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NEWSLETTER

Commonly Asked *Bartonella* Questions- Revisited©

Evelyn E. Zuckerman, Editor **Fall 2023** **Vol. 22, Number 4**

In This Issue:

The Fall 2023 issue of the NVL Newsletter ends the 22nd year of our Newsletters (88 issues in total). This issue will revisit the Summer 2004 Vol.3, No.3 Newsletter for answers to some of the commonly asked questions concerning *Bartonella*.

Commonly Asked *Bartonella* Questions:

Bartonella Testing:

1. Why do you require the age and diagnosis for all Bartonella tests on the submission form?

Answer: It is very important for us to know the age and diagnosis for all cats and dogs being tested for *Bartonella* because we make specific recommendations regarding therapy or re-testing based on these factors and the test result. For example, kittens under 6 months of age who have a typical *Bartonella* inflammatory disease, but test negative or +1 (uninfected) for *Bartonella*, should be re-tested 2 months later. These kittens may be incubating *Bartonella* infection, which is causing the inflammation, but not enough time has elapsed for the production of detectable antibody. In this regard, 11 of 65 (17%) kittens retested 8 weeks later were positive (infected). This is important for eventual therapy recommendations and for the public health implications.

2. What is the earliest age a kitten should be tested for Bartonella?

Answer: Any age kitten should be tested because kittens are more likely to transmit *Bartonella* to people, especially children, due to their playful nature. Although antibody in kittens may be of maternal origin, we recommend that all Fe*Bart*® test positive (+3 or +4) kittens be considered infected and should be treated.

3. What is the occurrence of "false negative" FeBart® tests?

Answer: About 3% of *Bartonella* infected cats do not produce detectable antibody and thus test negative.[1,2] This is not truly a "false negative" in that the test is not in error. A similar situation occurs in people with *Bartonella*-induced cat scratch disease. Only 80% of people with CSD are antibody positive.

4. In multi cat households, where one cat tests positive for Bartonella, should I just treat the other cats rather than test all of them?

Answer: **No No No No!!!** It is very poor veterinary medicine to indiscriminately treat cats with antibiotics without knowing if they are infected with the organism for which you are treating. The possibility of creating antibiotic resistant strains of bacteria is likely with this approach.

5. There are 6 known Bartonella species in pet cats, what species does the FeBart® test detect?

Answer: The short answer is all of the feline *Bartonella spp*. There are presently 6 recognized *Bartonella* species that infect pet cats. The most common species in cats is *Bartonella henselae*. Unlike other serological tests, the Fe*Bart*® test detects all 6 species and even species from other animals such as dogs, cattle, deer, and humans. Our test is a western immunoblot where we purify our isolate of *Bartonella*, break it up into component proteins which are then separated by gel electrophoresis into individual proteins based on their sizes (molecular weights).[1] The approximate 20 proteins are then transferred to nitrocellulose paper strips and reacted with cat or dog sera. The numerous antibodies found in infected cats, dogs and people react with the bacterial proteins and give a "fingerprint" of the immune reaction. The antibodies are cross-reactive with the various homologous proteins of the different *Bartonella* species (Figures 1 & 2).

Fe*Bart*® Western Blot (WB) Test

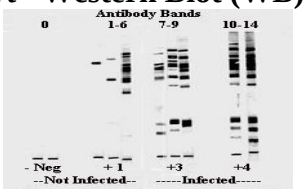


Figure 1. Grading system for the Fe*Bart*® Western Blot Test. – and +1: not infected, and +3 & +4: infected.[3]

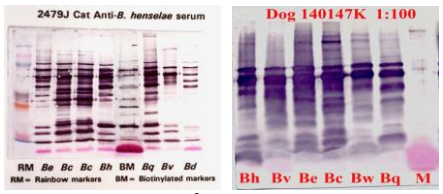


Figure 2 Left. Fe*Bart*® Western Blot test is able to detect all 6 feline *Bartonella* and is able to detect the cross-reacting proteins from other *Bartonella*. This figure shows the detection of proteins from *Be B. elizabethae*, *Bc B. clarridgeiae*, *Bh B. henselae*, *Bq B. quintana*, *Bv B. vinsonii*, and *Bd B. weissi* by an infected cat's serum.
Figure 2 Right. Seropositive dog showing cross-reactivity to 6 *Bartonella* species: *B. henselae*, B. *vinsonii*, *B. elizabethae*, *B. clarridgeiae*, *B. weissi (bovis)*, and *B. quintana* (M= mol. wt. markers).

