume and red serum due to haemoglobinaemia.

Feline Haemoplasmosis

Haemoplasmosis arises due to infection with one of the following feline haemoplasma species: *Mycoplasma haemofelis, 'Candidatus M. haemominutum'* or *'Candidatus M. turicensis' (Willi et al 2006).* These species differ in pathogenicity with *M. haemofelis* being the most pathogenic, often resulting in a severe haemolytic anaemia during acute infection. The induced anaemia is usually regenerative in type, unless concurrent disease or retrovirus infection hampers this, and cats may also have positive slide agglutination and Coombs' tests due to the presence of IMHA. Identification of organisms on blood smear examination is notoriously difficult and the diagnostic test of choice is now the use of polymerase chain reaction (PCR) tests which are able to determine which haemoplasma species the cat is infected with.

PK Deficiency

PK is an enzyme critical to RBC energy metabolism and production. If RBCs are deficient in PK, they haemolyse. PK deficiency is an autosomal recessive inherited trait seen particularly in Abyssinian and Somali breeds. A molecular based genetic test is available to identify affected (homozygous) and carrier (heterozygous) cats.

NON-REGENERATIVE ANAEMIAS

Non-regenerative anaemias develop because a diseased or abnormal bone marrow fails to replace ageing RBCs.

Causes

Primary marrow disorders tend to cause moderate to severe anaemia whilst systemic disorders usually produce mild subclinical anaemia only.

- Primary Bone Marrow Disorders
  - Pure red cell aplasia (PRCA)
  - Aplastic anaemia/pancytopenia
  - Myelodysplastic syndromes (MDS)
  - Myeloproliferative diseases
  - Myelophthisis – filling of the marrow space with neoplastic cells or fibrous tissue (myelofibrosis)
- Systemic Causes of Bone Marrow Suppression
  - Anaemia of inflammatory disease (AID)
  - Chronic renal failure (CRF)
  - Retrovirus-associated

Diagnostic Features

There is minimal anisocytosis and polychromasia and a low reticulocyte count. RBCs are usually of a normal size and staining (normocytic and normochromic) although FeLV infection and myelodysplasia can cause a macrocytosis. Iron deficiency anaemia will typically be microcytic and hypochromic with a mild degree of regeneration. Concurrent leukopenias & thrombocytopenias may occur due to the bone marrow abnormalities affecting more than one cell line.

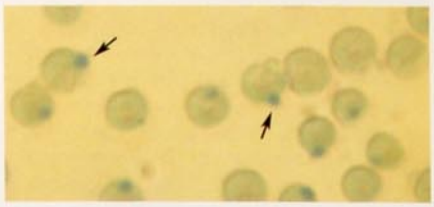


Figure 3: New methylene blue stained feline blood smear showing blue-green Heinz bodies protruding from the surface of many erythrocytes (examples are arrowed). This cat was suffering from onion toxicity.

Pure red cell aplasia (PRCA)

Here selective RBC bone marrow depletion causes anaemia. This can arise secondary to FeLV subtype C infection which is invariably fatal, or can be immune-mediated, as reported in young FeLV negative cats *(Stokol and Blue 1999)* in which some cats are Coombs' test positive. In the latter case immunosuppressive treatment is said to often be effective.

Aplastic Anaemia/Pancytopenia

Here, all haematopoietic cell lines in the bone marrow are affected ie. RBCs, white blood cells and platelets. FeLV, FIV, parvovirus, toxoplasmosis, ehrlichiosis and FIP are potential infectious causes of pancytopenia. Pharmacological agents such as griseofulvin (particularly when given to FIV infected cats), chloramphenicol and some chemotherapy agents can also induce pancytopenia. Some cases are idiopathic with no identifiable underlying cause. More recently a report found aplastic anaemia arose in association with CRF in cats and it has been suggested that starvation (via the negative protein balance present associated with cachexia) may contribute to the development of marrow aplasia *(Weiss 2006a).*

Myelodysplastic Syndromes (MDS)

MDSs are characterised by maturation defects in the bone marrow of one or more of the haematopoietic cell lines. These are usually characterized by the presence of a hypercellular marrow but with concurrent cytopenias evident in the peripheral blood picture. Dyshaematopoiesis (abnormal cell production) is evident and a macrocytosis may be present in the RBC line. Myelodysplasia is often associated with FeLV infection in cats *(Shimoda et al 2000)* although a recent report found only 36% of cats with MDS were FeLV positive *(Weiss 2006b).* Secondary dysmyelopoiesis can arise due to IMHA in which the immune system targets the bone marrow resulting in a non-regenerative anaemia, and differentiation of this from primary MDS can be difficult as both can show autoagglutination. MDS cases tend to have higher numbers of blast cells in the bone marrow. Some MDS cases respond to differentiating agents (such as cytosine arabinoside), anabolic steroids or haematopoietic growth factors but some go on to develop a true leukaemia with excessive numbers of blast cells.

