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The purpose of this manuscript is to provide a brief review of the emerging clinical issues associated with Bartonella species and hemoplasma (previously Haemobartonella species) infections of cats and dogs.

**Feline bartonellosis.** Cats have proven by culture or DNA amplification to be infected by *Bartonella henselae*, *B. clarridgeiae*, *B. koehlerae*, *B. quintana* and *B. bovis*. Antibodies against *B. elizabethae* have been detected in some cats but these results should be interpreted cautiously because of the serological cross reactivity among *Bartonella* spp. Cats are the main reservoir hosts for *B. henselae* and *B. clarridgeiae* and are likely to be the reservoir for *B. koehlerae*. *Bartonella henselae* is the most common cause of Cat Scratch Disease as well as bacillary angiomatosis, and peliosis hepatis, common disorders in humans with AIDS. *Bartonella* spp. are thought to have both intra-endothelial and intra-erythrocytic phases of infection.

Based on results of seroprevalence studies, culture, or polymerase chain reaction (PCR) assay, cats are commonly exposed to or infected by *Bartonella* spp.. The organism is transmitted between cats by *Ctenocephalides felis* and so prevalence is greatest in cats from regions where fleas are common. In a recent study in the United States, we collected fleas from cats and attempted to amplify *Bartonella* spp. DNA from flea digests as well as the blood of the cat. The prevalence rates for *B. henselae* in cats and their fleas were 34.8% and 22.8%, respectively. The prevalence rates for *B. clarridgeiae* in cats and their fleas were 20.7% and 19.6%, respectively. Results are similar in other studies performed around the world. *Bartonella henselae* survives in flea feces for days after being passed by infected *C. felis*. Infected flea feces are likely to contaminate cat claws during grooming and then *Bartonella* are inoculated into the human when scratched. It is also possible that open wounds are contaminated with infected flea feces.

Most cats with serological evidence of exposure to a *Bartonella* spp., a *Bartonella* spp. cultured from blood, or microbial DNA amplified from blood by PCR assay are clinically normal. However, *Bartonella* spp. infection of cats has also been associated directly or indirectly with a variety of clinical manifestations like fever, lethargy, lymphadenopathy, uveitis, gingivitis, and neurological diseases [Figure 1]. How often cats become ill from *Bartonella* spp. infections is unknown and more information is needed. For example, the association of *B. henselae* infection to uveitis in a cat was first made in an individual case with uveitis.

Figure 1: Bilateral anterior uveitis in a cat that is consistent with bartonellosis
Bartonella and Haemobartonella in cats and dogs: current knowledge

Bartonella infection. Cats that are culture-negative or PCR-negative and antibody-positive and cats that are culture-negative or PCR-negative and antibody-positive are probably not a source of flea, cat, or human infection. However, bacteremia can be intermittent and false-negative culture or PCR results can occur, limiting the predictive value of a single battery of tests. With PCR, false positive results can occur and positive results do not necessarily indicate that the organism is alive. While serologic testing can be used to determine whether an individual cat has been exposed, both seropositive and seronegative cats can be bacteremic, limiting the diagnostic utility of serologic testing. Thus, testing healthy cats for Bartonella spp. Infection is not currently recommended in the United States. Testing should be reserved for cats with suspected clinical bartonellosis. If the results of Bartonella tests are negative in a clinically ill cat, the organism is not likely the cause of the clinical syndrome unless the infection was peracute and serological testing was used as the diagnostic test. If the results of Bartonella tests are positive, the agent remains on the differential list, but other causes of the clinical syndrome must also be excluded.

In experimental studies, administration of doxycycline, tetracycline, erythromycin, amoxicillin-clavulanate, or enrofloxacin can limit bacteremia but does not cure infection in all cats. To date, use of antibiotics in healthy cats has not been shown to lessen the risk of cat scratch disease. In addition, treating healthy cats with antibiotics that do not eliminate infection may predispose to resistant strains of the organism. Thus in the United States, treatment is generally recommended for clinically ill cats. If clinical bartonellosis is suspected, I prescribe doxycycline at 10 mg/kg, PO, daily, formulated into a flavored suspension (to avoid esophageal strictures) for 7 days as my initial therapeutic trial. If a positive response is achieved, I continue treatment for 2 weeks past clinical resolution of disease or for a minimum of 28 days. If a poor response is achieved by day 7 or doxycycline is not tolerated and I still believe bartonellosis is a valid differential diagnosis, I consider azithromycin or a fluoroquinolone as second choices. In my experience, Bartonella spp. positive cats that have failed to respond after administration of 2 different drugs with presumed anti-Bartonella activity generally have another cause of the clinical syndrome.

