



NATIONAL VETERINARY LABORATORY

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NEWSLETTER

Feline *Bartonella* Test Results and More Public Health Implications

Evelyn E. Zuckerman, Editor

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In This Issue:

In the winter 2004 issue of the NVL Newsletter we will summarize our *Bartonella* test results to date and give several more examples of public health risks to cat owners and veterinarians. A Gallup survey shows that most pet cats in the United States are adopted strays, a risk factor that doubles the likelihood for *Bartonella* infection. *Bartonella* testing of all cats is becoming routine in many practices.

Bartonella Test Results

We have performed 35,684 FeBart® *Bartonella* tests between November 1999 and December 31, 2003. The following tables summarize our findings. *Bartonella* infection is widespread in pet cats.

Bartonella Pathogenesis

Bartonella have a strong tendency to adhere to endothelial cells which leads to the wide and varied tissue pathogenesis observed in cats, dogs, and people.

FeBart® Test:

During our 5-year development of an accurate serological test for *Bartonella* infection we compared IFA, ELISA and western blot (WB) tests and found the WB to be the most accurate. The data in the following tables are from the FeBart® WB test. To date we have tested 35,684 cats, 333 dogs, 5 horses, 5 cougars, 2 lions and 1 serval. Forty-five percent of the cats tested were positive, the majority of which were cats that had chronic inflammatory diseases. The percent of cats infected with *Bartonella* appears to be constant with the increased numbers tested (Table 1). The occurrence of *Bartonella* in dogs will be the subject of a future Newsletter.

Table 1 FeBart® Tests of Cats to 12-31-2003

Cats	# Tested	# Infected	% Infected
Healthy*	9,704	3,714	38%
Disease	25,980	12,255	47%
Totals:	35,684	15,969	45%

* Many with infection risk factors

Approximately 50% of cats with inflammatory diseases in various organ systems test positive and are infected with *Bartonella* (Table 1). A positive test may indicate: 1) that *Bartonella* is the sole etiological agent for the disease, 2) that

Bartonella is a co-etiological agent for the disease, 3) that *Bartonella* is not causing the disease but is infecting the cat. In the following table, the infection rate in cats with inflammatory diseases is compared to the base-line infection rate in healthy cats with no reported *Bartonella* infection risk factors (X).

Table 2 *Bartonella*-Infection: Cats* with Inflammatory Diseases

Diseases	No. Tested	No. Infected	% Infected	Difference / X
Healthy: No Risk Factors	840	170	20%	X
Oral Disease	19,823	9,932	50%	2.5X
Resp. Diseases	4,933	2,471	50%	2.5X
Ocular Diseases	3,767	1,820	48%	2.4X
GI Diseases	1,522	747	49%	2.5X
Skin Diseases	399	211	53%	2.7X
Other Bart. Diseases	2,534	1,216	48%	2.4X
Total	32,978	16,397	50%	2.5X

* Many cats had multiple inflammatory diseases, thus totals in Table 2 exceed the total number of cats tested.

Human *Bartonella* Diseases

We have investigated numerous additional cases of feline *Bartonella*-induced human diseases during the past 6 months. The following are descriptions of the cases and the associated cats.

Case 1: Veterinarian: Cat Scratch Disease

A 34-year-old female veterinarian practicing in the New York City metropolitan area was diagnosed with Lyme disease 13 years earlier. In March of 2003 she began to have severe headaches, fevers, enlarged lymph nodes and a stiff neck. She consulted a local physician who treated her with antibiotics which did not alleviate her symptoms. After again seeing her physician she was told to "get married and go on a vacation." With that recommendation in mind she consulted an infectious disease specialist at a major medical center who was suspicious of *Bartonella* infection and cat scratch disease, even though there was no history of a cat scratch or bite. Her *Bartonella* antibody test was positive for *Bartonella quintana*. *Bartonella quintana* has not yet been isolated from cats but is likely to be an additional *Bartonella species* capable of infecting pet cats. She was treated with azithromycin for 3 weeks and her

symptoms promptly resolved within the first 2 weeks of therapy. We tested her serum by WB and found her to be more reactive to *Bartonella henselae* than to *Bartonella quintana*. The doctor remains healthy, happy and single!

Case 2: Chorioretinitis

A 56-year-old grandmother living in Texas adopted a stray kitten 2 years after completing chemotherapy for breast cancer. Several weeks later she, and her grandchildren, developed a flu-like illness with fever, chills and aches. The children rapidly improved but the grandmother developed tender lymph nodes under both sides of her jaw and a persistent fever of 103-104°F. She was treated with azithromycin for 3 days but did not improve. Two weeks later a "fog" developed in her left eye that progressed into very blurred vision. An infectious disease specialist then submitted serology for *Bartonella* that was highly positive (1:1024). She was again treated, not with azithromycin, but her vision did not improve. Two weeks later she developed muscle and joint pain but was still not treated specifically for *Bartonella*. After her kitten tested +4 strongly *Bartonella* positive and after consulting her veterinarian, Dr. Stanley Zbylot, Spring Creek Animal Hospital, Tomball, Texas, the woman returned to her physician, with our *Bartonella* brochure in hand, and strongly requested azithromycin treatment for 21 days. Her physician agreed and the clinical improvement was rapid and dramatic, her muscle and joint pain resolved and her blurred vision improved by about 70%. However, there appears to be some permanent loss of vision due to retinal scarring.

Her ophthalmologist advised her "to get rid of the kitten." We reassured her that this was not necessary and the kitten has been treated with azithromycin for 21 days.