Bartonella Therapy:

6. Should healthy Bartonella infected cats be treated?

Answer: **YES**. All healthy *Bartonella* infected cats should be treated to prevent disease occurrence in the cat, to prevent transmission to people, and to remove the host reservoir of infection for fleas, ticks and possibly mites.

7. Why do you recommend 21 days of azithromycin therapy when, in humans, azithromycin is usually given for only 5 days?

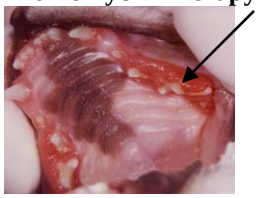
Answer: Azithromycin (Z-Pack) therapy in humans is usually only 5 days for respiratory infections but is given for up to 6 weeks when treating *Bartonella* diseases.[3,4] We, and others have shown that it is necessary to treat infected cats for at least 21 days since *Bartonella*, although not an obligatory intracellular parasite, does live in macrophages, endothelial cells and red blood cells.[5,6,7] Thus, in order to penetrate these cells, it is necessary to treat for a long period as is done for Lyme Disease.

8. How soon should I see clinical improvement after treatment of Bartonella infected cats with inflammatory diseases if Bartonella is the cause of the inflammation?

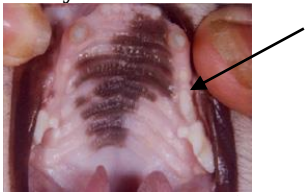
Answer: The time required to see therapy responses can vary depending on the initial duration (chronicity) of the disease (Figure 3).

Figure 3.

Severe Gingivitis in a 6-month-old kitten Before Azithromycin Therapy



After 28 Days- 100% Resolved



Case photographs courtesy of:
Jan Corbishley, B.S.
Oradell Animal Hospital, Paramus, NJ

Most cats that respond start to show improvement after 10 to 14 days of therapy. As seen in these photographs, of a 5-month-old

Bartonella-infected kitten with severe gingivitis, complete resolution occurred after 28 days. As many inflammatory conditions can have multiple co-infectious causes, improvement of 50-80% can occur by elimination of *Bartonella* leaving the remaining factors still active. If no improvement occurs by 21 days, we suggest continuing therapy with the same antibiotic for another 21 days. In some cats the inflammatory condition may not improve at all, which indicates that *Bartonella* is not the cause of the condition.[5,6]

9. How do you explain when a cat with URI or gingivitis has a 100% clinical response, but there is no titer decrease in the comparative titer test?

Answer: Here the cause of the disease was something other than *Bartonella* which was in the cat, but **was not** causing the inflammatory conditions, even though there was elimination of the *Bartonella* infection. The reverse situation can also occur, where there is no clinical improvement in the inflammatory disease but there is a marked titer decrease indicating elimination of the infection. Here the interpretation is that *Bartonella* **is not** the cause of the disease.

10. Should Bartonella infected pregnant cats be treated?

Answer: No studies have been done regarding the effects of azithromycin or rifampin therapy in pregnant cats thus we recommend that infected pregnant cats not be treated until after they have their litters and their kittens are weaned.

Therapy Evaluation:

11. How can we determine if the Bartonella infection has been eliminated after therapy?

Answer: The best way to determine if *Bartonella* has been eliminated after therapy is to do a **comparative therapy titration test**.[5,6] We compare the titer from the first sample, which we have saved frozen, with an after-therapy sample submitted **6 MONTHS AFTER THE END OF THERAPY**. A 4-fold or greater drop in titer indicates elimination of *Bartonella* infection.

