

Canine Bartonellosis

Bruno B. Chomel, DVM, PhD, University of California, Davis

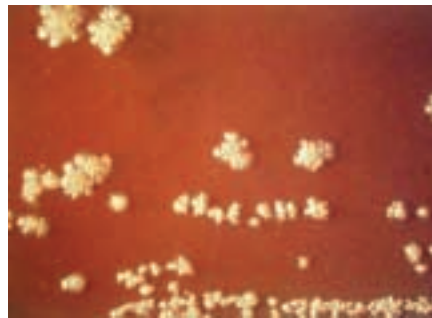
P Profile

DEFINITION

An infection caused by various *Bartonella* species or subspecies in domestic dogs causing a wide spectrum of clinical signs from subclinical infection to severe clinical manifestations, including granulomatous hepatitis, granulomatous lymphadenitis, and most commonly endocarditis. Infection in dogs appears to be more common in tropical environments (up to 65% of dogs in these areas are seropositive) than in temperate or cold climates (< 5%).¹ Canine bartonellosis is suspected to be a vector-borne infection, but the true vectors have yet to be identified. However, ticks could be involved for some of the *Bartonella* species that infect dogs.^{2,3}

SIGNALMENT

Species. *Bartonella vinsonii* subspecies *berkhoffii* infection has been reported mainly in dogs and some wild canids, such as coyotes in California.^{1,3,4} Domestic cats are the main reservoir for *B. henselae*. However, this *Bartonella* species has been diagnosed in a few clinical cases in dogs and a recent study has shown seropositivity for this bacterium in a high percentage of dogs.⁵ Similarly, cats are the main reservoir for *B. clarridgeiae*, but this species has also been isolated from domestic dogs and associated with endocarditis and liver disease.¹ Finally, a few clinical cases in dogs were caused by



Bartonella henselae culture on rabbit blood agar

species usually found in rodents (*B. washoensis* and *B. elizabethae*).¹

Breed Predislection. Seropositivity was mainly observed in herding dogs and dogs living in rural areas;^{2,6} toy breeds were less commonly affected.⁶ Endocarditis is primarily reported in large to medium-sized breeds.⁷

Age and Range. Unknown (not enough data available). Endocarditis is usually seen in middle-aged dogs (median age, 8.5 years in a case series).⁷

Gender. No predislection.

CAUSES / PATHOPHYSIOLOGY

Bartonella are fastidious, Gram-negative organisms that have a specific tropism for red blood cells and endothelial cells and are usually transmitted by insect vectors.^{1,3} Endocarditis is probably the result of chronic *Bartonella* infection in dogs and is char-

acterized by a preferential localization on the aortic valve.⁷ *Bartonellae* stimulate several cellular functions of endothelial cells, resulting in cell invasion, proinflammatory activation, suppression of apoptosis, and stimulation of proliferation, which may culminate in vasoproliferative tumor growth.⁸

RISK FACTORS

For *B. vinsonii* subspecies *berkhoffii*, several risk factors have been associated with seropositivity in dogs. Dogs living in rural environments (especially on farms) and that were allowed to roam outdoors as well as those presenting with heavy tick and/or flea infestations were more likely to have antibodies against *B. vinsonii berkhoffii* (odds ratio [OR] 14 and 5.6, respectively).² Seropositivity to tick-borne pathogens (mainly *Ehrlichia* species, *Anaplasma phagocytophilum*, *Babesia canis*) was more commonly seen in dogs seropositive for *Bartonella*.^{2,9} In another study, when compared with sporting breeds, herding dogs were more likely to be seropositive for *Bartonella* species (OR, 2.23; 95% confidence interval (CI), 1.11 to 4.48), whereas toy breeds were less likely to have antibodies against *Bartonella* species (OR, 0.26; CI, 0.08 to 0.80).⁶

CLINICAL SIGNS

In dogs, infection with *Bartonella* species is known to cause endocarditis, but it has also been commonly associated with arrhyth-

continues

mias, myocarditis, peliosis hepatis, granulomatous lymphadenitis, granulomatous rhinitis, and granulomatous and lymphocytic hepatitis.^{3,10-13} In addition, the clinical spectrum of *Bartonella* species infection has expanded on the basis of serologic evidence, and may include such clinical signs as anterior uveitis, choroiditis, cutaneous vasculitis, meningoencephalitis, splenomegaly, polyarthritis, lameness, nasal discharge, or epistaxis.^{6,14} Thrombocytopenia, immune-mediated hemolytic anemia, neutrophilic leukocytosis, and eosinophilia are the most commonly detected hematologic abnormalities in dogs seropositive for *B. vinsonii berkhoffii*.¹⁴ While these clinical and laboratory abnormalities have been reported, any one of them alone would not be sufficient to indicate the need for *Bartonella* testing.