To lessen the likelihood of acquiring a Bartonella spp. infection from a cat, the following are adaptations of what is recommended to HIV-infected people and other cat owners by the Centers for Disease Control and the American Association of Feline Practitioners.

- **Flea control should be initiated and maintained year-round.**
- If a family member is immunocompromised and a new cat is to be acquired, adopt a healthy cat > 1 year of age and free of fleas.
- Immunocompromised individuals should avoid contact with cats of unknown health status.
- Declawing of cats is generally not required but claws should be trimmed regularly.
- Bites and scratches should be avoided (including rough play with cats).
- Cat-associated wounds should be washed promptly and thoroughly with soap and water and medical advice sought.
- While Bartonella spp. have not been shown to be transmitted by saliva, cats should not be allowed to lick open wounds.
- Keep cats indoors to minimize hunting and exposure to fleas and other possible vectors.

**Canine bartonellosis.** *Bartonella vinsonii* subsp. *berkhoffii* was initially isolated from a dog with endocarditis in North Carolina in 1993. Since that time, dogs in multiple areas of the world have been shown to seroreact with *B. vinsonii* subsp. *berkhoffii* antigens. *Bartonella vinsonii* (berkhoffii) is thought to be tick borne. Serum of some dogs also seroreacts with *B. henselae* and *B. claridgeiae* antigens; these Bartonella spp. are transmitted by fleas. Bartonella spp. that have been isolated from dogs or from which DNA has been amplified from blood or tissues include *B. vinsonii* (berkhoffii), *B. hense- lae*, *B. claridgeiae*, *B. walthoiensis*, and *B. elizabethae*. Each of these organisms potentially can induce illness in dogs. Dogs infected with a *Bartonella* spp. are commonly co-infected with other agents like *Ehrlichia* spp. which may play a role in the pathogenesis of disease.

Clinical findings or syndromes most frequently attributed to Bartonella spp. infections of dogs include endocarditis, fever, arrhythmias, hepatitis, granulomatous lymphadenitis, cutaneous vasculitis, rhinitis, polyarthritis, meningonecephalitis, thrombocytopenia, anemia, eosinophilia, mononcytosis, immune-mediated hemolytic anemia, epistaxis, and uraemia. *Bartonella vinsonii* (berkhoffii) and *B. henselae* seem to be the most likely species to be associated with clinical disease. Serum antibodies can be detected in both healthy and clinically ill dogs and so do not correlate always to illness. Some Bartonella spp., in particular *Bartonella vinsonii* (berkhoffii), can be difficult to culture and so amplification of DNA by PCR assay is often used to confirm infection. If positive test results are detected in a clinically ill dog and there is no other obvious explanation for the illness, treatment is indicated. Some clinicians believe that azithromycin is the treatment of choice, but controlled studies are lacking. Fluoroquinolones, alone or in combination with amoxicillin, were apparently effective for the treatment of some dogs with suspected clinical bartonellosis. Doxycycline may also be effective. No matter which drug is used, a minimum of 4-6 weeks of treatment is usually needed. In one study, successfully treated dogs became seronegative.

**Feline hemoplasmosis.** The large and small forms of Haemobartonella felis are gram-negative, epicyclic parasites of feline erythrocytes that have been reclassified as mycoplasmas. The new
name for large form (Ohio isolate) is Mycoplasma haemofelis (Mhf). The proposed name for the small form (California isolate) is ‘Candidatus Mycoplasma haemominutum’ (Mhm). Strains evaluated in the United States and the United Kingdom are genetically similar.

A potentially pathogenic, genetically distinct species was amplified from a clinically ill cat in Switzerland. The proposed name is ‘Candidatus M. turicensis.’ In at least two studies of experimentally infected cats, Mhf is apparently more pathogenic than Mhm; all Mhm inoculated cats became clinically ill whereas Mhf inoculated cats were generally subclinical.

