1. In reality (i.e. based upon evidence) we do not know how to treat bartonella infections in cats, dogs or people, so the following suggestions are made based upon a small number of experimental animal treatment studies or clinical experience in treating canine or feline bartonellosis (predominantly mine), with extrapolation from human case-based treatment evidence.

2. Doxycycline alone is not an effective treatment to eliminate infections associated with any *Bartonella* species. Experimental evidence from cats and clinical evidence in treating dogs supports the lack of efficacy for this antibiotic, particularly when given for periods of at least 4 weeks at 5 mg/kg every 12 hours (i.e. the recommended dose and treatment period for canine ehrlichiosis).

3. Because of the rapid development of resistance, when compared to several other antibiotic classes, azithromycin is not recommended as a first line antibiotic. Once resistance develops, *B. henselae* isolates are resistant to all macrolides. If azithromycin is used to treat bartonellosis, another antibiotic that maintains high plasma levels should be used concurrently.

4. Because the treatment needs to be long in duration (6 weeks to 3 months), because more than one antibiotic is needed (expense), and because of antimicrobial resistance concerns associated with the indiscriminate use of antibiotics, diagnostic confirmation of bartonellosis (recommended), or a very high index of suspicion (less than optimal) for this infection, is an important clinical consideration.

5. Aminoglycosides are the only known cidal antibiotics for treatment of bartonellosis. Their use in human endocarditis patients in France has decreased hospitalization times and decreased the need for surgical heart valve replacement. 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 endocarditis and myocarditis patients). Thus, the combination of doxycycline and amikacin would be a reasonable initial antibiotic combination to treat canine or feline endocarditis cases.

6. For elimination of *Bartonella* (like the closely related alpha Proteobacteria *Brucella*), a therapeutic cure is not easily achieved, therefore monitoring serology (antibody titers tend to drop rapidly (weeks to a couple of months) with effective therapy) and BAPGM enrichment blood cultures (Galaxy Diagnostics, www.galaxvdx.com) at 2 and 6 weeks after completion of antibiotic therapy can be used to infer a therapeutic cure. Proving a therapeutic cure is challenging and perhaps impossible.

7. For long term therapy doxycycline and enrofloxacin in dogs and doxycycline and pradofloxacin in cats should be considered, until other antibiotics or antibiotic combinations are proven to be effective. A combination of two antibiotics with different modes of action, one achieving high blood concentrations and the other achieving high intracellular concentrations is seemingly needed to eradicate Bartonella infections. Pradofloxacin has better MICs than enrofloxacin, but pradofloxacin has only been approved for use in cats in the United States. Ciprofloxacin has less favorable MICs compared to enrofloxacin and pradofloxacin, and because of variable (at times poor) intestinal absorption following oral administration, ciprofloxacin is not recommended for treatment of bartonellosis in dogs.
8. For canine cases with CNS involvement doxycycline and rifampin in combination has been used successfully, but the use of rifampin is not recommended in cats.

9. For dogs that are reasonably stable (for example Bartonella polyarthritis) try starting one antibiotic (for example doxycycline at 5 mg/kg every 12 hours) and then add the second antibiotic 5-7 days later. The reason to not start both antibiotics simultaneously is associated with a Jarisch Herxheimer-like reaction, which is a common occurrence in cats and dogs during the initial treatment for this infection. The reaction (lethargy, fever, potentially vomiting) tends to occur 4-7 days after starting antibiotics (but is even more delayed in some animals) and is a result of bacterial injury/death and cytokine release, presumably after achieving high intracellular antibiotic concentrations. Because the patient’s condition can be worse than before starting antibiotics, the clinician often suspects an adverse drug reaction and either stops or switches antibiotics. This reaction (lethargy, fever, vomiting) generally lasts only a couple of days. Giving anti-inflammatory steroids for a few days may help dogs through this period. Unless clinical deterioration continues to progress, it is best to continue the antibiotics that were initially started. The fact that the antibiotics induced a reaction is most likely a reflection of adequate intracellular and intravascular drug concentrations resulting in bacterial death.

10. For cats, a combination of doxycycline (5 mg/kg every 12 hours with water flush after every oral dose) and pradofloxacin (5 mg/kg every 12 hours) is the recommended therapy, until clinical or experimental research treatment trails provide evidence of a more optimal therapy. As above, if the veterinarian and owner elected to treat a *Bartonella* sp. bacteremic cat, it is important to treat for an adequate duration (minimum of 6 weeks) to eliminate the infection and prevent development of resistance. A major concern relative to inadequate treatment durations is the potential for subsequent transmission of a resistant *Bartonella* strain to a family member or veterinary worker, which could have legal implications. Also as above, post-Treatment serology and BAPGM enrichment blood culture/PCR (Galaxy Diagnostics, RTP, NC) should be used to support therapeutic elimination.

Selected References: