Proceedings of the
World Small Animal Veterinary Association
Sydney, Australia – 2007

Hosted by:

Australian Small Animal Veterinary Association (ASAVA)
Australian Small Animal Veterinary Association (ASAVA)
Australian Small Animal Veterinary Association (ASAVA)

Next WSAVA Congress

33rd Annual
World Small Animal Veterinary Association
14th FECAVA Congress

DUBLIN, IRELAND
20th - 24th August 2008
FELINE HAEMOPLASMOSIS
Remo Lobetti BVSc MMedVet (Med) PhD Dipl ECVIM (Internal Medicine)
Bryanston Veterinary Hospital
PO Box 67092, Bryanston, 2021, South Africa
Email: rlobetti@mweb.co.za

Causative Agent

The organism causing feline infectious anaemia was first described in 1942 from a cat in Pietermaritzburg, South Africa and was classified as *Eperythrozoon felis*, a protozoan belonging to the Order Hemopozoida and Family Anaplasminidae. Subsequent re-classifications placed the Anaplesminidae in the bacterial Order Rickettsiales as the Family Anaplasmataceae and *Eperythrozoon felis* and *Haemobartonella felis* were considered identical. Based on phylogenetic analysis of 16S rRNA gene sequences, *Haemobartonella felis* has been reclassified within the genus as *Mycoplasma* as 3 separate species, namely *M. haemofelis*, *M. haemominutum*, and most recently, *M. turicensis*. The latter was discovered in a Swiss pet cat with a history of severe haemolytic anaemia, and phylogenetic analyses revealed that this agent is most closely related to rodent haemoplasma species, namely, *Mycoplasma haemomuris* and *Mycoplasma coccoides*.

These three haemotropic mycoplasma species are collectively referred to as the feline haemoplasmas.

Epidemiology

Haemoplasmosis has a worldwide distribution with blood transfusion and tick and flea feeding the proposed modes of transmission. Experimental transmission has been shown to occur by oral, intraperitoneal and intravenous inoculation of infective blood. In contrast with the situation in dogs, the presence or absence of the spleen has little effect on transmission of the disease in cats. Other non-proven modes of transmission include in vitro, via nursing and other insect vectors such as mosquitoes.

Pathogenesis

The incubation period of the disease varies between 6-17 days and has a range of 20-34 days. The disease can be divided into the pre-parasitaemic, acute, recovery, and carrier phase. The period from the first to the last major parasitaemic episode is known as the acute phase with anaemia and other clinical signs developing during this phase. Some cats in the acute phase show signs that are inapparent or very mild whereas more severe cases that are left untreated may result in death. The acute phase is followed by the recovery phase during which time parasites may still be found but the haematocrit returns to normal. After the recovery phase it appears that most, if not all, infected animals become carriers. Parasites may occasionally be found during the carrier stage but decreases in haematocrit tend to be less severe. Relapses can occur under stressful conditions such as pregnancy, starvation, neoplasia, and other infections. However, immunosuppressive
drugs and corticosteroids do not seem to induce a relapse of the disease. Cats that recover from haemoplasmosis do not appear to have immunity. Risk factors for haemoplasmosis are anaemia, FeLV or FIV infection, history of cat bite abscesses, less than 3 years of age, and roaming outdoors.

Clinical Manifestations

Infection with *M. haemofelis* often causes a severe haemolytic anaemia, whereas *M. haemominutum* infections do not usually induce clinical signs, although some reports have documented a mild or moderate anaemia. It has also been suggested that co-infection with *M. haemominutum* and feline retroviruses may result in anaemia. The pathogenic potential of *M. turicensis* seems to depend on cofactors but has been reported to result in haemolytic anaemia.

The clinical signs of haemoplasmosis are generally non-specific. Infected animals may exhibit depression, lethargy, anorexia, weight loss, weakness, and pale mucous membranes. Icterus is variably present. In the acute phase, pyrexia may be apparent whereas chronically infected cats tend to be normothermic. A hepato-splenomegaly and generalized lymphadenopathy may be present. Cats with secondary haemoplasmosis are usually much sicker than animals manifesting the primary disease. In addition to the signs related to the underlying disease, the animals are usually moderately to severely anaemic.

