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NEWSLETTER

Bartonella: Quick Reference Sheet©

Evelyn E. Zuckerman, Editor **Spring 2005** **Vol. 4, Number 2**

In This Issue:

In the Spring 2005 issue of the NVL Newsletter we will give a complete summary (Quick Reference Sheet) of *Bartonella* infections in cats and dogs.

Bartonella Quick Reference Sheet

Background:

Bartonella are bacteria that cause chronic inflammatory diseases in any tissue in cats, dogs and humans. Cats and dogs act as reservoir hosts for many *Bartonella* species and the bacteria are found in the plasma, tissues, in erythrocytes, macrophages and importantly in endothelial cells. Cats can be bacteremic for years, or even for life, and thus serve as reservoirs for human infection.

Transmission:

Bartonella are transmitted mainly by arthropod vectors, fleas and ticks, in cats and dogs.

Although not proven, it seems likely that they may also **very rarely** be transmitted directly among cats by scratches and bites, as occurs in the zoonotic transmission from cats to humans. For the most part, direct transmission cat to cat does not occur and infected cats may be kept with uninfected cats while being treated.

Diseases:

Bartonella cause inflammatory diseases in any tissue because of their strong tendency to adhere to and penetrate endothelial cells, the components of capillaries. They induce inflammatory cytokines in those tissues and a chronic inflammation ensues. What makes some tissues, like the gingival and respiratory tissues and eye, more susceptible is unknown.

Most Accurate *Bartonella* Test:

After 5 years of research comparing culture isolation with serology, our data showed that the most accurate and reproducible test for detection of *Bartonella* infection in cats is the serologic detection of antibodies to the bacteria using the western blot (WB). Multiple studies have shown that the WB is the most accurate and sensitive serologic assay for many microorganisms. It is used in human medicine to confirm ELISA positive HIV screening tests, Lyme positive serology and several others. In veterinary medicine it is also used to confirm FIV ELISA positive serology.

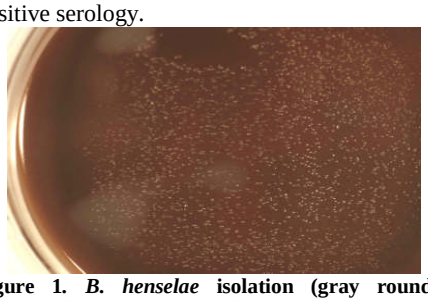

Figure 1. *B. henselae* isolation (gray rounded colonies) from the blood of a 6-month-old kitten. >1,000 *Bartonella*/ml was isolated after 35 days in blood agar culture. Isolation is not a very sensitive assay for detection of *Bartonella* infections.

Comparative tests of serology and PCR for *Bartonella* detection in cats have not been performed but in humans with cat scratch disease, only 64% are PCR positive whereas 84% are serologically (antibody) positive. Detection of antibodies is an amplification system when antibodies coexist with etiological agents as they do in FIV and *Bartonella* infections in cats.

Fe*Bart*® Western Blot (WB) Test

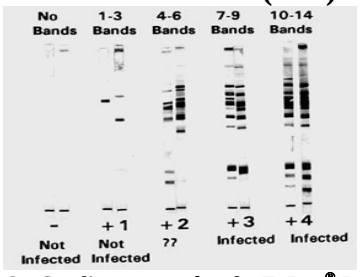

Figure 2. Grading system for the Fe*Bart*® Western Blot (WB) Test. – and +1 not infected, +2 30% of cats infected, +3 & +4 infected.

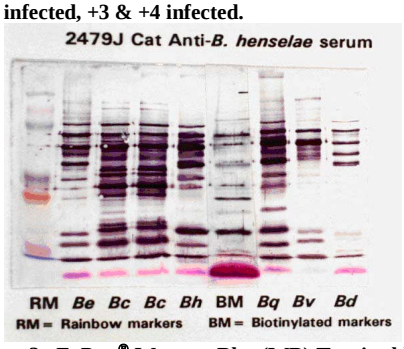

Figure 3. Fe*Bart*® Western Blot (WB) Test is able to detect all 6 feline *Bartonella* and is able to detect the cross-reacting proteins from other *Bartonella*. This figure shows the detection of proteins from *Be B. elizabethae*, *Bc B. clarridgeiae*, *Bh B. henselae*, *Bq B. quintana*, *Bv B. vinsonii*, and *Bd B. weissii* by an infected cat's serum. Thus, our WB test can detect any *Bartonella* that infects cats or dogs which is not always the case for the IFA or ELISA *Bartonella* tests (see below).