This case illustrates that some people may be more susceptible to *Bartonella* infection due to the immunosuppressive effects of chemotherapy. It is important for veterinarians to inform cat owners about *Bartonella*, especially people adopting stray kittens, and any member of the household who is immunosuppressed due to chemotherapy, an organ transplant or HIV infection. It also illustrates the need for a prompt diagnosis and appropriate effective long-term specific antibiotic therapy for *Bartonella* in order to avoid retinal scarring. Eye disease is common

in people infected with *Bartonella* and there are numerous publications concerning *Bartonella*-induced eye diseases in humans (see references in our laboratory notes)¹⁻⁴. Table 3 summarizes our *Bartonella* test results for cats being tested due to public health concerns.

Table 3
Public Health Reasons for Testing
Cats for *Bartonella*

Concern	No. Tested	No. Infected	% Infected
Cat Scratch Disease- house	337	215	64%
Immunosuppressed person	35	12	34%
Organ transplant	38	15	40%
Chemotherapy	27	10	37%
HIV infection	6	4	67%
Children in house	77	30	39%
Cat going to nursing home	16	7	44%
Totals:	536	293	55%

Case 3: Meningoencephalitis & Chorioretinitis

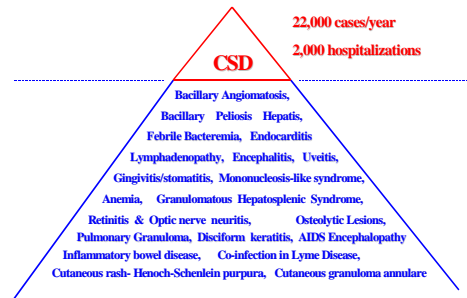
The Pennsylvania family of a 42 year-old woman with a 2.5 year-old cat adopted a 4-week-old stray barn kitten with fleas. The kitten was treated for the flea infestation and was otherwise healthy. Six months later the kitten jumped off the woman's lap leaving a slight scratch on the left knee with a hind claw. Two weeks later a red papule developed at the site followed a week later by lymphadenopathy of the left inguinal lymph nodes, a persistent fever of 101.5°F, and headaches. The woman's mother, a retired nurse living in Florida, diagnosed the condition by telephone as cat scratch disease (CSD). Her physician apparently did not include CSD in his differential diagnosis and gave her a short course of antibiotics (not azithromycin or doxycycline) with no improvement.

A week later she was seen at her local hospital where a clinical diagnosis of CSD was made and she was treated with azithromycin for 5 days (Editorial Comment: not long enough). Shortly after completing treatment the woman had grand mal seizures and was flown to a regional referral hospital where a brain MRI was within normal limits. A PCR on the CSF was negative for *Bartonella*, but her serology for *Bartonella* was positive. She lapsed into a coma for 3 days, was placed on a respirator, and was given intravenous azithromycin, doxycycline and rifampin combination for 5 days (rifampin and doxycycline pass through the blood brain barrier). She recovered rapidly and fully and walked out of the hospital on the 6th day. She was treated with oral azithromycin for an additional 21 days and remains healthy.

This case illustrates the lack of awareness among some physicians of the diverse nature of the clinical signs of *Bartonella* infection in their patients and the rapid response to the appropriate antibiotic therapy¹⁻⁴. The clinical syndrome of CSD is only the "tip of the iceberg" of *Bartonella* diseases (Figure 1). The kitten and the adult cat in this household were both +4 strongly *Bartonella* positive. We thank Antech Diagnostics for assisting us in contacting the referring veterinarian in this case.

Figure 1

Cat Scratch Disease: The Tip of the *Bartonella* Iceberg



Case 4: Veterinary Office- Group-Test

Four members of a veterinary office in the New York Metropolitan area asked to be tested for *Bartonella* for research purposes. The 2 veterinarians were healthy, an office manager reported periodic fevers of unknown origin, and a veterinary technician complained of persistent low-grade fevers and a chronic condition. We found 1 of the healthy veterinarians and the veterinary technician to be serologically positive. Although healthy, the veterinarian was one of the strongest human WB reactors that we have detected. He remains healthy, without treatment, 6 months after the test. The veterinary technician was negative by a licensed human *Bartonella* test. A recent study from Japan found that approximately 4% of veterinary technicians, working 5 years or longer, had acquired cat scratch disease.⁵

Case 5: Mononucleosis-like Syndrome⁶

An 18 year-old girl living in Florida was scratched by a neighbor's 8-week-old stray kitten. Seven weeks later she developed a mononucleosis-like syndrome, fever, and fatigue, followed by loss of vision in one eye.⁶ Optic neuritis was diagnosed and a serological test for *Bartonella* was recommended by an ophthalmologist due to a swollen optic nerve and characteristic retinal lipid exudates that form a macular star. She was hospitalized due to severe headaches and meningitis but has recovered completely 6 weeks after therapy. Her serological test was positive for *Bartonella henselae* and the kitten was a strong +4 *Bartonella* positive.

Case 6: Pulmonary Infiltrates- Pneumonia

After receiving our *Bartonella* laboratory notes and Newsletters, Dr. Carl Myers from Theodore Veterinary Hospital, Theodore, Alabama thought of a client who runs a cat rescue home (>100 cats) who has had numerous cats with chronic inflammatory diseases. One particular cat, with intractable URI for 14 months, came to mind and he called the owner to come in with the cat for a *Bartonella* test. The 47 year-old woman had been treating the cat for the past 14 months and was often scratched and bitten while treating the cat. The cat tested positive for *Bartonella* and Dr. Myers instituted azithromycin therapy, which totally resolved the longstanding URI. During the clinic visit the woman mentioned that she also developed chronic respiratory disease, "like her cat," that was also refractory to antibiotic therapy. During the 14 months of her respiratory illness she had radiological evidence of pulmonary infiltrates and had been tested for many agents including HIV

and TB. All tests were negative. Her illness became so severe that she required the use of an oxygen machine for more than 6 months. She also reported chronic headaches and blurred vision.