In a recent study, we collected fleas from cats and attempted to amplify hemoplasma DNA from flea digests as well as the blood of the cat. The prevalence rates for Mhf in cats and their fleas were 7.6% and 2.2%, respectively. The prevalence rates for Mhm in cats and their fleas were 20.7% and 23.9%, respectively. In addition, fleas ingested Mhm and Mhf from infected cats when feeding. In one cat, we documented flea feeding to transfer Mhf. However, when we fed Mhf or Mhm infected fleas to cats, infection was not documented. In other studies, hemoplasmas have been transmitted experimentally by IV, IP, and oral inoculation of blood. Clinically ill queens can infect kittens; whether transmission occurs in utero, during parturition, or from nursing has not been determined. Transmission by biting has been hypothesized. Red blood cell destruction is due primarily to immune-mediated events; direct injury to red blood cells induced by the organism is minimal.

Clinical signs of disease depend on the degree of anemia, the stage of infection, and the immune status of infected cats. Coinfection with FeLV can potentiate disease associated with Mhm. Clinical signs and physical examination abnormalities associated with anemia are most common and include pale mucous membranes, depression, inappetence, weakness, and occasionally, icterus and splenomegaly. Fever occurs in some acutely infected cats and may be intermittent in chronically infected cats. Evidence of coexisting disease may be present. Weight loss is common in chronically infected cats. Cats in the chronic phase can be subclinically infected only to have recurrence of clinical disease following periods of stress.

The anemia associated with hemoplasmosis is generally macrocytic, normochromic. Chronic nonregenerative anemia is unusual in cats with hemoplasmosis. Neutrophilia and monocytosis have been reported in some hemoplasma-infected cats.

Diagnosis is based on demonstration of the organism on the surface of erythrocytes on examination of a thin blood film or PCR assay (Figure 2). Organism numbers fluctuate and so blood film examination can be falsely negative up to 50% of the time. The organism may be difficult to find cytologically, particularly in the chronic phase. Thus, PCR assays are the tests of choice due to sensitivity. Primers are available that amplify a segment of the 16S rRNA gene common to both hemoplasmas. Real-time PCR to quantify hemoplasma DNA has now been titrated and can be used to monitor response to treatment.

Since hemoplasmosis and primary immune hemolytic anemia are difficult to differentiate, cats with severe, regenerative hemolytic anemia are often treated with glucocorticoids and antibiotics. Doxycycline has less side effects than other tetracyclines in cats and so is preferred. I usually administer doxycycline as a flavored suspension (to avoid esophageal strictures) at 10 mg/kg, PO, every 24 hours for 7 days. If there is a positive response and the cat is tolerating the drug, I continue treatment for 28 days. If autoagglutination is evident, I generally prescribe prednisolone at 1 mg/kg, PO, every 12 hours for the first 7 days or until autoagglutination is no longer evident. Tetracyclines utilized to date appear to lessen parasitemia and clinical signs of disease but probably do not always clear the organism from the body and so recurrence is possible. In cats intolerant of doxycycline, enrofloxacin given at 5 mg/kg, PO, every 24 hours for 14 days was tolerated by cats and is equally effective or more effective than doxycycline. Administration of marbofloxacin gives similar results. Azithromycin was not effective for the treatment of hemoplasmosis in one study. Imidocarb administered at 5 mg/kg, IM, every 2 weeks for at least 2 injections was used successfully in the management of five naturally-infected cats that had failed treatment with other drugs. Blood transfusion should be given if clinically indicated.

To attempt to prevent hemoplasma infections, it might be prudent to control fleas. Cats should be housed indoors to avoid other potential vectors and fighting. Clinic blood donor cats should be screened for hemoplasmas by PCR assay prior to use.

Canine hemoplasmosis. Previously, it was believed that dogs were occasionally infected by Haemobartonella canis, an organism transmitted by Rhipicephalus sanguineus. Based on genetic analysis, dogs are now known to be infected by 2 distinct species, M. haemocanis and ‘Candidatus M. haematoparvum.’ While the distribution of these agents is largely unknown, both species have been amplified from dogs in the United States and Europe. For example in France, 71 of 460 dogs were positive for DNA of one or both of the organisms. It is possible that M. haemocanis infection is more common in kennel raised dogs than in pet dogs. Neither organism appears to be a significant primary pathogen. However, after splenectomy or other forms of immune suppression, latent infection can be activated and result in hemolytic anemia. Because results of cytology can be falsely negative, PCR assay may be needed to prove infection. Treatment with tetracycline derivatives with or without glucocorticoids can control the hemolytic anemia. However, similar to feline hemoplasmas, antibiotic therapy is unlikely to eliminate the infection. PCR assay positive dogs should not be used as blood donors. Tick control should be maintained to attempt to lessen risk of infection.
Selected References

**Feline bartonellosis**


**Canine bartonellosis**


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