Myeloproliferative Disorders

Neoplastic proliferation e.g. in a leukaemia, can result in inhibition of haematopoiesis and resulting cytopenias, including anaemia.

Anaemia of Inflammatory Disease (AID)

AID is an extremely common cause of anaemia in

the cat, occurring in association with many diseases such as infections and neoplasia. The anaemia is mild to moderate (PCV >17%), normocytic and normochromic and clinical signs are rare. AID can develop quite rapidly in the cat (within 3-4 days) suggesting that a shortened RBC lifespan, as well as reduced RBC production, contributes to the development of anaemia. Iron sequestration by the macrophage system, erythrocyte sequestration and impaired bone marrow response to erythropoietin are all thought to contribute to the development of AID.

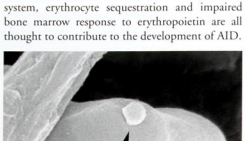


Figure 5: Scanning electron microscopic photo of a feline erythrocyte infected with a *Mycoplasma haemofelis* organism (arrowed). Note the attachment of the organism to the surface of the erythrocyte.

Chronic Renal Failure (CRF)

Up to 40% of cats with CRF are anaemic due to decreased renal erythropoietin production, bone marrow inhibition by uraemic toxins, decreased RBC survival, blood loss due to gastrointestinal ulceration or thrombocytopathia, and impaired iron utilization (a component of AID). Aplastic anaemia has also recently been associated with CRF *(Weiss 2006a)*.

Retrovirus Infection

Several mechanisms already mentioned above (e.g. PRCA, IMHA, AID) can contribute to retrovirus-infected associated anaemia but most cases show evidence of non-regenerative anaemia. FeLV and FIV testing can be done on blood and bone marrow samples.

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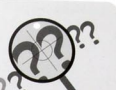
What is your DIAGNOSIS?



by Gabriele Habacher DVM MRCVS Fort Dodge Feline Fellow

Chloe, a 2 year female neutered cat was presented at the University of Bristol with dyspnoea. Three days prior to presentation her owners reported an increase in her respiratory rate.

Right lateral radiographic view of the chest obtained after drainage of 150mls of pleural effusion.

That morning however Chloe had deteriorated and her tachypnoea had progressed to dyspnoea.

Emergency clinical examination revealed dyspnoea and tachycardia (260bpm). Chloe was orthopnoeic and appeared to show a restrictive breathing pattern. Her mucous membranes were pink and moist and the CRT was < 2 seconds. Lung sounds were not audible in the ventral lung field bilaterally and chest percussion was suggestive of a fluid line at the level of 1/3 of the chest height. During examination, Chloe became dyspnoeic and started open mouth breathing. Oxygen was administered immediately via a face mask which settled Chloe down.

The chest was clipped and aseptically prepared for thoracocentesis. 150mls of pink-tinged fluid was drained. Chloe improved markedly during thoracocentesis. Her dyspnoea resolved and both the respiratory rate (40 breaths/minute) and heart rate (200bpm) decreased.

A thorough clinical examination was carried out at that point and no other abnormalities were detected apart from reduction of cranial rib spring. A thoracic radiograph was performed under mild sedation post drainage.

1. **What are your differential diagnoses for a restrictive breathing pattern?**
2. **Describe the radiographic abnormalities?**
3. **What further tests or procedures would you perform to give a definite diagnosis?**
4. **What treatment would you suggest?**

Answers on page 7

Case Challenges in Feline Medicine

School of Veterinary Science, Langford, nr Bristol

4th March 2009

Dealing with the severely ill, injured or unstable patient can be a hectic but rewarding experience. Often quick decisions have to be made about what tests are necessary to confirm or rule out a condition. Cases that you are likely to encounter in practice will be used to illustrate these areas.

