



Bartonellosis of the Cat & Dog

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In vitro susceptibility data do not correlate with in vivo effectiveness for many antibiotics, especially when only 1 antibiotic is administered.²

Overview

Common *Bartonella* spp of the cat and dog

- *B clarridgeiae*
- *B henselae*
- *B koehlerae*
- *B vinsonii* subsp *berkhoffii*

Note: Infections with other *Bartonella* spp have been documented in cats and dogs.¹

Based on in vitro testing in humans, most *Bartonella* spp are susceptible to a large number of antibiotics; however, data on in vitro susceptibility do not correlate with in vivo effectiveness for many antibiotics, especially when only 1 antibiotic is administered.²

- Phylogenetically, the genus *Bartonella* is in the Alphaproteobacteria class and therefore is very closely related to the genus *Brucella*.
- Similar to the treatment of brucellosis, **successful therapeutic elimination of *Bartonella* spp organisms can typically require coadministration of 2 antibiotics with different modes of action** (extrapolated from available animal and human treatment data).

Doxycycline

Cats, dogs: 10 mg/kg PO twice a day for 28-42 days^{3,4}

- To avoid esophagitis, use with suspension or perform water flush after administering each oral dose.

Doxycycline is a tetracycline antibiotic that inhibits protein synthesis by binding aminoacyl-tRNA to the 30S ribosomal subunit in the mRNA translation complex. Based on a laboratory study involving cats infected by blood transfusion, administration of doxycycline (5 mg/kg PO twice a day) for 2 or 4 weeks did not consistently clear *B henselae* or *B clarridgeiae* from the blood.³ In a separate trial, when doxycycline (50 mg PO once a day) was administered for 28 days to 9 cats naturally infected with *Bartonella* spp, all cats remained positive on polymerase chain reaction (PCR) assay on day 35 and 6 cats remained positive on day 58.⁴

Although laboratory treatment studies in dogs have not been published, dogs infected with *Bartonella* spp have failed 3 months of doxycycline (5 mg/kg PO twice a day) administered for the treatment of concurrent ehrlichiosis.⁵

- Doxycycline should *not* be recommended as the sole antibiotic treatment of bartonellosis in cats or dogs.
 - More than 1 antibiotic is often needed for therapeutic elimination (see **Closing Remarks**, page 21).

Minocycline

Cats: 8.8 mg/kg PO once a day for 28-42 days⁶

Dogs: 10 mg/kg PO twice a day for 28-42 days⁷

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Like doxycycline, minocycline is a tetracycline antibiotic that inhibits protein synthesis by binding aminoacyl-tRNA to the 30S ribosomal subunit in the mRNA translation complex. Recently, the increased cost and decreased availability of doxycycline have sparked interest in using minocycline as an alternative antibiotic in both cats and dogs. A recent pharmacokinetic study found that one 50-mg capsule administered orally once a day would be appropriate for most cats.⁶

Based on clinical reports, GI upset can occur in both dogs and cats. No clinical or laboratory-based treatment studies have been performed to assess the efficacy of minocycline treatment of bartonellosis in cats or dogs.

- As with doxycycline, minocycline should *not* be recommended as the sole antibiotic treatment.

Pradofloxacin

Cats: 5-10 mg/kg PO once or twice a day for 28-42 days⁸ (also, author experience)

Dogs (not approved in United States): 5-10 mg/kg PO once or twice a day for 28-42 days (anecdotal)

- Per US labeling,⁹ do not use in dogs. —Throughout Europe and in other countries, pradofloxacin is available for the treatment of bartonellosis in dogs.

Pradofloxacin is a fluoroquinolone antibiotic

that disrupts bacterial replication by inhibiting DNA gyrase, thereby preventing DNA replication, and by blocking topoisomerase IV, which is a bacterial strategy to resist antimicrobials.

In an experimental infection model, pradofloxacin had beneficial anti-*Mycoplasma haemofelis* effects similar to doxycycline and appeared to provide more effective long-term clearance of *M haemofelis* organisms than did doxycycline when administered (5 mg/kg PO twice a day) for 14 days.¹⁰ However, reports of pradofloxacin efficacy for treating *Bartonella* spp infections (or coinfections with hemotropic *Mycoplasma* spp) in naturally or experimentally infected cats have not been published to date.