After hearing this, Dr. Myers urged his client to take our *Bartonella* Cat Owner brochure to her physician and insist that a *Bartonella* test be done. Her physician was convinced and submitted a *Bartonella* serological test, which proved to be "inconclusive." However, her physician thought that she may be infected with *Bartonella* and instituted doxycycline therapy for 21 days. There was a dramatic improvement in her condition within 10 days of the start of therapy. Her breathing became normal; she did not require an oxygen machine, and her headaches resolved. In obtaining the information for this Newsletter the woman mentioned that her 13 year-old son has also been chronically ill with fevers and persistent headaches. We urged her to consult the boy's physician regarding the possibility of *Bartonella* infection.

This case again illustrates the diverse nature of *Bartonella* clinical symptoms in people and the fact that *Bartonella* is "below the radar" of many physicians due to the diverse clinical presentations. However, with this patient's association with numerous stray cats, *Bartonella* should have been a primary consideration.

Editor's Note:

We are often asked if people living in households with *Bartonella* infected cats, or veterinarians and their employees, should be tested or treated for *Bartonella*. Some have asked if veterinarians and veterinary technicians should be tested yearly or bi-yearly. We recommend that healthy people need not be tested or treated. However, persons with chronic conditions, any of those listed in Figure 1, should consult their physicians with the information that they have been exposed to a *Bartonella* infected cat. It is important that the physician truly consider *Bartonella* as a possible cause for the illness and it may be necessary to insist that they consider this organism as occurred in **Case Reports 1, 2, 3, and 6**. We thank Dr. Donald DeForge, Silver Sands Veterinary Center, and Milford CT for calling our attention to these questions.

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Bartonella references can be obtained at:

www.nlm.nih.gov/



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NEWSLETTER

Bartonella: What is the Veterinarian's Legal Responsibility?

Evelyn E. Zuckerman, Editor

Spring 2004

Vol. 3, Number 2

In This Issue:

In the Spring 2004 issue of the NVL Newsletter we will discuss the veterinarian's moral and legal responsibility regarding the zoonotic potential of feline and canine *Bartonella*.

Current Aspects:

Bartonella are major pathogenic agents for feline and canine diseases and are responsible for at least 24 human diseases, some of which can be fatal. Although human *Bartonella* infections and *Bartonella* diseases are not reportable to the CDC, several state health departments now require that they be reported (Table 1). This shows the increasing medical concern and interest in *Bartonella*. It is ironic that those states that require reporting are in geographic areas of the country where reservoir animal *Bartonella* infections (cats & dogs) are lowest.

Table 1
 State Health Departments That Require Reporting of *Bartonella* Infections or Diseases

Health Department	<i>Bartonella</i> Reporting Requirement
CDC	No
Minnesota	Yes
Oklahoma	Yes
Wyoming	Yes
Wisconsin	Yes
46 Other States	No

It is important for veterinarians to recognize their responsibility to their patients and to their clients regarding the zoonotic potential for feline and canine *Bartonella*. *Bartonella* testing should be routine for all cats and for dogs with *Bartonella*-type diseases.

Bartonella in Small Animals:

As of this writing, 5 species of *Bartonella* have been found in both cats and dogs (Table 2). Although cats have infected far more people than dogs, more canine *Bartonella* species have been recovered from humans (Table 3).

Table 2 Pet Animal *Bartonella*

<i>Bartonella</i>	Cats	Dogs
<i>B. henselae</i>	Yes	Yes
<i>B. clarridgeiae</i>	Yes	Yes
<i>B. elizabethae</i>	Yes	Yes
<i>B. koehlerae</i>	Yes	No
<i>B. weissii</i>	Yes	No
<i>B. washoensis</i>	No	Yes
<i>B. vinsonii</i>	No	Yes

Table 3

Bartonella Isolated from Humans

<i>Bartonella</i>	Animal Origin
<i>B. henselae</i>	Cat & Dog
<i>B. clarridgeiae</i>	Cat & Dog
<i>B. elizabethae</i>	Cat, Dog, Rat
<i>B. washoensis</i>	Dog & Squirrel
<i>B. vinsonii</i>	Dog & Vole
<i>B. grahamii</i>	Mouse
<i>B. quintana</i>	Human
<i>B. bacilliformis</i>	Human

Numerous wild and domestic animals are reservoirs for various *Bartonella* species and may also act as a source of infection for humans. Infection of humans from these animals probably occurs via transmission of *Bartonella* via arthropod vectors and not by contact as occurs from cats.

Veterinarian's Legal Responsibility

Many practitioners have asked our opinion regarding their legal responsibility and exposure regarding *Bartonella*. Although we cannot give legal advice, there are several factors to consider. The current knowledge regarding *Bartonella* is substantial. The prototype *Bartonella* disease, cat scratch disease, was first described in France in 1889. Most cat owners have learned of "cat scratch disease" or "cat scratch fever" from general publications such as newspapers and magazines. In this regard, Time magazine highlighted cat scratch disease as an important zoonosis in their February 23, 2004 issue.