The emphasis of this course will lie on diagnostic dilemmas and the process of clinical decision making. We will highlight how to prioritise tests in a practice setting. Small group discussions will be followed by a thorough analysis of the cases including tips and tricks that will help you on a day to day basis.

Examples of specific areas to be covered:

- **The seizuring cat**
- **The blocked cat**
- **The jaundiced cat**
- **The dyspnoeic cat**
- **The anaemic cat**

Speakers:

Prof Tim Gruffydd-Jones
BVetMed PhD DipECVIM-CA MRCVS
Andrea Harvey
BVSc DSAM(Feline) DipECVIM-CA MRCVS
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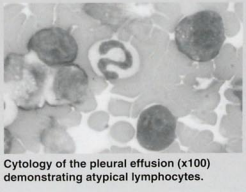
What is your DIAGNOSIS?

ANSWERS

1. Restrictive breathing patterns are characterised by an inability to extend the lungs appropriately. Differential diagnoses would include pleural space diseases (i.e. masses, pleural effusion, pneumothorax, constrictive/fibrosing pleuritis), pulmonary parenchymal or airway disease, thoracic wall disease and diaphragmatic rupture.

2. This is a right lateral view of the chest which was obtained after drainage. A small volume of residual pleural effusion is present. A soft tissue or fluid opacity can be seen in the cranial mediastinum. The trachea is deviated dorsally. Both of these findings are suggestive of the presence of a cranial mediastinal mass.

3. Haematology (including blood smear evaluation) and biochemistry allow assessment of the general health status and establish the presence of paraneoplastic syndromes. FeLV/FIV tests to determine retrovirus status should be performed. Samples of the obtained fluid should be sent for cytological and biochemical analysis and often allows a conclusive diagnosis. Ultrasound guided fine needle aspiration (FNA) or Tru-Cut biopsies of the cranial mediastinal mass may be of value to determine its nature. Ultrasound of the abdomen can help to assess the extent of the disease and potential involvement of abdominal organs/lymph nodes.



Cytology of the pleural effusion (x100) demonstrating atypical lymphocytes.

Chloe's haematology and biochemistry were unremarkable. Her FeLV status was positive on ELISA and confirmed with PCR. Cytology of the pleural effusion demonstrated atypical lymphocytes and was consistent with lymphoblastic lymphoma. In cases of lymphoblastic lymphoma, cytological examination is almost always diagnostic for lymphoma, thus further FNAs or Tru-Cut biopsies of the cranial mediastinal mass are not always carried out.

4. Treatment with a CHOP based protocol was initiated and Chloe showed a favourable response to chemotherapy. Her dyspnoea completely resolved within the first 2 weeks of treatment. The only side effects noticed were an episode of neutropenia, and loss of her whiskers which have grown back since. Chloe finished her 14-week chemotherapy protocol three weeks ago and has remained in remission since. We are hoping that she will continue to do well.

DISCUSSION

In the past most mediastinal lymphomas were associated with FeLV. Reduction of FeLV as a result of widespread vaccination programmes have contributed to a significant drop in the incidence of this form. Nowadays a high proportion of cats with mediastinal lymphomas are FeLV negative. A predisposition of Siamese and Orientals has been recognised for a long time. A much smaller proportion of these are now FeLV positive, but a familial form has been recognised in these breeds.

Dyspnoea as seen in Chloe's case is the most common presenting sign. Most commonly it is caused by the presence of a large mediastinal mass and/or pleural effusion. In the latter, thoracocentesis can offer temporary relief and facilitate further investigations such as radiography which may help to confirm the presence of a cranial mediastinal mass. Even though lymphoma is the most likely cause in this location, other differential diagnoses such as thymoma need to be ruled out. In case of a thymoma the pleural effusion would not be expected to contain lymphoblasts. If no conclusive diagnosis can be determined on basis of cytological examination of the pleural effusion FNAs or Tru-Cut biopsies of the cranial mediastinal mass would be indicated.

Mediastinal lymphoma is considered to be one of the most chemotherapy responsive anatomic forms of lymphoma with response rates being as high as 90%. Combination protocols such as COP achieve a very high and typically rapid response rate and are straightforward to use in practice. Protocols using doxorubicin seem to achieve the highest response rate and can be saved as a rescue protocol.

