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NEWSLETTER

Bartonella in Kittens and *Bartonella* Therapy Evaluation

Evelyn E. Zuckerman, Editor **Winter 2003** **Vol. 2, Number 1**

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.[1, 2.3]

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.

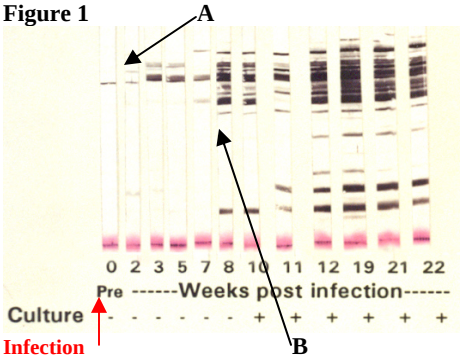
Detection of Early Infection:

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

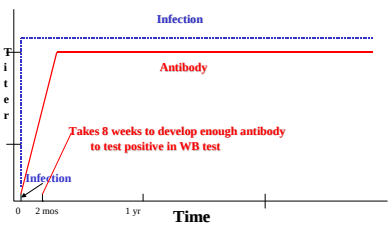
Figure 1



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.[1, 2]

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.

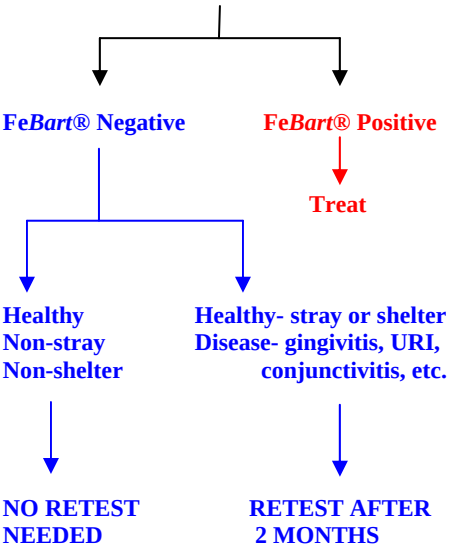
Why Are Kittens More Likely to Transmit *Bartonella* to Humans?

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 Tests for Kittens:
All newly introduced kittens, at any age, should be screened for *Bartonella* infection at their first examination. Since the Fe*Bart*® 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 Fe*Bart*® 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.

Fe*Bart*® 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 Fe*Bart*® 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



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.

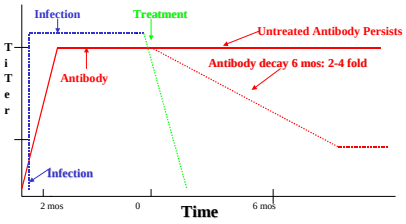
Bartonella Therapy

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.[4] 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

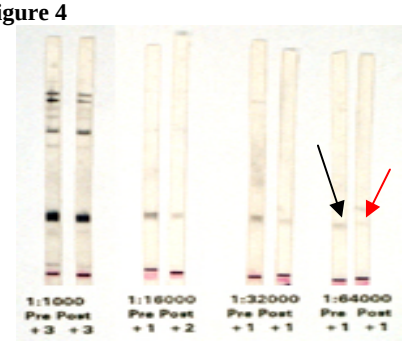
Antibody Decay After _Bartonella_ Therapy



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).

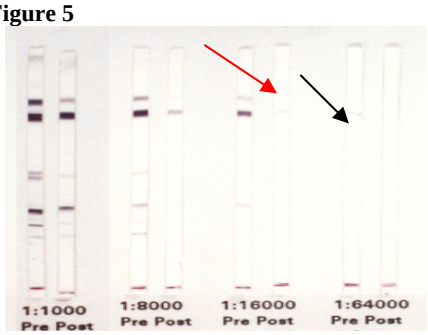
The screening test for infection, the Fe*Bart*® test, is too sensitive to use for detection of decreased titers since it is performed at a single dilution of 1:100. Many infected cats have titers of 1:256,000 or greater. Therefore, the therapy titration test is required for determination of successful *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 FE*BART*® TEST FOR THERAPY EVALUATION.**

Figure 4



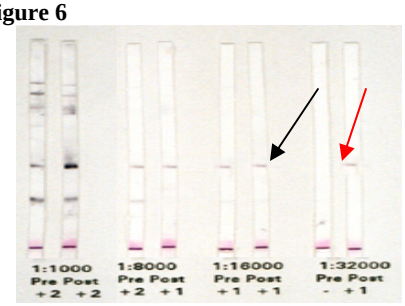
No Therapy: There is no decrease in titer after 3 years in this untreated *Bartonella*-infected cat.