In the 1970s there even was a popular Rock & Roll song by Ted Nugent titled CAT SCRATCH FEVER. The medical and veterinary literature has more than 1300 *Bartonella* articles. There have been numerous publications in veterinary journals (Table 4) regarding *Bartonella* infections in cats and dogs. Finally, the new source for much information, the INTERNET, has many good, and not so good, sites where *Bartonella* information can

be obtained. In addition, our *Bartonella* test has been available for more than 4 years.

Table 4

Number of *Bartonella* Articles in Veterinary Journals

Journal	Cat	Dog
Adv Vet Med	1	1
Am J Vet Res	3	1
J Am Anim Hosp Assoc	1	1
J Am Vet Med Assoc	2	5
J Fel Med & Surg	4	0
J Vet Med Sci	3	0
J Vet Diag Invest	2	1
Vet Clin NA	1	2
Vet Immun & Immunopath	3	2
Vet Microbiol	7	0
Vet Ophthal	0	1
Vet Parasitol	0	1
Vet Quarterly	2	0
Vet Record	5	2
Vet Research	2	0
Totals:	36	17

Considering the large amount of current *Bartonella* information, it seems unlikely that veterinarians can claim a lack of information as a defense.

The following case histories are given as cautionary examples.

Veterinary Specialist

A nationally known veterinary specialist had been treating a client's cat for a chronic inflammatory condition for several months. The cat was not responding well to different antibiotics. When the *Bartonella* test became available, the specialist thought that *Bartonella* might be the cause of the condition. After receiving a positive *Bartonella* test result from this laboratory, the veterinarian changed the antibiotic therapy to Azithromycin and there was a prompt clinical improvement. However, at that time, the client reported that he had been hospitalized for 10 days with "CAT SCRATCH FEVER" and, when he found that his cat was being treated for the same bacterium, he asked the veterinarian when he first learned of *Bartonella*. Fortunately the client was understanding and did not seek a legal remedy, maybe because his beloved cat had finally been cured of its chronic disease.

Kids, Kittens and Bartonella

As was discussed in our Winter 2003 Newsletter, kittens are more likely than adult cats to transmit



Bartonella to people, especially children. Children often allow kittens to lick their face and to sleep with them. Boys play more roughly than girls with kittens and are more likely to be scratched or bitten and thus are more likely to develop cat scratch

disease (CSD) more often than girls.

Two Boys and a Kitten:

A suburban family, living in the northeast, found a 3-month-old stray kitten in their backyard. The kitten was thin, alert, playful, and loaded with fleas. The family immediately took the kitten to their veterinarian who examined the kitten, began vaccination, tested for FeLV and FIV, and dispensed flea medication. Although the veterinarian had performed numerous *Bartonella* tests on cats with inflammatory diseases he did not recommend a test of this kitten. Two months later the 7 year old boy in the household was hospitalized with cat scratch disease with cervical lymphadenopathy, a high fever, and neurological signs. The boy recovered rapidly after receiving intravenous antibiotics.

Approximately 5 weeks later, the boy's friend, who lived 2 houses away became severely ill with neurological signs, confusion, agitation, and was unresponsive to verbal stimuli. He too was hospitalized and, after a MRI and an abdominal biopsy, was diagnosed with "cat scratch disease." This boy, who did not own a cat but played with his friend's kitten, did not have the typical prodromal CSD signs of fever and lymphadenopathy following a known cat scratch or bite. He too was treated with antibiotics and recovered rapidly.

The kitten was taken back to the veterinarian where the owner requested a *Bartonella* test. The kitten was FeBart[®] positive, a very strong positive +4 by western blot. Although this family did not blame the veterinarian nor seek legal recourse, the veterinarian might have been able to prevent these 2 cases of severe CSD had he tested the kitten at the first visit.

Blood Donors

Two young sisters, living in a northern state, adopted two 8-week-old healthy littermate kittens from a neighbor who owned the queen. The kittens were robust and free of fleas. The family brought the kittens to their veterinarian for a routine health exam and vaccination. The kittens were free of enteric parasites and were tested for FeLV, but were not tested for *Bartonella*. Approximately 6 months later, a neighbor's dog severely mauled one of the kittens, which necessitated a blood transfusion. The kitten received a transfusion from one of the long-time hospital blood donors, an adult cat that was

adopted by the hospital after a client found it as a stray. The donor had been tested for FeLV, FIV was fully vaccinated, and was in good health but had never been tested for *Bartonella*.

The kitten recovered rapidly but developed a severe upper respiratory disease and conjunctivitis about 3 weeks after release from the hospital.

Repeated treatment with various antibiotics did not resolve the URI or the conjunctivitis over a 6-month period. One day the mother of the 2 girls came into the office and reported that her



husband, who had been treating the kitten at home, and one of her daughters had both developed CSD. The husband developed blurred vision in one eye, a severe chronic fatigue syndrome and had an IgG *B. henselae* titer of 1:512. The daughter had cervical lymphadenopathy, fever and severe headaches. Her IgG titer was 1:1,024. They both were treated with Azithromycin and recovered completely. The owner requested *Bartonella* tests of both kittens. Only the kitten who received the blood transfusion was *Bartonella* positive. After reviewing the case, the hospital tested the blood donor cat and found it too was *Bartonella* positive. Although it cannot be proven, it is likely that the blood donation transmitted *Bartonella* to the injured kitten who subsequently transmitted the infection to two people in the household. No legal action was taken.