Survival times are generally very good but may be shorter in FeLV positive cats with mediastinal lymphoma. Cats with mediastinal lymphoma that were alive after an induction phase of 15 weeks, had a median survival time of >728 days (range 120 to >1491 days).

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ABSTRACTS

Effect of Feline Interferon-Omega on the Survival Time and Quality of Life of Cats with Feline Infectious Peritonitis

Susanne Ritz, Hermann Egberink, Katrin Hartmann

*J Vet Intern Med 2007; 21:**1193-1197***

Feline infectious peritonitis (FIP) is a worldwide occurring disease of feline corona virus in the cat. Although survival data have been poorly documented it is regarded as an invariably fatal disease.

In more recently published case series, feline interferon-omega (FeIFN-ώ) has been speculated to increase survival times however no controlled studies were available to assess its efficacy. The aim of this study was to evaluate the efficacy of FeIFN-ώ in cats with a confirmed diagnosis of FIP in a placebo-controlled double-blind trial.

Thirty seven cats were randomly assigned to an intervention or a placebo group. In all cats the diagnosis of FIP was confirmed by the detection of FCoV antigen in macrophages in the effusion, characteristic histological signs of biopsies of the liver, mesenteric lymph nodes, kidney, spleen and omentum and/or positive immuno-histochemical staining of FCoV antigen in macrophages. The intervention group (n=20) received 10^6 U/kg (0.1ml/kg) FeIFN-ώ subcutaneously every 24 hours for 8 days, then once a week for a total of 1 year or until euthanasia. Cats of the placebo group (n=17) received 0.1ml physiological saline at the same schedule. Additional treatment consisted of glucocorticoids, amoxicillin-clavulanic acid, dalteparin natrium and Feliserim consisting of antibodies against feline herpesvirus, feline calicivirus and feline parvovirus in order to increase protection against these infectious diseases.

All cats were hospitalised for the first 8 days and follow-up examinations were performed on days 7, 14, 30, 90, 180 and 360. The owners were asked to record respiratory rate, weight, length of sleeping time, eating, playing and grooming behaviour at home in a provided diary.

Eighty-seven per cent were domestic shorthair cats, 8% British Shorthair, and 5% Persians. Twenty cats were younger than 6 months and 34 cats (92%) had developed the disease younger than 24 months. 36 out of 37 cats presented with effusions, most of them with ascites (92%). There was no statistical difference in any variable on day 0 between intervention and control group. On day 7, lymphocyte count was significantly lower in the FeIFN-group. On day 14, statistical evaluation was abandoned because only 5 cats remained in the study.

Cats survived between 3 and 200 days (median: 9 days). Thirty-two of 37 cats survived fewer than 4 weeks. However, the difference in survival times between the intervention and control group was not significant. There was only one long-term survivor (> 3 months), and the cat was in the FeIFN- group.

Seven cats improved in their general condition during treatment (2 cats receiving FeIFN-ώ and 5 cats receiving placebo). Concurrent problems developed in five cats during treatment after which they deteriorated rapidly and died or had to be euthanized. The effusion resolved in 6 cats (3 cats receiving FeIFN-ώ and 3 cats receiving placebo). It relapsed in all 6 cats a few days before they were euthanized.

This study shows no statistically significant difference in the survival time of cats treated with FeIFN-ώ versus placebo or any other variable evaluated. Reasons for the lack of efficacy of FeIFN-ώ compared with placebo are uncertain. Insufficient tissue concentrations, drug interactions, different serotypes of FCoV and late initiation of treatment may play a role. In experimental studies, survival time increased significantly from 5 to 14 days when IFN treatment was initiated before virus inoculation which is in the field impossible. Other studies using IFN therapy for suspected FIP lack a confirmed diagnosis, thus longer survival times could be attributed to other disease processes.

Levetiracetam as an adjunct to phenobarbitone treatment in cats with suspected idiopathic epilepsy

Kerry Smith Bailey, Curtis W Dewey, Dewan M Boothe et al

J Am Vet Med Ass 2008, 232(6): 867-872

Phenobarbitone is currently the drug of choice for treatment of cats with idiopathic epilepsy. However, in those instances when treatment with phenobarbitone alone is ineffective, administration of phenobarbitone contraindicated because of concomitant medical conditions, or phenobarbitone treatment is associated with unacceptable side effects, alternative anticonvulsant drugs are needed. Historically, drugs of second choice are diazepam and bromide. These have however been associated with potentially fatal idiosyncratic hepatotoxicosis and eosinophilic lung disease respectively.

