

CLINICAL AND HEMATOLOGIC FEATURES OF INFECTION

M. haemofelis and *M. haemominutum*

The clinical signs and hematologic features of *M. haemofelis* and *M. haemominutum* infection in the cat are different. Acute infection with *M. haemofelis* is associated with a massive parasitemia of the red blood cells, causing a severe and sometimes fatal hemolytic anemia. This parasite has been shown to produce clinical signs of disease including lethargy, anorexia, fever, and anemia in naturally and experimentally infected cats. However, the pyrexia is intermittent and spikes when parasite numbers are highest in the peripheral blood. Splenomegaly and icterus, which are principally due to extravascular hemolysis are occasionally seen. The anemia associated with *M. haemofelis* infection is typically regenerative, showing anisocytosis and polychromasia with an increase in the absolute number of reticulocytes. However, the severity of the anemia depends on the stage of infection and the hematocrit may fall to less than 20% at peak parasitemia.

Healthy cats that were experimentally infected with the smaller red cell parasite, *M. haemominutum*, however developed only minimal clinical signs of acute disease and negligible hematologic changes. In this study, the cat's hematocrit declined throughout the course of infection with *M. haemominutum*, but never fell below the reference range for the cat. Single and occasionally multiple organisms were detected on each erythrocyte with the peak in parasitemia concurrent to the nadir of the hematocrit. However, there is some concern that the difference in pathogenicity between *M. haemofelis* and *M. haemominutum* may be merely dose-dependent effects. Additional studies are needed to better define the difference in virulence between these two red cell parasites in the cat.

In a recent study, cats that were experimentally coinfectd with FeLV and *M. haemominutum* developed a more severe anemia than cats infected with this parasite alone. Further, it was suggested that chronic infection with *M. haemominutum* may induce myeloproliferative disease in FeLV infected cats. Chronic *M. haemofelis* infection may also promote neoplastic transformation of hematopoietic cells in FeLV infected cats. The possible sequelae of chronic infection by these haemotrophic parasites in cats have not been fully defined. However, it cannot be assumed that these infections are of no consequence. It is also important to recognize that despite an intense immune response and/or antibiotic treatment, cats that are infected with either *M. haemofelis* or *M. haemominutum* probably remain chronic carriers of the parasite.

M. haemocanis

In the dog, two forms of *M. haemocanis* infection have been reported. The acute form of the disease is characterized by the presence of many RBC parasites and rapidly developing anemia, which is most often found in immunocompromised or splenectomized dogs. Acute infection also may be observed in non-splenectomized dogs that have various concurrent infections including babesiosis, ehrlichiosis and septicemia. The clinical signs may include anorexia, lethargy, weight loss, and fever. Packed cell volumes (PCV) as low as 11% have been reported with evidence of anisocytosis, nucleated red blood cells and polychromasia on the peripheral blood smear. Spherocytes, positive results of direct Coombs testing, and thrombocytopenias also have been occasionally reported. In severe cases, acute hemolytic anemia may result in death. More commonly, the dog recovers from acute disease but remain chronically infected.

A chronic form of infection also has been reported in non-splenectomized dogs, which produces no definitive clinical signs. In this form of infection, the parasites are found only periodically and in low numbers in the peripheral blood. Chronic infection has been associated with mild anemia, leukopenia, and listlessness in experimentally infected dogs. Further, these dogs may have a ravenous appetite with pica.

There are also rare reports of *M. haemominutum* infection in the dog, however the significance of the infection is unknown. Further, the prevalence of *M. haemocanis* in the canine population remains to be determined. In the dog, the infection is usually subclinical and often unrecognized until the spleen has been removed. It is our experience that *M. haemocanis* infection may be a widespread, latent disease in kennel-raised dogs. Thus, the potential exists for these latent infections to adversely affect or confound research results. As previously suggested, if an investigator desires to use splenectomized dogs for experimental procedures, or a surgeon is contemplating the splenectomy of a canine patient, development of acute haemoplasmosis as a possible complication must be considered.