Cat Scratch Disease Can Be Costly

An 18-year-old Georgia college student was earning money over the summer by painting houses. He was painting the house of women who had collected 10 cats that lived in and around her house. The boy did not own a cat nor did he like cats. However, one day while painting around the foundation he was scratched by one of the semi-feral cats. The owner was conscientious and had most of the cats seen regularly by her veterinarian. Most cats had been tested free of FeLV and FIV but none had been tested for *Bartonella*. The veterinarian had performed almost 100 *Bartonella* tests on cats with inflammatory diseases but she had not recommended testing healthy cats. Two weeks after the scratch, a raised red papule appeared and persisted at the site of the scratch. The boy eventually developed severe CSD with several sequelae that required hospitalization and a resulting \$21,000 hospital bill. The boy was uninsured and had to postpone returning to college in order to earn money to pay for the hospitalization. No legal action was taken.

Cancer Patients and Cats

A 58-year-old woman, living in the south, had been treated for breast cancer which consisted of surgery and chemotherapy. She had 3 middle-

aged cats that were regularly seen by her veterinarian who had become aware of her health issues. The cats were in good health and up-to-date on their vaccinations. After learning of the owner's chemotherapy, the veterinarian recommended *Bartonella* tests for all of her cats but the owner declined. About a year after completion of therapy, the owner developed severe headaches, joint pains, and blurred vision in one eye. Following several weeks of diagnostic tests, she went into a coma and was transported to a major medical center. After further extensive tests, a serological test for *B. henselae* was strongly positive, 1:1,024 IgG titer. She was treated with intravenous antibiotics and made a prompt recovery. The veterinarian was relieved that her client had recovered but was worried that she had not asked this susceptible client to sign a release stating that she had declined *Bartonella* tests of her cats. No legal action was taken.

Veterinarian's Legal Responsibility Regarding Bartonella

After reading these case histories (not actual cases but composites of numerous instances) it is apparent that these veterinarians might have been at some risk of legal action. Although we cannot give legal advice, we feel that veterinarians should be aware that they might be legally responsible when they give no information or give misinformation regarding the public health risks of feline and canine *Bartonella*.

Our Recommendations:

1. Discuss *Bartonella* with all cat owners, especially new kitten owners, and recommend that all cats, especially kittens, be tested. If the owner declines, a signed written statement may be warranted.
2. Be especially diligent to discuss *Bartonella* with any person who is immunosuppressed, has been treated for cancer, has had an organ transplant, is HIV-infected or has AIDS, and families with children less than 10 years old.
3. Test all blood donor cats for *Bartonella* infection and treat all infected donors.
4. Caution owners of infected cats to avoid being scratched or bitten while treating their cats. It is often helpful to have one person restrain the cat while another administers the medication.
5. If any cat owner or hospital employee is scratched or bitten by an infected cat, immediately thoroughly clean the wound and apply alcohol and peroxide.
6. We do not recommend that **healthy** owners of *Bartonella* infected cats obtain a human *Bartonella* test.
7. However, any owner of an infected cat or veterinary hospital employee **with chronic disease symptoms**, related to *Bartonella* infection, (Newsletters Vol. 1, No 2 Spring 2002 and Vol. 2, No 2 Spring 2003) should immediately see their physician and be sure to STRESS that they are concerned about *Bartonella* infection or "CSD."
8. Although there are no reports of medical problems with pregnant women or their unborn fetuses, they should be careful around *Bartonella* infected cats.
9. **IT IS TIME TO CONSIDER FELINE AND CANINE BARTONELLA AS SERIOUS VETERINARY AND HUMAN PATHOGENS.**



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NEWSLETTER

Commonly Asked *Bartonella* Questions Summer 2004

Evelyn E. Zuckerman, Editor

Vol. 3, Number 3

In This Issue:

The Summer 2004 issue of the NVL Newsletter will answer 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 FeBart® 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 4-6% 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. We recommend treating only *Bartonella* test positive cats. This may actually result in a monetary saving for your clients considering the expense of antibiotic therapy and considering the prevalence of *Bartonella* infection in healthy cats (~20%).

5. There are 6 known *Bartonella* species in cats. What species does the FeBart® test detect?

Answer: There are presently 6 recognized *Bartonella* species that infect pet cats. Unlike other serological tests, the FeBart® 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.

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

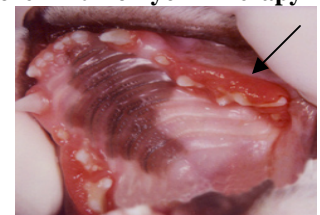
penetrate these cells, it is necessary to treat for a long period as with Lyme Disease.

8. How soon should I see clinical improvement after treatment of *Bartonella* infected cats with inflammatory diseases?

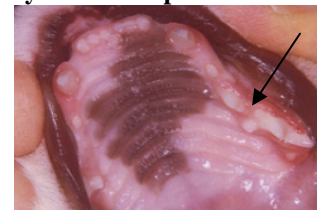
Answer: The length of time required to see therapy responses can be variable depending on the initial duration (chronicity) of the disease. Most cats that respond show improvement by 10 to 14 days from the start of therapy. As seen in the photographs below of a 5 month-old *Bartonella*-infected kitten with severe gingivitis, marked improvement (80%) occurred by 14 days and complete resolution by 28 days. If no improvement occurs by 21 days we suggest re-treatment for an additional 21 days with azithromycin or rifampin. In some cats (~17%) the inflammatory condition may not improve at all, which indicates that *Bartonella* is not the cause of the condition.^{5,6}

