

# NATIONAL VETERINARY LABORATORY

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## NEWSLETTER

### *Bartonella* in Kittens and *Bartonella* Therapy Evaluation<sup>©</sup>

Evelyn E. Zuckerman, Editor

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#### In This Issue:

In the winter 2003 issue of the NVL Newsletter we will explain the biology and public health risks of *Bartonella* infection in kittens. In addition, therapy recommendations and evaluation for *Bartonella* infection and *Bartonella*-induced diseases will also be discussed.

#### **Bartonella** in Kittens

Kittens are special additions to a household and usually become a child's best friend within minutes of arrival. Therein lies the possible danger!

#### Background:

Pet cats can be infected with at least 6 species of *Bartonella* and any age cat is susceptible to infection. However, the medical literature shows that many severe cases of cat scratch disease in humans, especially in children, are associated with transmission from kittens.<sup>1, 2, 3</sup>

#### Pathogenesis of *Bartonella* Infection:

Cat and dog fleas and ticks all can carry and transmit *Bartonella* from cat to cat and probably from cat to dogs and cat to humans. However, it seems possible, although not proven, that direct cat-to-cat transmission via scratches and bites, can transmit *Bartonella* from cat to cat as often as direct cat to human transmission occurs.

Once the organisms are introduced into cats or kittens they multiply rapidly and become disseminated throughout the body. This dissemination is aided by the presence of pili, hair-like structures on the outer membrane of the bacteria, which cause them to clump together in a sticky mass and to attach themselves to erythrocytes. Erythrocytes with adherent *Bartonella* are then circulated throughout the body. The pili, along with a protein called deformin, allow *Bartonella* to stick to erythrocytes and endothelial cells in capillary rich tissues such as the oral cavity, the respiratory tract, the eyes, and the gastrointestinal tract and thereby establish foci of infection in these tissues.

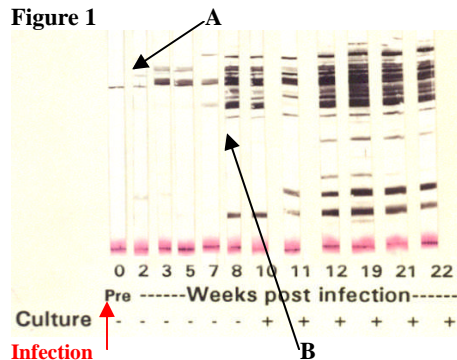
#### Detection of Early Infection:

Few studies have been performed where the timing of infection and the ability to detect that infection have been correlated. Isolation of the bacteria from the blood of experimentally infected cats is a poor method of detection since the ability to culture this organism from known infected cats or people is poor. *Bartonella* can be cultured from the blood of infected cats only about 55% of the time.

The best way to study early infection in cats is to follow the development of antibody against *Bartonella*. We inoculated a small amount of infected blood into an adult cat and followed the development of antibodies against the bacteria and the ability to isolate the bacteria from the blood (Figure 1).

#### Antibody Development After Infection

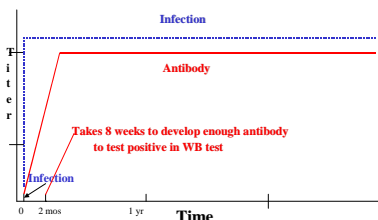
Figure 1



As can be seen in Figure 1, it takes about 3 weeks after infection for antibody to begin to form (arrow A) and 8 weeks before there is enough antibody to consider this cat serologically positive (arrow B). Bacteria were first isolated from the blood at week 10.

Figure 2

#### *Bartonella* Infection Coexists with Antibody



The kinetics of antibody formation is important for our understanding of the infection of kittens, under 6 months of age, and the ability to detect infection by serological tests.

#### Kittens and *Bartonella*:

Kittens quickly become welcome members of many households each year and become the special friends of the children in those households. Children often allow kittens to lick their faces, to eat from their plates and to sleep in their beds. They also play more vigorously with the kittens than do the adults in the households thereby receiving playful bites and scratches more frequently than the adults. Boys, more often than girls, play more roughly with their newfound friends and thus develop cat scratch disease more often than girls.<sup>1, 2</sup>

Kittens can become infected with *Bartonella* from arthropod vectors (fleas & ticks) and possibly from direct contact from adult cats, from their queens by grooming and parental care or via an infected queen's milk. Transmission by direct contact to cats or kittens has not been demonstrated and is only presented here as speculation.

