

## Testing Cats for Infection with *Bartonella* species

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*Bartonella* species are fastidious gram-negative bacteria that are highly adapted to a mammalian reservoir host, within which these bacteria usually cause a long-lasting intraerythrocytic bacteremia. These two facts are of particular importance to veterinarians, as an increasing number of animal reservoir hosts have been identified for each of the various *Bartonella* species. *Bartonella henselae*, *B. quintana*, *B. koehlerae* and *B. clarridgeiae* have been isolated from the blood of cats and have been detected using molecular methods in cat fleas. Elimination of fleas is critical to prevent infection or re-infection of cats with these bacteria. *Bartonella* infection is a frequent occurrence in feral cat populations, in shelters, among outdoor cats in flea-endemic regions and in open multi-cat households that periodically introduce flea-infested cats or kittens.

The extent to which members of the genus *Bartonella* are pathogenic for cats remains unclear. Depending upon the prevalence of fleas, *B. henselae* bacteremia has been documented by conventional blood culture in 5 to 41% of healthy cats worldwide. Due to the high prevalence of non-clinical infection among various feline populations; it is obvious that cats, fleas and *B. henselae* share a long and highly adapted evolutionary relationship. However, dogs (reservoir host) infected with *B. vinsonii* subsp. *berkhoffii* and cats (reservoir host) infected with *B. henselae* can develop both develop endocarditis with the respective reservoir-adapted *Bartonella* species. In addition, strain variation in pathogenicity among *B. henselae* isolates appears to be responsible for the development of granulomatous and neurological disease in cats. Recently, using the BAPGM platform we isolated *B. vinsonii* subsp. *berkhoffii* genotype II (canine reservoir) from a cat with recurrent digital osteomyelitis. Subsequently, we sequenced the same genotype from a paraffin block containing the original osteomyelitis lesion, surgically excised eighteen months earlier. This case suggests that non-reservoir adapted *Bartonella* sp. can induce a chronic bacteremic disease in cats and that an optimized diagnostic approach (the BAPGM platform) is required to document bacteremia.

### Diagnostic Testing:

When to test and how to test cats for evidence of *Bartonella* infection has been in a state of rapid change over the past few years. I am increasingly of the opinion that BAPGM enrichment blood culture followed by PCR amplification and DNA sequencing should be the test of choice for documenting infection with a *Bartonella* sp. in a cat, dog, horse or human patient. As clinicians, we need to know if a cat is bacteremic, not whether the cat has been exposed to a *Bartonella* sp. at some previous time point. **The expense of antibiotics, the long duration of treatment required to eliminate the infection, the need to use non-first line antibiotics, and the increasing zoonotic concerns surrounding this genus of bacteria justify proving bacteremia or no bacteremia in each and every patient.**

Unfortunately, bacterial isolation, conventional or real time PCR following direct DNA extraction (standard test offered by most commercial diagnostic laboratories) from patient samples, and antibody tests (ELISA, Western blot or IFA) all have diagnostic limitations. Serology can only determine prior exposure to a *Bartonella* species. Therefore, regardless of the serological testing modality selected, detection of antibodies does not confirm active infection and unfortunately the lack of antibodies does not rule out active infection (seronegative bacteremia). In addition, most diagnostic laboratories test against only one *Bartonella* species (*B. henselae*), which may not confirm exposure to other clinically relevant species. Recent evidence suggests that there is minimal to no crossreactivity among various

*Bartonella* sp. that infect cats. As a subset of bacteremic cats do not have detectable *B. henselae* antibodies, a negative antibody test does not consistently rule out active infection.

The diagnosis of *Bartonella* infection can be confirmed by culturing the organism from aseptically-obtained patient samples, including blood, cerebrospinal fluid, lymph node or other tissue aspiration samples, cavitory effusions, joint or ocular exudates or from surgical biopsies. Our research group optimized a novel, chemically modified, insect cell culture-based liquid culture medium (*Bartonella*/alpha-Proteobacteria growth media, BAPGM) that supports the growth of *Bartonella* species. Subsequently, this patented enrichment culture approach (the BAPGM platform) was licensed from North Carolina State University by Galaxy Diagnostics ([www.galaxydx.com](http://www.galaxydx.com)) for animal and human *Bartonella* testing purposes.

Although the BAPGM platform provides the most sensitive modality to document *Bartonella* infection in a patient sample, the highly fastidious nature of these bacteria makes diagnostic detection challenging. Because cats (and likely dogs and human patients) develop a relapsing pattern of bacteremia, all BAPGM platform test results would be negative if the cat was not bacteremic (i.e. the organism was in tissues, not in the blood sample) at the time of sample collection. Therefore, ideally a clinician would want both serological (antibody= exposure) results and BAPGM platform (active infection) results for for each feline patient, particularly when determining if a cat poses a zoonotic risk for family members.

**Because of the emerging zoonotic importance of this genus, it is important to document the presence or absence of infection, therefore antibody tests (ELISA, IFA, Western blot) are no longer recommended as stand alone or sole diagnostic tests.**

#### References:

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