Severe Gingivitis

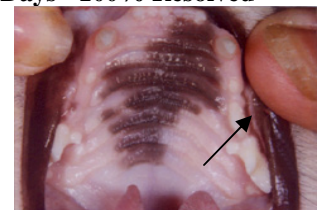
Before Azithromycin Therapy



14 Days- 80% Improved



28 Days- 100% Resolved



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

9. What are the adverse side effects of azithromycin and rifampin therapy in cats?

Answer: As in humans, azithromycin therapy can induce GI upset resulting in vomiting and diarrhea. There are no reports of other more severe adverse effects, although recently a case report has associated azithromycin therapy with an aplastic anemia in a cat.⁸ Adverse reactions with rifampin therapy consist of allergic reactions, pruritis, redness, and swelling of the face and paws. **If you feel that you have seen an adverse reaction to azithromycin or rifampin please let us know so that we can compile this information.**

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 only way to determine if *Bartonella* has been eliminated after therapy is to run a comparative therapy titration test.^{5,6} We compare the titer from the first sample, which we have saved frozen, with a sample submitted **6 MONTHS AFTER THE END OF THERAPY**. A 4 fold or greater drop in titer indicates successful *Bartonella* therapy.

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

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 4-fold or greater 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 therapy titration test before 6 months will not detect a sufficient decrease.

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

Answer: The comparative titer is reported in a range of 0-fold or greater decrease with the median

being a 4-fold decrease. For cats with no titer decrease or with only a minimal 2 fold decrease, where the inflammatory condition has not completely (100%) resolved, we recommend re-treatment with either azithromycin or rifampin for 21 days. We cannot make any recommendation if the exact (%) clinical response is not indicated. In addition, we need these data to properly assess our therapy protocol outcomes, which will allow us to modify our treatment recommendations if indicated by the data.

Bartonella Biology:

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

Answer: Yes, dogs are carriers of 6 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 recent study found 34% of ticks in New Jersey were carriers of *Bartonella*.⁹ We have found 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 that pregnant owners of *Bartonella* infected cats avoid contact until the cat has been treated by another family member.

More than 1400 *Bartonella* references can be obtained at: www.nlm.nih.gov/

We will be presenting 2 papers at the 4th International *Bartonella* Meeting in Uppsala, Sweden in August. One paper describes ocular *Bartonella* diseases (coauthors Dr. Kerry Ketring, All Animal Eye Clinic, Cincinnati, OH and Dr. Craig Fischer and Dr. Melanie Mineo, Animal Eye Clinic of Florida, Clearwater, FL) and the other describes feline diseases and therapy. We thank the thousands of practitioners who have helped us obtain these data. We will report any new information obtained from investigators from around the world in future Newsletters.

REQUEST FOR PHOTOS:

Please contact us if you have taken before and after therapy photographs of *Bartonella* infected cats with inflammatory diseases and would like to share them with us for inclusion in our Newsletters. We would also like photos of *Bartonella* infected dogs with inflammatory diseases.

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NEWSLETTER

4th International *Bartonella* Conference

August 26-28, Uppsala, Sweden

Fall 2004

Vol. 3, Number 4

Evelyn E. Zuckerman, Editor

In This Issue:

The fall 2004 issue of the NVL Newsletter will cover the feline and canine papers presented at the 4th International *Bartonella* Conference that was held August 26-28 at The Evolutionary Biology Centre, Uppsala University in Uppsala Sweden. The human *Bartonella* reports and pathogenesis papers will be covered in the next issue of our Newsletter.

The Conference:

The conference was attended by about 100 scientists from around the world: Japan, Russia, France, Germany, Sweden, Italy, Israel, Switzerland, United Kingdom, Peru, South Korea, and the United States. Two elegant conference dinners were given, one in the Saluhallen (marketplace) and the other at the elegant Orangeriet, Linnaeus Garden. The Orangeriet, Linnaeus is the home of the noted Swedish scientist Carolus Linnaeus. The setting was historic, elegant and the food was excellent.



The Orangeriet, Linnaeus
The home of the Swedish scientist
Carolus Linnaeus

Carolus Linnaeus (1707-1778) was Sweden's most famous biologist. In 1744 he suggested the centigrade scale which perfected the thermometer, reversing the temperature scale of Anders Celsius so that 0 represented the freezing point of water and 100 represented the boiling point. Linnaeus also invented the practice of naming all species by 2 names (binomial) a *genus* name followed by a *species* name (*Bartonella henselae*) and began the practice of grouping species hierarchically into orders, classes and kingdoms. It was fascinating to have been able to stand in his beautiful home library and examine the preserved specimens that he used in his work.

The Scientific Sessions:

The scientific sessions were comprised of 17 oral presentations and 17 posters during the 3-day meeting. Six papers covered feline *Bartonella* whereas 2 papers described canine *Bartonella*. Two abstracts from our Laboratory were accepted for inclusion in the meeting. Dr. Hardy gave a 45 minute presentation on feline *Bartonella* other inflammatory diseases, with

emphasis on ocular diseases, and *Bartonella* therapy (see abstracts in this Newsletter). *Bartonella* infection in humans, sheep, cattle, woodland rodents, insects, and the mechanisms of *Bartonella* pathogenesis and genome analysis comprised the remaining presentations.

Canine and Feline Papers:

***Bartonella*-Induced Ocular Inflammatory Diseases of Cats.**

Hardy, WD, Jr.¹, Zuckerman, E¹, Ketring, K.², Fischer, C.³ and Mineo, M.³
¹National Veterinary Laboratory, Inc., Franklin Lakes, NJ, ²All Animal Eye Clinic, Cincinnati, OH, and ³Animal Eye Clinic of Florida, Clearwater, FL.