#### Why Are Kittens More Likely to Transmit *Bartonella* to Humans?

*Bartonella* organisms are found in the blood plasma, inside erythrocytes and endothelial cells and in tissues of infected cats. In order to be transmitted to people, the organism must be present on the claws (scratch), in the mouth (bites) or on the fur (contact- no abrasion) of infected cats. Infected kittens are rapidly growing and have changing dentition leading to the probability that *Bartonella* can leak into the oral cavity. The loss of kitten teeth or oral trauma due to rough play, chewing and playful fighting, can lead to *Bartonella* in the oral cavity. Cats groom themselves frequently thereby depositing *Bartonella* organisms from the oral cavity onto their fur or claws. The fact that kittens and children are both more playful toward each other presents the conditions needed for the zoonotic transmission from kittens to children. Boys tend to play more roughly with kittens than do girls which is reflected in the higher incidence of cat scratch disease in boys.

# Bartonella Therapy

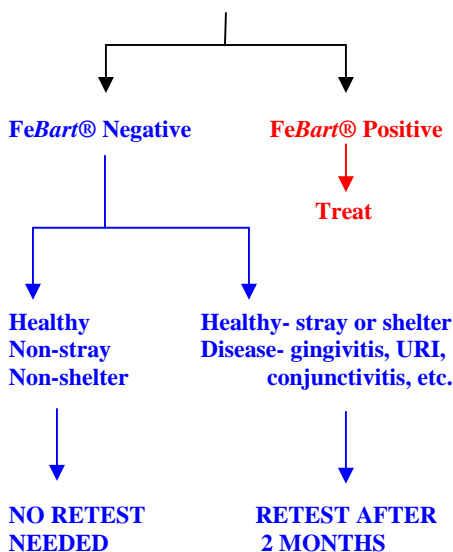
## Bartonella Tests for Kittens:

All newly introduced kittens, at any age, should be screened for *Bartonella* infection at their first examination. Since the FeBart® test (western blot) is a test for antibody against various *Bartonella* proteins, a positive test in a kitten may represent maternal antibody or kitten antibody. The western blot technique is so sensitive that it can detect maternal antibody up to 7-8 months in many kittens. Irrespective of the source of antibody, all FeBart® test positive kittens should be considered infected and treated for their infection. Some kittens with maternal antibody will be treated needlessly, however truly infected kittens are too dangerous to allow to go untreated.

FeBart® test negative kittens, 6 months or younger, present a different problem for the practitioner. The negative test is most likely (95% or greater) to represent a truly uninfected kitten. However, we have tested several kittens, under 6 months of age with *Bartonella*-like diseases (gingivitis, URI, conjunctivitis, etc.), from stray or shelter backgrounds, who when retested 8 weeks later, were found to be FeBart® test positives. The first test was apparently taken, during the 8-week period, between infection and the kitten's production of antibody. *Bartonella* appear to be able to infect young kittens and induce an inflammatory disease before the development of detectable antibody. We have developed a *Bartonella* test algorithm for kittens under 6 months of age, and recommend retesting healthy negative kittens if they were obtained as strays or from shelters and all kittens, with *Bartonella*-like diseases coming from the same environments.

## Bartonella Test Algorithm for Kittens

### Test Any Age Kitten



### Summary:

*Bartonella* cause more diseases in pet cats than do FeLV and FIV and, unlike the viruses, are a known significant public health risk.

**We recommend *Bartonella* tests for all cats, especially kittens.**

## RECOMMENDATIONS:

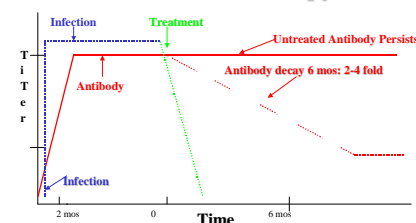
Approximately 80% of healthy *Bartonella*-infected cats clear their infections with 10 days of azithromycin therapy (10mg/kg once daily). In addition, approximately the same percentage of *Bartonella*-infected cats with a *Bartonella* disease show clinical improvement of 50% or greater with the same therapy. However, in order to improve the percentage of anti-bacterial and disease therapy responses, we are revising our therapy recommendation for infected cats.<sup>4</sup> We recommend 21 days of azithromycin or rifampin therapy at the same dose (see NVL Newsletter volume 1, number 1, winter, 2002).