Levetiracetam is a novel antiepileptic drug which has been used in people. Pharmacokinetic studies have shown that the drug is well absorbed orally and does not undergo hepatic metabolism. In humans, a wide safety margin is reported with the most common side effects being somnolence, asthenia, headaches, and dizziness.

The study was conducted as a non-comparative clinical trial. Cats with idiopathic epilepsy that received phenobarbitone were eligible for enrolment if they were having seizures despite treatment, they had unacceptable side effects or unacceptably high serum phenobarbitone concentrations. A seizure log was maintained by the owners. Cats were treated with levetiracetam at a dosage of 20 mg/kg PO every 8 hours for a minimum of 3 months. Phenobarbitone administration was continued, and dosage changes were made only on basis of serum phenobarbitone concentrations. Cats were considered to have responded to levetiracetam treatment if the percentage reduction in seizures frequency was >50%. Seizure frequency, safety and tolerability were analysed. Serum concentrations were measured to assess bioavailability.

Twelve cats met the inclusion criteria. Eleven cats were domestic shorthair cats, 1 was a Siamese. Nine cats were castrated males and 3 spayed females. Median age at the onset of seizures was 2 years (range, 0.25 to 19 years). Physical and neurological examinations were normal prior to treatment with levetiracetam. Median duration of phenobarbitone treatment was 7 months (range, 1 week to 46 months). Ten of the 12 cats continued to have seizures while being treated with phenobarbitone including 1 cat with and episode of status epilepticus and two cats with episodes of cluster seizures. Serum phenobarbitone concentrations were high in 4 of these cats. Before instigation of levetiracetam 3 cats were treated with other anticonvulsant drugs in addition to phenobarbitone (potassium bromide; gabapentin; potassium bromide, zonisamide and phenytoin). Eleven of the 12 cats were still receiving levetiracetam at the end of the clinical trial, with follow-up times ranging from 6-24 months (median, 9 months). As accurate seizure logs were not maintained for 2 cats, efficacy data were available from only 10 cats. For these cats, median seizure frequency prior to treatment with levetiracetam (2.1 seizures per month; range, 0.8-42.4) was significantly greater than after initiation of treatment with levetiracetam (0.42 seizures per month; range, 0 – 1.25). Seven cats were considered to have responded to levetiracetam treatment (>50% reduction in seizure frequency). This included 3 cats without any recorded seizure activity since starting treatment. Percentage reductions in seizure frequency for the 3 cats that did not respond to levetiracetam treatment were 4%, 12.5%, and 34.9%. For 7 cats (4 responders and 3 non-responders), information was available on the number of seizures that occurred during the 3 months immediately before treatment and the 3 months after initiation treatment and showed no significant difference. Two of the 12 cats reportedly developed mild adverse effects in association with levetiracetam. These included mild inappetence and lethargy and resolved without any change in medications after 1-2 weeks. Administration of levetiracetam was discontinued in one cat in which seizure frequency only reduced by 4%. This cat had also signs mild cerebellar ataxia and was changed to zonisamide, which controlled the seizures although ataxia persisted.

In 8 of the 12 cats, serum levetiracetam concentrations were highest 2 hours after drug administration and in 2, after 4 hours. Elimination half life was calculated as 19 hours in 1 cat, but was < 6 hours in the remaining 11 cats.

Results of the present study suggested that levetiracetam may be an effective anticonvulsant when given in addition to phenobarbitone treatment in cats with idiopathic epilepsy and that serum drug concentrations could be achieved with an 8-hour dosing interval. However, longterm follow-up is needed to evaluate the efficacy because in dogs and people, the drug has been associated with a subsequent return to baseline values ("honeymoon period"). Of the 7 cats in the present study that were followed up > 8 months, 5 were classified as responding to treatment. Additional studies will be needed to determine whether levetiracetam will result in only transient decreases in seizure activity.