- Because pradofloxacin achieved better bacterial minimum inhibitory concentrations (MICs) than did enrofloxacin and because there is no evidence of retinal injury in cats receiving pradofloxacin,¹¹ a combination of doxycycline and pradofloxacin has been preferentially used by the author for treatment of feline bartonellosis.
- No experimental data support treatment efficacy of pradofloxacin in dogs.

Enrofloxacin

Cats: 5 or 10 mg/kg PO once a day for 28-42 days¹²

- Due to the refractory nature of treating *Bartonella* spp infections, shorter durations and lower drug doses are not effective.

DNA = deoxyribonucleic acid, GI = gastrointestinal, MIC = minimum inhibitory concentration, mRNA = messenger ribonucleic acid, PCR = polymerase chain reaction, tRNA = transfer ribonucleic acid



A combination of doxycycline and amikacin would be a reasonable initial strategy for treatment of canine or feline endocarditis, with the addition of an oral fluoroquinolone at discharge.

tive for these intracellular bacteria. Thus, enrofloxacin may be used anecdotally at higher doses and for longer durations than labeled.

- Based on clinical evidence, cats are at risk for retinotoxicity at doses >5 mg/kg PO once a day.
 - With the recent availability of pradofloxacin, **enrofloxacin is no longer recommended by the author as sole or combination therapy in cats.**

Dogs: 5-20 mg/kg PO once a day for 28-42 days¹²

- Due to the intracellular nature of *Bartonella* spp infections, it is possible that a longer duration of therapy is more important to achieve a therapeutic cure than use of a high-dose, short-duration therapy.

Like pradofloxacin, enrofloxacin is a fluoroquinolone antibiotic that disrupts bacterial replication by inhibiting DNA gyrase and thereby preventing DNA replication. Treatment with enrofloxacin (5 mg/kg PO twice a day) for 14 or 28 days was well tolerated by cats and was as effective as or more effective than doxycycline.³

Based on in vitro testing using *B henselae* isolates from cats and a human isolate, enrofloxacin achieved better bacterial MICs than did ciprofloxacin.^{13,14}

- Because of variable absorption of ciprofloxacin in dogs and because therapeutic elimination of bartonellosis can be challenging in bacteremic dogs, administration of enrofloxacin (5 mg/kg PO twice a day) in combination with doxycycline (5-10 mg/kg PO twice a day)

has been used by the author for the treatment of dogs with bartonellosis.

Amikacin

Cats: 10-14 mg/kg IV, IM, or SC once a day for 7-10 days⁷

Dogs: 15-30 mg/kg IV, IM, or SC once a day for 7-10 days⁷

Amikacin sulfate is a semisynthetic aminoglycoside antibiotic that binds to the bacterial 30S ribosomal subunit, causing misreading of mRNA and leaving the bacterium unable to synthesize proteins vital for its growth.¹⁶ Because aminoglycosides are dose-dependent nephrotoxins,¹⁵ renal function should be monitored before therapy; during therapy, daily urine sediments should be screened for granular casts indicative of tubular toxicity.

Aminoglycosides are the only known bactericidal antibiotics for treatment of bartonellosis.¹⁶ Their use in human patients with endocarditis has decreased the length of hospitalization stays as well as the need for surgical heart valve replacement.¹⁷ Therefore, using amikacin during hospitalization, and for a longer duration if monitoring is adequate, should be considered during the initial treatment of seriously ill bartonellosis patients, notably those with endocarditis and myocarditis.

- The combination of doxycycline and amikacin would be a reasonable initial antibiotic strategy for treatment of canine or feline endocarditis, with the addition of an oral fluoroquinolone at time of discharge (extrapolated from human data).

Rifampin

Dogs only: 5 mg/kg PO once a day for 6 weeks to 3 months⁷

Rifampin inhibits bacterial DNA-dependent RNA synthesis by inhibiting bacterial DNA-dependent RNA polymerase. For canine patients with central nervous system (CNS) involvement, doxycycline and rifampin in combination have been successfully used anecdotally, but the use of rifampin in cats is not recommended.

Azithromycin (Not Recommended)

Cats, dogs: Do not use for treatment of feline or canine bartonellosis.

Azithromycin is an azalide, a subclass of macrolide antibiotics. Because of the rapid development of resistance, as compared with several other antibiotic classes, azithromycin is not recommended as a first-line antibiotic for bartonellosis. Once resistance develops, *B henselae* isolates are resistant to all macrolides.

