Feline Hemotropic Mycoplasmas

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KEYWORDS

• *Haemobartonella* • Anemia • Feline immunodeficiency virus
• Feline leukemia virus • Polymerase chain reaction • Zoonosis

Hemotropic mycoplasmas (hemoplasmas) are small (0.3–0.8 μm), unculturable epierythrocytic bacteria that can cause severe hemolytic anemia. These organisms infect a variety of mammalian species and are distributed worldwide. The organism causing disease in cats was previously known as *Haemobartonella felis*, and the disease is referred to as feline infectious anemia. Sequence analysis of the 16S rRNA genes of *Haemobartonella* spp has shown that they belong to a group of fastidious mycoplasmas.[1–3] Over the last 2 decades, the development and application of molecular genetic tests for these organisms had led to a greatly improved understanding of the hemoplasma epidemiology and pathogenesis. Several new hemoplasma species have been discovered in cats, which appear to vary in their pathogenicity, responsiveness to antimicrobial drugs, and ability to form a carrier state.[4–6]

ETIOLOGY AND EPIDEMIOLOGY

Organisms associated with the surface of the feline erythrocyte were first identified in South Africa in 1942, in an anemic cat, and were named *Eperythrozoon felis*.[7] Approximately 10 years later, similar organisms were recognized in cats in the United States in Colorado, and intraperitoneal injection of blood from an infected anemic cat into research cats resulted in anemia in the inoculated cats.[8] In 1955, based on their morphology, the name *Haemobartonella felis* was suggested for the organisms.[9,10] The infection was recognized in cats from other US states[11,12] and several other countries worldwide.[13–23]

With the advent of polymerase chain reaction (PCR) assays in the 1990s, amplification of DNA from *Haemobartonella* spp and *Eperythrozoon* spp became possible. Sequence information from amplified 16S rRNA gene DNA revealed the close similarity of these organisms to mycoplasmas, and *Haemobartonella felis* was renamed *Mycoplasma haemofelis* (Mhf).[2] Around the same time, another epierythrocytic organism was detected in California in a cat that was coinfected with feline leukemia virus (FeLV). This organism was approximately half the size of Mhf, and much less

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pathogenic.[4] Initially referred to as the small form, or California variant of *Haemobartonella felis*, the name "*Candidatus* Mycoplasma haemominutum" (Mhm) was subsequently given to this organism (the "*Candidatus*" term for newly described hemoplasmas is required for taxonomy purposes because the organisms cannot be cultured, and will be removed when more information becomes available to support their classification).

Three years later, a third hemoplasma, "*Candidatus* Mycoplasma turicensis" (Mtc), was identified in Switzerland (Latin, *Turicum*, Zurich).[5] This organism has subsequently been reported from Australia, Brazil, Canada, Germany, Italy, Japan, South Africa, United Kingdom, and United States.[24–32] Mtc was discovered using PCR, and has never been identified on blood smears using cytologic examination. In one study, inoculation of 2 specific pathogen-free cats with this organism resulted in mild anemia in one cat and severe anemia in the other, although the cat with severe anemia was also immunosuppressed with glucocorticoids.[5] The same isolate caused mild anemia in 3 additional glucocorticoid-treated cats in a separate study, and the degree of anemia was proportional to the organism load inoculated.[33] Mtc has also failed to cause anemia when inoculated into specific pathogen-free cats.[33,34] Circulating organism loads in cats infected with Mtc, as determined using quantitative PCR assays, have typically been very low.[24,25,33,34] Inoculation of Mtc into research cats was followed by a sharp decline in organism numbers around day 40 post inoculation, and all cats became negative by day 45 post inoculation.[34] Intermittent low-level positive PCR results were detected at later time points in some cats, suggesting that complete elimination of the organism had not occurred. In another study, spontaneous clearance of infection occurred at 10 to 21 weeks post inoculation.[33]

MYCOPLASMA HAEMOFELIS

Using cytologic evaluation of blood smears, Mhf appears as cocci to small (0.6 μm) rings and rods, sometimes forming short chains of 3 to 6 organisms. In most epidemiologic studies that use PCR to detect infection, Mhf is the least prevalent of the 3 feline hemoplasmas, being found in 0.5% to 6% of sick cats visiting veterinary hospitals, although in a few geographic locations Mtc is less prevalent (**Fig. 1**).[24–30,32,35] Experimental inoculation of cats with Mhf results in moderate to severe anemia, and cats infected with Mhf sometimes demonstrate fluctuations in organism loads over the course of infection, with peak organism numbers correlating with dramatic declines in the hematocrit.[4,34,36,37] Young cats may be more susceptible to infection and disease.[27,34]

"CANDIDATUS MYCOPLASMA HAEMOMINUTUM"

Most infections with Mhm are chronic and not associated with anemia or other clinical abnormalities. Mhm can be detected using PCR in as many as one-fifth to one-half of cats visiting veterinary hospitals for a variety of reasons, with the prevalence of infection generally increasing with age.[24–30,32,35,38] Inoculation of cats with Mhm can initially be followed by a mild decrease in hematocrit, but the hematocrit generally normalizes after 4 to 6 weeks.[34,36] After infection, organism numbers (as determined using quantitative PCR assays) gradually increase, then reach a plateau.[36] The prevalence of infection in anemic cats has been the same, or lower than the prevalence of infection in nonanemic cats, implying that infection with Mhm is not associated with anemia.[6,24,38,39] Furthermore, inoculation of glucocorticoid-treated, splenectomized cats with Mhm was not associated with development of anemia, and subsequent coinfection with *Bartonella henselae* also did not precipitate development of anemia.[40]