12. Why can't we just re-test cats with the FeBart® test after treatment rather than the more expensive comparative titration test?

Answer: In most cats a Fe*Bart*® positive result will not change for years, even after successful therapy, because the Fe*Bart*® screening test is performed at a 1:100 dilution. In contrast, in the comparative titration test, 4 dilutions are performed for the pretreatment sample and 4 for the post treatment sample, in order to determine if there is a titer decrease. Some cat titers are as high as 1:2,048,000 and thus will remain well above the 1:100 screening dilution that is used in the Fe*Bart*® test, long after *Bartonella* has been eliminated. About 88% of treated cats show a decrease titer indicating elimination of *Bartonella* infection.

13. Why do we have to wait 6 months after the end of therapy to do the comparative titration test to determine if therapy is successful?

Answer: It takes 6 months for the antibody titer to decrease 2-to-32-fold after removal of an antigen, in this case *Bartonella*.[5,6] Antigenic stimulation of memory T cells and B cells must be turned off allowing the preformed antibody to be catabolized over a 6-month period. Approximately 20% of treated cats will show sufficient antibody titer decrease by as early as 3 to 4 months. However, for most cats, performing the comparative therapy titration test before 6 months after the end of therapy will not accurately detect a sufficient decrease in titer.

14. Why do you need to know the percent improvement after therapy on the test submission form when we request the comparative therapy titration test?

Answer: A titer decrease is reported in a range of 0 to 64-fold decrease with most being a 4-fold decrease. For cats that have no titer decrease, or a minimal 2-fold decrease, we recommend retreatment with a different *Bartonella*-sensitive antibiotic **(not the original antibiotic again)** such as rifampin, doxycycline, azithromycin, or Veraflox for 21 to 42 days. After unsuccessful *Bartonella* therapy, using a different antibiotic should lessen the chance of developing antibiotic resistant strains of *Bartonella*. Another therapy titration test should be performed 6 months after the completion of this second therapy. We need to know the % clinical response of the inflammatory disease so we can interpret the *Bartonella* etiology of the disease for you.

Bartonella Biology:

15. Are dogs susceptible to Bartonella infection and what are the diseases caused by Bartonella in dogs?

Answer: Yes. Dogs can be carriers of 5 species of *Bartonella* and they develop very similar inflammatory diseases (except oral inflammatory diseases) that have been described in cats and humans. However, the incidence of infection is lower in dogs than in cats and tends to be highest in areas where ticks are common. In this regard, a study found 34% of ticks in New Jersey were carriers of *Bartonella*.[9] We have found *Bartonella* infected dogs with the following conditions: lymphadenopathy, chronic fevers of unknown origin, uveitis, polyarthritis, heart disease, liver disease, and skin granulomas.

16. How are Bartonella transmitted; can they be transmitted directly from cat to cat?

Answer: *Bartonella* are mainly transmitted among most animals by arthropod vectors. Fleas and ticks are major vectors for transmission among cats and dogs.[10] Ear mites may be able to transmit *Bartonella* among cats but direct proof of this has not yet been obtained. Sand flies and lice transmit human *Bartonella* among certain populations of people, inner city homeless (lice) and people living in the Andes Mountains (Sand flies). Direct, non-vector, transmission of feline and canine *Bartonella* occurs via scratches, bites and contact with fur, to people. Fleas and ticks may also transmit *Bartonella* from cats and dogs to people. Direct cat to cat (non-vector) transmission probably does occur rarely by bites and scratches. It probably occurs as often as does cat to human transmission.

17. Are there any adverse effects of Bartonella infection in pregnant women?

Answer: We have often been asked if *Bartonella* can cause medical problems in pregnant women. A literature search has not revealed any publications concerning *Bartonella* infection during pregnancy. However, experimental *Bartonella* infection in cats does cause reproductive problems.[11] Thus, it is advisable for pregnant owners of *Bartonella* infected cats to avoid contact until the cat has been treated by someone else.

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More than 6,000 *Bartonella* references can be obtained at: www.ncbi.nlm.nih.gov/pubmed and www.natvetlab.com