Dx Diagnosis

CLINICAL DIAGNOSIS

Clinical diagnosis is problematic, as the clinical spectrum of *Bartonella* infection in dogs is just being established. *Bartonella* infection should be suspected in cases of endocarditis or cardiac abnormalities (arrhythmias, myocarditis), especially when the aortic valve is affected. It also should be suspected in dogs with prolonged or intermittent fever, lethargy, or unexplained lameness or in unexplained granulomatous disease. Similarly, a diagnostic test for *Bartonella* infection should be considered when there is clinical or epidemiologic suspicion of a tick-borne infection. Thrombocytopenia, anemia, neutrophilic leukocytosis, and eosinophilia are the most commonly detected hematologic abnormalities in dogs seropositive for *B. vinsonii berkhoffii*.¹⁴

DIFFERENTIAL DIAGNOSIS

In cases of endocarditis, blood culture should be done to exclude any conventional bacterial endocarditis (caused by bacteria,

PCR = polymerase chain reaction

such as *Streptococcus* or *Staphylococcus*). In cases of vegetative endocarditis, especially on the aortic valve, suspicion of *Bartonella* infection should be high. Among other causes of culture-negative endocarditis, *Coxiella burnetii* (Q fever) infection should be considered.

Because of the broad spectrum of clinical signs, bartonellosis can be confused with several tick-borne infections, such as Lyme disease, ehrlichiosis, anaplasmosis, or babesiosis. Therefore, *Bartonella* serologic testing should be included in any "tick-borne diseases" panel.

SEROLOGIC TESTING

In dogs, individual serologic testing mainly consists of indirect immunofluorescent antibody testing against *B. vinsonii berkhoffii*. However, in dogs with a high clinical suspicion for infection, testing against other *Bartonella* species that have been recently isolated or detected by PCR in dogs, especially *B. henselae* and *B. clarridgeiae*, should be done.

Serologic testing is good for initial screening of infected dogs. A titer 1:64 or greater is usually considered indicative of exposure to the agent. In suspected clinical cases, testing two samples at 2-week intervals is strongly suggested to evaluate the kinetics of the infection. As in humans, *Bartonella* endocarditis cases are usually characterized by high titers (>1:512) and cross-reactivity with several *Bartonella* antigens occurs.⁷ Due to this cross-reactivity, isolation or PCR is necessary to confirm the infecting *Bartonella* species.

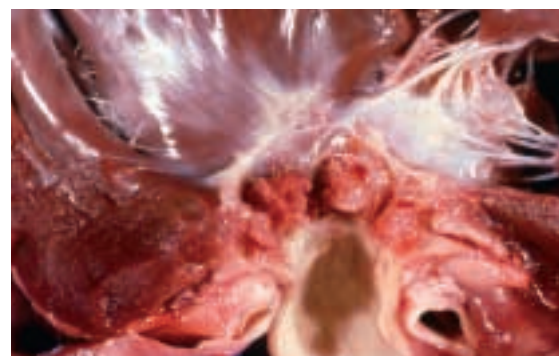
BLOOD CULTURE

Culturing *Bartonella* from blood is very difficult, even when dogs have endocarditis.^{1,3} Isolation is done using lysis-centrifugation

tubes (Wampole Istatat 1.5) or EDTA tubes (plastic tubes are the most convenient). Whole anticoagulated blood is plated, usually after freezing to induce red blood cell lysis, onto fresh rabbit blood agar and incubated for at least 4 weeks at 35°C with 5% carbon dioxide. The isolate is then identified using PCR techniques and partial sequencing. Such testing can only be done in a few diagnostic laboratories across the country.^{1,3} (See Aids & Resources.)

EXTRACTION OF DNA

Extraction of DNA from tissue samples with PCR testing is also a common method of diagnosis and has been more successful than culture in dogs. Frozen tissues or fresh biopsies can be easily tested. PCR extraction from paraffin-embedded tissues is more cumbersome, but possible. Testing should be done in laboratories familiar with these fastidious organisms, and laboratories should be contacted for specific instructions for sample collection and submission.