IFA *Bartonella* Test

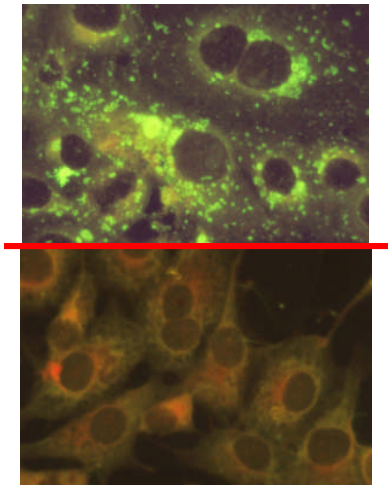

Figure 4. The IFA *Bartonella* test developed in our laboratory was not as accurate or as reproducible as our western blot test for detecting *Bartonella* infected cats. *Bartonella* were grown in feline cells in cell culture and used as targets for the detection of antibody in cat sera. Top panel: antibody-positive test showing apple green fluorescence of *Bartonella* in infected cells. Bottom panel: antibody-negative test.

PCR *Bartonella* Test

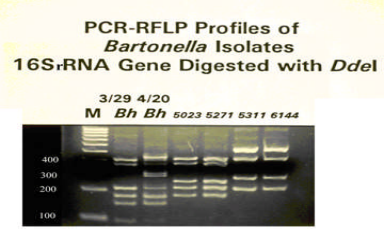

Figure 5. PCR test developed with our collaborators to compare our different *Bartonella* isolates. Only 64% of people with cat scratch disease are PCR positive whereas 84% are antibody positive.

ELISA *Bartonella* Test

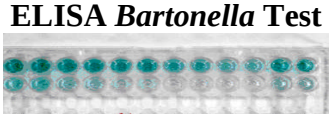

Figure 6. *Bartonella* ELISA test developed in our laboratory was the least accurate and reproducible of all the serological assays.

Public Health:

Bartonella originating from cats can infect people and cause at least 24 chronic inflammatory diseases and may even rarely cause fatalities. Contrary to some publications, **MORE IMMUNOCOMPETENT PEOPLE ARE INFECTED BY CAT *BARTONELLA* THAN IMMUNOSUPPRESSED PEOPLE.** However, immunosuppressed people are more likely to have severe consequences and more likely to die from their *Bartonella* infection.

Treatment:

Bartonella are susceptible to several antibiotics. Azithromycin has been shown to be the most effective antibiotic for *Bartonella* infections in humans and cats. It should be noted that high dose long-term therapy is required since many, though not all, *Bartonella* live intracellularly in erythrocytes, macrophages and endothelial cells.

Antibiotics of choice are:

Azithromycin: 10 mg/kg SID for 21 or more days
Rifampin*: 10 mg/kg SID for 21 or more days
Doxycycline: 10 mg/kg BID for 6 weeks (careful of esophageal strictures)
Only infected cats, WB +3 or +4, should be treated.

*** Rifampin can be used as a single drug. However, we have had numerous reports of allergic reactions in cats treated with rifampin. Reactions consist of reddened and itchy ears, face, nose, and paws, swelling of the face and paws, abdominal pain and general unease.**

DO NOT TREAT UNTESTED CATS OR CATS THAT ARE WB +1 OR -NEGATIVE WITH AZITHROMYCIN. Azithromycin is an excellent human antibiotic and we must use it specifically and judiciously in veterinary medicine.

Therapy Evaluation:

The Comparative Titration Test is the **ONLY** way to determine if therapy has eliminated *Bartonella* infection. The regular screening WB will remain positive for years, even after elimination of infection, because it is performed at a 1:100 serum dilution and infected cats can have very high antibody titers, some 1:2,048,000. The titration test compares the titer of antibody in the original sample (saved in our freezer) with the post-therapy sample taken:

6 MONTHS OR LONGER AFTER THE END OF THERAPY.

The titration test is more expensive because, unlike the screening single WB Fe*Bart*® test, we must use 8 WB strips, 4 for the original sample and 4 for the 6-month post therapy sample, to determine the comparative endpoints (Figures 7, 8 & 9). If the titer decreases 4 fold or greater the therapy has been successful in eliminating *Bartonella*. There is no reason to re-titer a cat that has already had a 4 fold or greater decrease titration test result. We cannot accurately test to determine if a cat has been re-infected.

Therapy Titration Tests

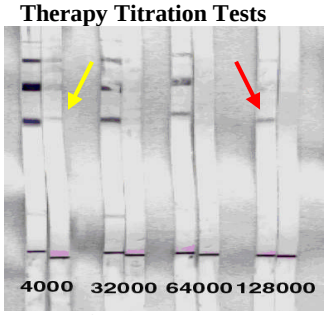

Figure 7. A 32 fold antibody titer decrease after azithromycin therapy. Pre-therapy titer 1:128,000 (red arrow) and post therapy titer 1:4,000 (yellow arrow). This indicates successful removal of the *Bartonella* infection.