Outcome of cats with low-grade lymphocytic lymphoma: 41 cases (1995-2005)

Micheal A Kiselow, Kenneth M Rassnick, Sean P McDonough et al

*J Am Vet Med Ass 2008; 232:**405-410***

Lymphoma in cats represents a diverse group of tumours that vary in cell type, rate of dissemination, and progression. Most lymphomas in cats are intermediate (35%) or high (54%) grade. Approximately 10% of lymphomas of cats are composed of small, relatively well-differentiated, neoplastic lymphoid cells and can be histologically described as low grade. In previous studies, cats with low grade lymphocytic lymphoma in the gastro-intestinal tract had improved response to treatment with chlorambucil and prednisolone, disease-free interval, and overall survival. The purpose of this study was to compare the clinical outcome of cats with low grade lymphocytic lymphoma affecting other organ systems and to evaluate factors associated with response to treatment, remission duration and survival.

Medical records from 1995-2005 were reviewed at the Cornell University Hospital. Only cats with a histopathologically confirmed diagnosis of low-grade lymphoma that were treated with a combination of prednisone and chlorambucil were included. Lymphoma was classified as gastro-intestinal if histological findings were restricted to stomach, small intestine, or large intestine. The disease was considered non-gastrointestinal when histological findings revealed low-grade lymphoma of any other organ system, with or without gastro-intestinal involvement. Biopsy findings were reviewed and immunophenotyping was performed. Response to treatment was categorised as complete (100% resolution of clinical signs for >30 days) or partial (>50% but < 100% resolution of clinical signs for > 30 days). Cats reported to have < 50% improvement of clinical signs or responses of less than 30 days were considered to be nonresponders.

Five hundred fifty seven cats were identified with high-grade lymphoblastic lymphoma. Of the 110 cats coded as having low-grade lymphocytic lymphoma, 69 were excluded for mis-diagnosis (other neoplasia or non-neoplastic disease, n=15), missing biopsy specimens (n=7), treatment other than prednisone and chlorambucil or no treatment (n=16) and for being lost to follow-up (n=31).

Fourty-one cats met all the inclusion criteria. Median age was 13 years (rage, 6-17 years). Most cats were either domestic short hair or domestic long hair (n=40). Duration of clinical signs ranged from 5 days to 49 months and consisted of weight loss (83%), vomiting (73%), anorexia (66%), diarrhoea (59%), and lethargy (n=39%). Lymphoma was confined to the gastrointestinal tract in 68% of the cats, whereas 32% cats had other organ systems affected. Extra-gastrointestinal tract sides included mesenteric lymph nodes (n=6), liver (n=10), spleen (n=1), and pancreas (n=1). Eighty-nine percent of lymphomas were determined to be T-cell lymphomas.

Information describing response to chemotherapy was not available for 2 cats, leaving 39 cats in the analysis. Response to treatment was recorded in 95% of these cats. Fifty-six per cent achieved a complete response and 39% achieved a partial response. Only 2 cats had no response to treatment. No differences were found between responders and non-responders, or between cats with partial/complete remission with respect to the analysed risk factors.

Of the 37 responders, 13 relapsed during the follow-up period. Twenty-four cats were still under observation at a median of 383 days (range 44-2.010 days). The overall median remission duration was 948 days. Of all risk factors analysed, only response to treatment was significantly associated with remission duration. Cats with a partial response had a 4.3 greater risk of progression or recurrence. The median remission for cats with partial response (n=15) was 428 days, for cats with a complete response (n=12) 897 days. Twenty-one cats were known to have died during the follow-up period. Nine of them died of concurrent disease of unknown causes. Median overall survival times for cats with lymphocytic lymphoma of the gastrointestinal tract and lymphocytic lymphoma of nongastrointestinal tract sites were 765 and 714 days respectively.

This study suggests that prognosis for cats with low-grade lymphocytic lymphoma treated with chlorambucil and prednisone is favourable. Ninety-two percent responded to treatment for a median of > 2.5 years (29 months for complete response; 14 months for partial response). Anatomic location does not appear to be prognostic for response to treatment, response duration, or overall survival time. However, response to chemotherapy has been confirmed as the main factor with consistent prognostic value.

Feline Update is published as a co-operative venture between Langford House and Fort Dodge Animal Health. Any correspondence should be addressed to Prof. T. Gruffydd-Jones, The Feline Centre, Department of Clinical Veterinary Science, University of Bristol, Langford House, Langford, BS40 5DU, or to Matthew Rowe BSc (Hons) at Fort Dodge Animal Health, Southampton, SO30 4QH.