TRANSMISSION

Lappin *et al.* recently showed that fleas infected with *M. haemofelis* can transmit parasites and produce disease in a susceptible cat, however transmission of *M. haemominutum* by fleas was not successful. It was suggested, however, that the low number of fleas used in the study might be responsible for these negative findings. Although the natural mode of transmission for *M. haemofelis* in the dog remains unknown, it is believed that the tick serves as an important reservoir and vector of infection. Blood transfusions from asymptomatic carrier dogs can also transmit infecting organisms to recipient dogs. However, it is likely that the recipient dog would need to be splenectomized or severely compromised for acute disease to occur.

DIAGNOSIS

The 16S rRNA gene is the basis for all the PCR assays developed to date for detection of haemotrophic mycoplasmas with several different primer pairs for detection of these parasites having been reported. During the past 3 years, more than 400 cats have been tested in the author's laboratory with both the Illinois and the California PCR assays for *M haemofelis* and 'Candidatus Mycoplasma haemominutum' infection, respectively (unpublished observations). About 12% of anemic cats were infected with *M haemofelis* compared with only 1.5% of nonanemic cats. However, 7.2% of anemic cats and 5.3% of nonanemic cats were infected with 'Candidatus Mycoplasma haemominutum.' The overall prevalence of infection in cats was about 20%. Jensen and colleagues developed a single PCR assay for the concurrent detection of both feline haemoplasma species. Using this assay, they found that 28% of blood samples from cats in which infection was suspected on the basis of fever, anemia, or microscopic evidence of parasitemia were positive for one or both feline haemoplasmas. *M haemofelis*, alone or in combination with 'Candidatus Mycoplasma haemominutum' accounted for infection in 17.1% of the suspect cats; whereas, none of the cats without clinical signs of infection (control cats) were infected with *M haemofelis*. However, 11% of suspect cats and 13.7% of control cats were infected with 'Candidatus Mycoplasma haemominutum.' The overall prevalence among suspect and control cats in that study was 19.5%. In a recent study in the United Kingdom using the same PCR assay, a prevalence of 18.5% for haemoplasma infection in cats was reported; however, 92% of the infections were due to 'Candidatus Mycoplasma haemominutum.' Thus, although the overall prevalence of haemoplasma infection in cats was similar in these 3 studies, there were notable geographic differences in the prevalence of specific parasites, particularly between the United States and the United Kingdom. The results of these studies emphasize the need to regularly test all donor cats for a haemotrophic *Mycoplasma* infection using a PCR-based assay.

ANTIBIOTIC TREATMENT

Although haemotrophic mycoplasmas are sensitive to tetracycline, the antibiotic must be given every 8 hours and drug-induced pyrexia in the cat may occur. Doxycycline, which also exhibits antimicrobial activity by inhibiting protein synthesis, is the preferred antibiotic. It is recommended that doxycycline be given twice daily per os at a dose of 5 to 10 mg/kg for up to 21 days. Gastrointestinal (GI) side effects due to irritation of the mucosa, may result in abdominal discomfort, vomiting, and anorexia in the cat and dog. There is also a report that doxycycline may induce esophagitis with esophageal stricture formation in cats. Recently, enrofloxacin (5 to 10 mg/kg, per os, every 24 h for 14 days) was shown to be equal or superior to doxycycline for treatment of haemoplasma parasite infections in the cat. The once-daily dosage and low incidence of side effects make its use attractive. Cases of acute and irreversible blindness and retinal degeneration have been reported in cats treated with enrofloxacin, however the prevalence of this toxicity is unknown. Azithromycin, which has been shown to control outbreaks of mycoplasma respiratory tract infections in humans, was ineffective as a treatment for these red cell parasites at a dose of 15mg/kg per os twice daily. Further, imidocarb dipropionate administered twice weekly at a dose of 5.0 mg/kg by intramuscular injection to cats with chronic *M. haemofelis* or *M. haemominutum*, failed to consistently clear the infection. Thus, treatment with doxycycline or enrofloxacin may effectively control acute infection in the cat, but none of the antibiotics tested to date consistently clear the parasites.

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