Background: *Bartonella* have a predilection to inflame vascular tissues in all host species. The eye is a very vascular organ that readily shows evidence of inflammation. There are numerous reports of human ocular diseases caused by *Bartonella* infection obtained from pet cats (Perinaud's oculoglandular syndrome, chorioretinitis, uveitis, retinal detachment, blepharitis, multifocal helioid choroiditis, disciform keratitis, orbital abscess). However, there are only several reports of *Bartonella*-induced ocular diseases in cats. **Methods:** 47,962 cats from throughout the United States (1,653 veterinary hospitals and 2 ophthalmology board-certified veterinarians, KK and CF) were serologically tested for *Bartonella* antibody, by a western immunoblot (WB). 5,711 (11.9%) of these cats had ocular diseases. Treatment of *Bartonella*-infected cats consisted of azithromycin or rifampin at 10mg/kg orally once daily for 10-21 days. Clinical therapeutic evaluations of 170 cats with ocular diseases were obtained and 70 (40%) of these were diagnosed, treated, and evaluated by the 2 board certified veterinary ophthalmologists (KK and CF). Post therapy WB titrations were done on 91 cats, 6 months after the end of therapy, to determine titer reductions indicating that *Bartonella* was eliminated. **Results:** 170 of 840 (20%) healthy cats, with no reported risk factors for *Bartonella* infection (flea exposure, etc.) were positive by WB. This group served as the base line *Bartonella* prevalence (X) for comparison with the *Bartonella* incidence in cats with ocular inflammatory diseases. *Bartonella* infection was found in a total of 2,772 of 5,711 (48.5%, 2.45X) cats with inflammatory ocular diseases: conjunctivitis 2,259 of 4,750 (47.6%), uveitis 364 of 667 (54.6%), corneal ulcer 53 of 98 (54.1%), keratitis 42 of 97 (43.3%), chorioretinitis 18 of 32 (56.3%), epiphora 13 of 27 (48.2%), glaucoma 16 of 21 (76.2%), and blepharitis 7 of 19 (36.8%). Clinical improvements after therapy were evaluated as follows: excellent 80-100%, good 60-79%, fair 50-59% and failure <50% improvement. There were 170 cats with conjunctivitis (111) and uveitis (59) available for clinical evaluation of therapy. Therapy results were: conjunctivitis- excellent 82 (74%), good 9 (8%), fair 5 (5%), and failure 15 (13%); uveitis- excellent 43 (73%), good 5 (9%), fair 3 (5%), failure 7 (12%), and worse 1 (1%). Thus, clinical improvement, due to *Bartonella* antibiotic therapy, occurred in 147 of the 170 (87%) cats. Therapy titration tests were done for 91 of the 170 cats that were clinically evaluated. A reduction in antibody titer occurred in 79 of the 91 (87%) treated cats indicating successful anti-*Bartonella* therapy. There were reductions in *Bartonella* antibody titers in 63 of 68 (93%) cats with improved clinical outcomes whereas 12 of 17 (71%) cats who did not improve clinically had titer reductions. Reductions in *Bartonella* antibody titers occurred in 4 of 6 (66.7%) cats where no clinical evaluation was available. **Conclusion:** *Bartonella* appears to cause a significant portion of ocular inflammatory diseases in cats and *Bartonella* antibiotic therapy was clinically effective in 87% of infected cats, even many who had been non-responsive to previous ophthalmologic therapies and some who were co-infected with other infectious agents, *Herpesvirus* and *Toxoplasma gondii*, known to cause ocular diseases in cats.

Epidemiology of Bartonella Infection in Domestic and Wild Carnivores. Bruno Chomel, *et al.* School of Veterinary Medicine, Univ. California, Davis, CA. Dr. Chomel reviewed the epidemiology of canine and feline *Bartonella*. He described a second case of endocarditis in a cat from New York that was originally tested +4 by our laboratory. He reported that *Bartonella* has been found in wild felids including Pumas, bobcats, lions, and cheetahs. He also noted that 3% of dogs in the eastern US and 10% of army dogs were seropositive. Most infected dogs were field dogs exposed to ticks and fleas. The clinical signs were often lameness, arthritis related to lameness, nasal discharge and epistaxis and splenomegaly. *Bartonella*, related to *B. clarridgeiae*, have also been isolated from wild canids, gray foxes and raccoons.

Comparative Medical Features of Canine and Human Bartonellosis. EB Breitschwerdt, *et al.*, College of Veterinary Medicine, North Carolina State University, Raleigh, NC. Dr. Breitschwerdt reviewed the similarities of *Bartonella* induced diseases in dogs and humans with emphasis on endocarditis. A significant increase in antinuclear antibodies in dogs infected with *B. vinsonii* (berkhoffii) was reported. He also noted that *B. henselae*, the predominant feline *Bartonella*, was found more often in dogs than has been previously described.

Identification of Swedish Bovine and Feline Bartonella Isolates by 16S rDNA Sequencing. Olsson Engvall, *et al.*, National Veterinary Institute, Uppsala, Sweden. Dr. Engvall reported a low prevalence (2.9%) of *Bartonella* infected cats in southern Sweden where fleas are endemic. In the colder northern portion of Sweden, where there are no fleas, no *Bartonella* infected cats have been reported. As would be expected, CSD occurs infrequently in Swedish patients.

Identification and Characterization of a Bartonella henselae Strain Isolated in Italy. L. Ciceroni, *et al.*, Istituto Superiore di Sanita, Rome, Italy. Dr. Ciceroni described DNA sequencing of several Italian *Bartonella* isolates. This group concluded that *Bartonella* are able to develop genotypic variability between genetically related strains. This may be significant in the ability to generate pathogenic strains capable of inducing different tissue tropisms and thus diseases in cats and humans. It may also make the development of a vaccine more difficult.