Clinical Pathology

During the acute phase, the cat may become anaemic (haematocrit < 20% and even < 10%). This anaemia is variable and is produced by a progressive, periodic (7 to 11 days) series of extravascular haemolytic episodes. During each episode the haematocrit falls precipitously for a day or so and then, remarkably, recovers over the next one or two days. This “response” or recovery is much more than the marrow regeneration can explain and is attributed to two mechanisms. First, some of the anaemia is caused by intravascular sequestration of erythrocytes and these cells are “released” during the response phase. Second, many of the erythrocytes are sequestered in the spleen, liver, lungs and bone marrow (RE system) where it has been shown that they are “cleansed” of parasites by macrophages and returned to the general circulation as “clean” cells although their half-life is still seriously reduced due to an increased fragility.

These episodes of anaemia are usually associated with a febrile reaction and often preceded by a short-lived increase in leukocyte count. Most documented cases and experimental studies show four or five such episodes. Cats that survive this series of haemolytic crises, during which they become progressively more anaemic, then enter a recovery phase (which is unremarkable, the haematocrit approaching the low-normal range within a month) and a subsequent asymptomatic carrier phase ensues.
There is almost invariably a Coombs’ positive state associated with the acute phase. Often, there is macroscopically detectable auto-agglutination (occasionally shown to be associated with cold agglutinins) and usually a microscopically detectable auto-agglutination. It is believed that both immunoglobulins and complement are involved but very little evidence has been published.

The decrease in the erythrocyte size has been attributed to increased osmotic fragility and decreased life span. Erythrophagocytosis is also evident in peripheral blood, bone marrow and spleen. As a result of these factors, the anaemia associated with haemobartonellosis is typically regenerative.

Although the haemolysis is extravascular, there is seldom any significant icterus or bilirubinuria. Severe, intravascular haemolysis, leading to haemoglobinuria and haemoglobinaemia is mentioned in some review articles but is not described in the greater majority of natural and experimental case studies.

**Diagnosis**

Since its first description, the organism has been diagnosed principally by the examination of Romanowski-stained (Giemsa, Wright’s, Diff-Quick®) blood smears. The organisms have been described as “blue staining, small rings (0.5µm), cocci or rods attached to the erythrocyte membrane”. The organisms may occur singly, in clusters and in chains. Electron microscopy has shown that the discoid organism lies in shallow depressions of the erythrocyte membrane where it is attached by a few “attachment points”. The differences in light microscopic appearance are probably associated with a “rounding up” in the thicker parts of the smear, leading to the “coccus” form and a “flattening” in the thinner parts of the smear (tails and edges), leading to the “ring” or “concave disc” appearance. Also in the thinner parts of the smear, this disc can occur on the periphery (edge) of the host cell. Here, it is then presented “edge-on” as it were, leading to the “rod” shape description. This, latter, presentation is the single most diagnostic, because the other forms are easily confused with various artefacts in and on the erythrocyte. In heavy parasitaemias, chains of organisms lying on the surface of the erythrocyte seem to “tip over” onto their side, presenting as a dark-staining groove with barely discernible indentations separating the individual organisms. Inexperienced microscopists find it difficult to distinguish the organisms from Howell-Jolly bodies, basophilic stippling and stain deposit. In South Africa and the USA, *Babesia felis* and *Cytauxzoon felis*, respectively, create additional confusion.

Fluorescence microscopy using acridine orange is much more reliable than Romanowski-staining. Unfortunately, it is not useful for practitioners as the cost of the equipment is prohibitive and the method is very labour intensive.

As the organism cannot be cultured outside the host, there are currently no serological tests available. However, recent experimental work using Western
immunoblot analysis has identified an immuno-dominant antigen, which could be used in the serological diagnosis of *H. felis*. Indirect fluorescent antibody testing and ELISA for erythrocyte-associated immunoglobulins have been described, but never came into general or commercial use.

In recent years, PCR has become “gold standard” for diagnosing infection.

**Therapy**

Haemoplasmosis is most frequently treated with either oral or parenteral tetracyclines with tetracycline, oxytetracycline, and doxycycline reportedly effective. However, oxytetracycline does not seem to clear the infection, as parasites may still be present three months after therapy. Other antimicrobials that have a reported beneficial effect include chloramphenicol, amoxicillin and the quinolone group; these are, however, not as effective as the tetracyclines. In addition to tetracycline therapy, treatment with an orally administered corticosteroid is indicated especially in the severely anaemic animals. The rationale behind this is that the anaemia associated with haemoplasmosis has an immune mediated pathogenesis. Immune-suppressive doses should be used and then gradually tapered down as the haematocrit rises. In severely anaemic animals, blood transfusion is required.

**Prevention**

The primary preventative measure is controlling the vector by routinely dipping or spraying animals, using tick collars or spot on preparations as well as spraying the premises. Because the disease can be transmitted via blood transfusions, all blood donors must be regularly evaluated for haemoplasmosis.