## Evaluation of Therapy- Therapy Titration:

There continues to be much confusion concerning the evaluation of effective *Bartonella*-infection therapy. The most practical method to determine if the therapy for *Bartonella* infection has been successful is to monitor the antibody levels. A 2 to 4 fold or greater decrease in the antibody titer indicates successful bacterial therapy. As with any antigen, initial stimulation leads to rising antibody titers whereas, removal of the antigen (bacteria), leads to eventual decrease in antibody titer.

Figure 3

### Antibody Decay After Bartonella Therapy

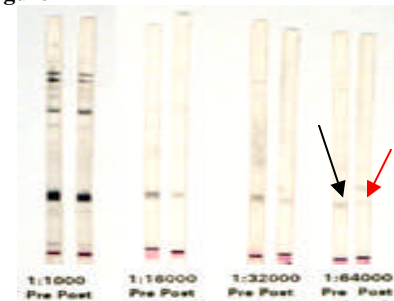


As seen in Figure 2, *Bartonella* infection leads to the production of detectable antibody, at high titers, by 8 weeks- rising titer. We found no decrease titers in 19 of 19 untreated *Bartonella*-infected cats (Figures 3 & 4). Conversely, removal of *Bartonella* by antibiotic therapy leads to the SLOW decrease in antibody titer as shown in Figures 3 & 5. It requires 6 MONTHS for the titer to decrease (antibody catabolism) 2 to 4 fold after clearance of *Bartonella*. When antibiotic therapy fails there is no decrease in antibody titer and there may even be an increase in titer (Figure 6).

The screening test for infection, the FeBart® test, is too sensitive to use for detection of decreased titers since it is performed at a single dilution of 1:100. Many infected cats have titers of 1:256,000 or greater. Therefore, the therapy titration test is required for determination of successful *Bartonella* therapy. This test consists of a total of 8 western blots, 4 blots for the pre-therapy sample (which we store in our freezers) and 4 blots for the post-therapy sample. Serial dilutions are tested for each sample to obtain end point titers for before and after therapy. A 2 to 4 fold or greater decrease indicates

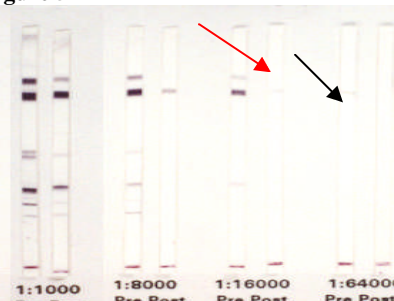
successful removal of the bacteria. **PLEASE DO NOT REQUEST THE SCREENING FEBART® TEST FOR THERAPY EVALUATION.**

Figure 4



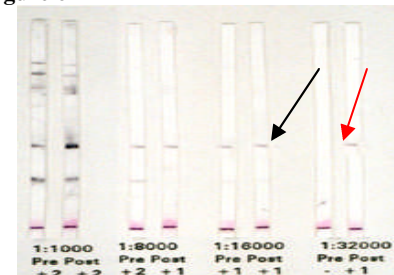
**No Therapy:** There is no decrease in titer after 3 years in this untreated *Bartonella*-infected cat.

Figure 5



**Successful Therapy:** *Bartonella*-infected cat treated with azithromycin- 10 mg/kg once daily for 21 days. There is a 4-fold decrease in titer which indicates effective *Bartonella* therapy. Pre-therapy titer is 1:64,000 (black arrow) whereas the post-therapy titer is 1:16,000 (red arrow).

Figure 6



**Therapy Failure:** Azithromycin failed to decrease the titer, in fact there was a 2-fold increase in the titer. Pre-therapy titer is 1:16,000 (black arrow) while the post-therapy titer is 1:32,000 (red arrow). *Bartonella* was isolated from the blood before and after therapy.

## References:

1. Kaplan, S., et al.: Morbidity and Mortality Weekly Report: March 15, 2002, Vol. 51/ No. 10.
2. E Eskow, et al.: Archives of Neurology 58: 1357-1363, 2001.
3. F Massei, et al. European Journal of Pediatrics 159: 416-419, 2000.
4. Hardy, WD, Jr., Zuckerman, EE, Corbishley, J, Gold, JWM<sup>2</sup>, Baron, P, Polsky, B, Gilhuley, K, Kiehn, TE, and Armstrong, DA. Efficacy of high dose, long duration Doxycycline or Azithromycin treatment for *Bartonella* infections in pet cats. International Conference of the American Society for Rickettsiology, Big Sky, Montana, August 17-22, 2001.

*Bartonella* references can be obtained at:  
[www.nlm.nih.gov/](http://www.nlm.nih.gov/)