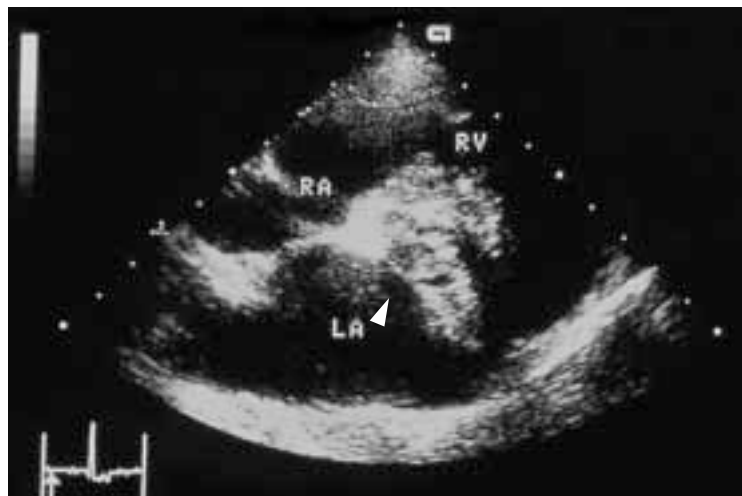


Canine *Bartonella* endocarditis with vegetative lesions on aortic valve

Tx Treatment

Studies have not yet been done to determine the efficacy of antibiotics in *Bartonella* infection in dogs. The use of antibiotics that achieve high intracellular concentrations, such as doxycycline, fluoroquinolones, or azithromycin, would be

required to eliminate intracellular infection. Based on data from other species, it is likely that antibiotics, such as doxycycline or tetracycline, could reduce the level of bacteremia during chronic infections. Treatment should continue for 4 to 6 weeks. Because azithromycin reaches high intracellular antimicrobial concentrations, it is suggested as a first-line antibiotic for treatment of *Bartonella* infections in dogs.¹⁴ However, if lesions of endocarditis are already well-established, antibiotic therapy may not be effective.



Two-dimensional echocardiogram (short-axis basilar) revealing aortic valvular infective endocarditis. Note the vegetative lesions (arrow) on the aortic valve cups at the center of the picture. LA = left atrium, RA = right atrium, RV = right ventricle

Follow-Up

PATIENT MONITORING

Patients should be monitored for negative blood culture (may be very difficult) and decreased antibody titers after treatment.¹⁴

PREVENTION

Canine *Bartonella* infections are likely to be vector-borne. A tick vector is strongly suspected for *B. vinsonii berkhoffii*³; therefore, prevention of tick infestation should be one of the main control measures in the clinical setting. Use of tick repellents and cleaning of the dog after a walk in high-risk terrain should be done systematically to prevent *Bartonella* as well as other tick-borne infections. Flea control measures are also important, as dogs may become infected with *B. henselae*, possibly when exposed to cat fleas, which are known to transmit the infection among cats.

COMPLICATIONS

Severe cardiac insufficiency and respiratory distress caused by fulminant cardiogenic pulmonary edema may occur in dogs with major vegetative lesions on cardiac valves caused by *Bartonella* infection.¹⁵

In General

RELATIVE COST OF TREATMENT

Depends on severity of clinical signs. Patients with endocarditis seen in emergency rooms for fulminant pulmonary edema can incur thousands of dollars in medical expenses (\$\$\$\$\$). The antibiotic treatment of dogs diagnosed with a *Bartonella* infection usually runs in the \$300 to \$600 range (\$\$\$).

PROGNOSIS

It is difficult to establish a clear prognosis for dogs with *Bartonella* infection, as the clinical spectrum of the infection in dogs is just being recognized. The prognosis is usually poor for most dogs with endocarditis,^{7,15} but one dog was documented to have survived over 3 years after the initial diagnosis.¹¹

FUTURE CONSIDERATIONS

Current clinical research is focused on identifying clinical entities associated with *Bartonella* infection in dogs and establishing the prevalence of infection in various dog populations. Furthermore, *Bartonella* species

other than *B. vinsonii berkhoffii* that infect dogs are being identified. Research is still greatly needed to determine which antibiotic, and at what dose, would most effectively control *Bartonella* infection in dogs. Finally, research is needed to confirm the role of ticks in the transmission of infection. ■

See Aids & Resources, back page, for references, contacts, and appendices.

Tx at a glance

- **Treat *Bartonella* infection with antibiotics with a high intracellular antimicrobial concentration:**
 - Doxycycline—10 mg/kg PO Q 12 H for 14 days to 4 weeks
 - Azithromycin—5 mg/kg PO Q 24 H for 4 weeks
 - Enrofloxacin—4 mg/kg PO Q 12 H for 4 weeks