Worldwide Prevalence of Bartonella Infection in Cats:

The following is a summary of the worldwide prevalence of *Bartonella* infection in cats based on reports from the 4th International *Bartonella* Conference and a review of the literature:

USA- North- 20% South-60%
 Hawaii- 89%
 Canada- 20%
 Caribbean- 70%
 Sweden- South- 3%, North- 0%
 United Kingdom- 40%
 France- 10-20%

Bartonella-Induced Inflammatory Diseases of Cats: An Increasing Spectrum. Hardy, WD, Jr., and Zuckerman, E.

National Veterinary Laboratory, Inc., Franklin Lakes, NJ.

Background: *Bartonella* species induce chronic inflammation in any tissue due to their tendency to adhere to vascular endothelium. The chronic *Bartonella* bacteremia in cats leads to the probability that many tissues will be inflamed. Our previous findings indicated that, as in humans, *Bartonella* cause inflammatory diseases in a wide variety of tissues in cats. We have continued to survey pet cats for *Bartonella* infection and have compiled data from cats treated for *Bartonella*-associated inflammatory diseases. **Methods:** 47,962 cats were serologically tested for *Bartonella* antibody, by a western immunoblot (WB), from throughout the United States (1,653 veterinary hospitals). Treatment of *Bartonella*-infected cats consisted of azithromycin or rifampin at 10mg/kg orally once daily for 10-21 days. Clinical evaluations of the therapy of 1,344 cats were obtained by collaborating veterinarians and post therapy WB titration tests, 6 months after the end of therapy, were done for 1,139 of these cats to determine the success of the *Bartonella* therapy. **Results:** 170 of 840 (20%) healthy cats, with no reported risk factors for *Bartonella* infection (flea exposure, etc.), were positive by WB. This group served as the base line prevalence of infection (X) for comparison with the occurrence of *Bartonella* in cats with inflammatory diseases. **Diseases:** A high incidence of *Bartonella* infection was found in cats with the following diseases: **Oral diseases:** 14,466 of 29,126 (49.7% 2.5X) cats, gingivitis 10,593 of 22,072 (48.0% 2.4X), stomatitis 2,905 of 5,285 (55.0% 2.75X), oral ulcers 968 of 1,769 (54.7% 2.75X); **Respiratory diseases:** 3,737 of 7,453 (50.1% 2.5X) cats, URI 3,266 of 6,567 (49.8% 2.5X), rhinitis 266 of 490 (54.3% 2.7X), sinusitis 205 of 396 (50.1% 2.5X); **Ocular diseases:** 2,772 of 5,711 (48.5% 2.45X) cats, conjunctivitis 2,259 of 4,750 (47.6% 2.4X), uveitis 364 of 667 (54.6% 2.75X), corneal ulcer 53 of 98 (54.1% 2.7X), keratitis 42 of 97 (43.3% 2.15X), chorioretinitis 18 of 32 (56.3% 2.8X), epiphora 13 of 27 (48.2% 2.4X), glaucoma 16 of 21 (76.2% 3.8X), and blepharitis 7 of 19 (36.8% 1.85X); **GI diseases:** 1,116 of 2,319 (48.1% 2.4X) cats, inflammatory bowel disease 243 of 487 (49.9% 2.5X), chronic diarrhea 460 of 952 (48.3% 2.4X), chronic vomiting 413 of 880 (46.9% 2.35X); **Other diseases:** lymphadenopathy 628 of 1,265 (49.6% 2.5X), fever of unknown origin 835 of 1,785 (46.8% 2.4X), liver disease 70 of 167 (41.9% 2.1X), heart disease 203 of 374 (54.3% 2.7X), neurological disease 43 of 105 (41.0% 2.0X), and diabetes mellitus 222 of 482 (46.1% 2.3X). **Therapy:** Clinical improvements were evaluated in 1,344 cats as follows: excellent 80-100%, good 60-79%, fair 50-59% and failure <50% improvement. Complete disease resolution occurred in 542 cats (40.3%), 90% improvement in 216 cats (16.1%), 80% improvement in 111 cats (8.3%), good 60-79% improvement occurred in 144 cats (10.7%), fair 50-59% improvement in 102 cats (7.6%), whereas there was no improvement (<50%) in 220 cats (16.4%) and the disease became worse in 9 cats (0.6%). Thus, 83% of the treated diseased cats improved >50%, while 64.7% improved 80% or greater. Many of these cats had failed previous empirical antibiotic and steroid therapy. Interestingly 10 of the 85 diabetic cats, that were evaluated, no longer required insulin maintenance and an additional 10 cats required significantly less insulin after *Bartonella* therapy. Overall, 936 of 1,139 (82.1%) of treated diseased cats had a 2 fold or greater reduction in their *Bartonella* antibody titers. *Bartonella* antibody titers decreased after therapy as follows: excellent improvement 663 of 722 (91.8%), good improvement 107 of 121 (88.4%), fair improvement 66 of 93 (71.0%), no improvement 96 of 194 (49.5%), and cats that became worse 3 of 9 (33.3%). **Conclusion:** *Bartonella* appears to cause a significant portion of chronic inflammatory diseases in various tissues in cats. Diseases similar to most of these feline *Bartonella*-associated diseases were first reported in humans and were caused by *Bartonella* transmitted from cats. *Bartonella* antibiotic therapy was clinically effective in 83% of these cats, even many who had been non-responsive to previous therapies and some who were co-infected with other infectious agents. In some cats, *Bartonella* appears to be one component of a polymicrobial disease process.

Feline Bartonella Prevalence