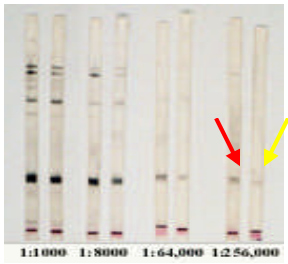

Figure 8. No antibody titer decrease after azithromycin therapy. Pre-therapy titer 1:256,000 (red arrow) and post therapy titer 1:256,000 (yellow arrow). This indicates unsuccessful removal of the *Bartonella* infection and this cat should be retreated with rifampin.

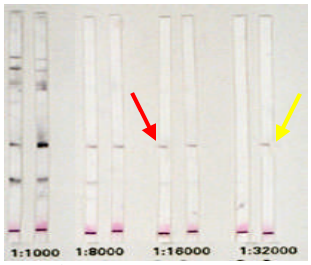

Figure 9. A 2 fold antibody titer INCREASE after azithromycin therapy. Pre-therapy titer 1:16,000 (red arrow) and post therapy titer 1:32,000 (yellow arrow). This indicates unsuccessful removal of the *Bartonella* infection and this cat should be retreated with rifampin.

Therapy Results:

We have evaluated 1,996 therapy titration tests as of August 2004 (Figures 10). Compared to the 20 cats who were not treated and had no titer decrease, 84% of treated cats had titer decreases of 2 fold or greater (Figures 10 & 11). These data show that appropriate antibiotic therapy can eliminate *Bartonella* infections in cats.

Figure 10

Therapy Titer Evaluation: *Bartonella*-Infected Cats

Titers:	#	Increase 2x or > WB Titer	No Decrease WB Titer	Decrease WB Titer: 2 Fold	4 Fold >
No Therapy	20	6	14	0	0
%	100%	30%	70%	0%	
Therapy	1,996	44	271	379	1,302
%	100%	2%	14%	19%	65%
			16%	84%	

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Antibiotic Comparison: 1,996 Therapy Titer Evaluations

Antibiotic	↑	No ↓	2 F	4 F	8 F	16 F	32 F	64 F	128 F
Azithromycin n 1,849	39 16%	258	356	790	314	67	18	4	3
Rifampin n 126	4 13%	12	20	46	39	4	1	0	0
Doxycycline n 21	1	1	3	8	5	3	0	0	0
Totals: 1,996	44	271	379	844	358	74	19	4	3
%	2	16% 14	19	42	18	3.7	1	0.2	0.1

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Figure 11. Titer reduction comparisons of azithromycin, rifampin and doxycycline therapy for *Bartonella* infection. All 3 antibiotics are effective, but azithromycin appears to be the most practical and has the least adverse side effects.

Laboratory Test Submission Forms: Data Requested

We have always requested that ALL clinical information be filled in on our laboratory Test Submission Forms and will ask that any missing information be faxed back to us. Why are we so OBSESSED with obtaining all the required information on our Test Submission Forms? The reasons are given below:

Age & Diagnosis: Both MUST be indicated in order to permit us to give you a proper interpretation of our test result. This is important both **MEDICALLY** and **LEGALLY**. For example, we recommend a re-test of any kitten less than 6 months old with an inflammatory disease who tests +1 or negative. Why? Because 17% of such kittens are infected and *Bartonella* is inflaming the tissues before enough antibody has been produced for us to detect. Yes, 17% retest positive (infected) 8 weeks later and thus are a **ZOONOTIC RISK TO THEIR OWNERS. These infected kittens may be missed if the age and diagnosis information is not indicated on the test submission form. If the cat's age is unknown, please estimate relative to younger or older than 6 months.**

Therapy Data: We **INSIST** that all therapy outcome data be recorded on the bottom of our Test Submission Form (Did the cat improve with therapy? What percent improvement occurred?). We need this information to interpret our titration data and give you the PROPER recommendation for re-treatment when it is indicated.

LEGAL LIABILITY: There have been, and will be, legal instances concerning a veterinarian's responsibility in *Bartonella* testing and recommendations to cat owners, especially owners of kittens in households with children. With complete information given by you on the Test Submission Form, and with correct recommendations based on our test results, we can give appropriate public health recommendations and be legally without fault. We insist on this for your and our protection.

***BARTONELLA* ARE SIGNIFICANT PUBLIC HEALTH RISKS TO VETERINARIANS, THEIR STAFF, AND CAT OWNERS**.