If azithromycin is used for treatment of bartonellosis, another antibiotic that maintains high plasma concentrations should be used concurrently. Based on in vitro testing, *B henselae* isolates from cats or humans rapidly developed resistance to azithromycin because of a homogenous single nucleotide substitution in the 23S rRNA gene.¹⁶ As a clinical example, *B henselae* and *B vinsonii* subsp *berkhoffii* were cultured on 3 independent occasions from blood and joint fluid samples, despite administration of nearly 4 months of nonconsecutive antibiotic (azithromycin) therapy in a dog.¹⁸

- Until additional experimental laboratory data are available to support its use, azithromycin is not recommended as a first-choice therapy or monotherapy for cats or dogs with bartonellosis.

Closing Remarks

Before instituting antibiotic therapy, diagnostic confirmation of bartonellosis (eg, bacterial isolation, enrichment blood culture/PCR, PCR from tissue or effusion) is an important clinical consideration for the following reasons.

- Treatment of bartonellosis requires long-duration antibiotic therapy (6 weeks to 3 months).^{19,20}
- More than 1 antibiotic is often needed (expense factor) for therapeutic elimination of the infection.^{19,20}
- Antimicrobial resistance is associated with indiscriminate use of any antibiotic.
- Documentation of *Bartonella* spp infection in a cat or dog has medically important implications for the health of the family.^{19,20}

For diagnostic confirmation and evaluation of therapeutic efficacy, monitoring results of serology (antibody titers tend to drop within weeks to months with effective therapy) and BAPGM enrichment blood cultures (Galaxy Diagnostics) before initiation of antibiotics and at 2 and 6 weeks after completion of antibiotic therapy is recommended.^{21,22}

Currently, no studies have confirmed the therapeutic effectiveness of any antibiotic or antibiotic combination for elimination of bartonellosis in a cat or dog. Because of persisting intracellular and extracellular intravascular and endotheliotropic bacteria within the host, therapeutic elimination of *Bartonella* spp infection has been

Monitoring the results of serology and BAPGM enrichment blood cultures is recommended before antibiotics are initiated and at 2 and 6 weeks after completion of therapy.^{21,22}

BAPGM = *Bartonella* alphaproteobacteria growth medium, CNS = central nervous system, DNA = deoxyribonucleic acid, MIC = minimum inhibitory concentration, mRNA = messenger ribonucleic acid, PCR = polymerase chain reaction, RNA = ribonucleic acid, rRNA = ribosomal ribonucleic acid



challenging, and recurrence after treatment is not uncommon in cats, dogs, or humans.^{21,22}

Bartonellosis can occur in association with immunosuppression or a concurrent disease process, and anecdotal evidence in dogs and humans has suggested that therapeutic immunosuppression (eg, corticosteroids, other immunosuppressive drugs) may facilitate localization of *Bartonella* spp to the heart valves, resulting in endocarditis.²³

For cats and dogs that are reasonably stable (eg, when treating *Bartonella*-linked polyarthritis),²⁴ the author recommends starting 1 antibiotic (eg, doxycycline at 5 mg/kg PO every 12 hours) and then adding the second antibiotic 5 to 7 days later. Initiation of both antibiotics simultaneously has been associated with a Jarisch-Herxheimer-like reaction,²⁵ a common occurrence during initial treatment of this infection. The reaction (eg, lethargy, fever, potential vomiting) tends to occur 4 to 7 days after the start of antibiotic therapy (but can be more delayed in some animals) and is presumably a result of bacterial injury or death and cytokine release by the host, possibly after high intracellular antibiotic concentrations have been achieved. Because the patient's condition can be worse than its condition before antibiotic therapy was initiated, the clinician may suspect an adverse drug reaction and either stop or switch antibiotics. This reaction generally lasts only a few days. In most instances, clinical experience has dictated that antibiotic treatment should be continued and symptomatic and

supportive therapies used as needed. Administration of antiinflammatory glucocorticoids for a few days in conjunction with antibiotics may help cats and dogs through this period. Unless clinical deterioration continues to progress, the author has found it best to continue the antibiotics that were initially started and discontinue glucocorticoids after initial signs of Jarisch-Herxheimer-like reaction have resolved (~72 hours).

Author Insight

Based on evolving medical evidence, the genus *Bartonella* represents an occupational risk for veterinary workers and others with extensive arthropod vector (eg, fleas, ticks, lice) exposures and extensive animal contact.^{26,27} Prevention of *Bartonella* spp infections in pets through year-round administration of acaricide products is of critical importance to prevent disease in cats, dogs, and their owners.²⁸

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