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.

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Bartonella references can be obtained at:
www.nlm.nih.gov/

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NEWSLETTER

Bartonella Diseases in Veterinarians, Their Families and Employees, and Their Cat Owner Clients

Evelyn E. Zuckerman, Editor **Spring 2003** **Vol. 2, Number 2**

In This Issue:

The spring 2003 issue of the NVL Newsletter will document the dangers of feline *Bartonella* for veterinarians, their families and employees and cat owners. These cases support our recommendation that all healthy cats, especially kittens, should be tested for *Bartonella*.

Bartonella and Veterinarians

Background:

Veterinarians and their employees are at higher risk for infection with *Bartonella* from cats than the general public.[1] In fact, one of the 6 feline *Bartonella* species, *Bartonella clarridgeiae*, was initially isolated from a veterinarian who was bitten by a 6-week-old kitten. In general, 20% of healthy pet cats in the USA are infected with *Bartonella*. Thus veterinarians and their staffs handle numerous infected cats in their daily occupation. A recent study found that 35 of the 233 (15%) veterinarians and veterinary technicians had antibody to *B. henselae* whereas only 7 of the 155 (4.5%) control group of medical students were antibody positive.[1]

Cat and dog fleas, and probably ticks, 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.

The oral cavity is the site for transfer of *Bartonella*, during grooming, to the nails and fur of infected cats. Cats can transmit the bacteria from their infected nails by scratches or from the fur by contact. The oral cavity is the obvious exit port for bite transmission to people. The presence of fleas is not needed for transmission of *Bartonella* from cats to humans. However, *Bartonella* probably occasionally are directly transmitted to people via cat and dogs fleas and ticks.

Bartonella infection and disease occur equally in people younger and older than 21 years of age.[2] In addition, *Bartonella* infection occurs more in immunocompetent than immunosuppressed people. Kittens are more likely to transmit *Bartonella*, especially to children, because they tend to playfully scratch and bite children more often than do adult cats. Boys are more often infected because they play more roughly with the kittens than do girls. Since kittens chew objects and have changing dentition, *Bartonella* are able to enter their oral cavity, through abrasions to their oral mucosa and through tooth sockets, to be transferred during grooming to the fur and nails. In this regard, cats with oral inflammatory disease: gingivitis, stomatitis, and oral ulcers, with inflamed and bleeding oral tissues are probably more likely to transmit *Bartonella* to people

Since *Bartonella* diseases are not reportable diseases an accurate incidence in humans has not been established. Previous estimates for cat scratch disease (CSD), only one of the 22 human *Bartonella* diseases, is 22,000 cases per year, of which 2,000 require hospitalization. CSD is the "tip of the iceberg" of a very large number (22) of little recognized *Bartonella* diseases of humans. The occurrence of all the *Bartonella* diseases (see Table below) in veterinarians, their family members or their employees has not been ascertained. It must be emphasized that many physicians are not familiar with the full range of *Bartonella* clinical diseases.[2, 3,4,5,6]

FELINE *BARTONELLA*-INDUCED DISEASES IN HUMANS

Previously Described Human Diseases:
Cat Scratch Disease
Bacillary angiomatosis & peliosis
Febrile bacteremia
Lymphadenopathy
Endocarditis & vegetative valvular disease
Uveitis
Neurological disorders
Anemia
Neuroretinitis- chorioretinitis
Osteomyelitis

Newly Described Human Diseases:
Inflammatory bowel disease
Mononucleosis-like syndrome
Co-infection with Lyme disease
Pulmonary infiltrates
Meningoencephalitis
Arthralgia & Myositis
Juvenile arthritis
Cutaneous rash- Henoch-Schenlein purpura
Cutaneous granuloma annulare
Disciform keratitis

Case Studies:

Veterinarian:

Case 1: Myositis

A 32-year-old male veterinarian, in small animal practice in New York City, developed muscle and joint pain that persisted for 4 years. Numerous diagnostic tests, including muscle biopsies, failed to find an infectious cause for his symptoms. Treatment by a rheumatologist consisted of corticosteroids which were effective in temporarily alleviating the discomfort. After learning about a case of myositis in a Florida cat, caused by *Bartonella*, that was cured by azithromycin therapy, the veterinarian sought a *Bartonella* test. His *Bartonella* serologic test was positive with an IgG titer of 1:128. Treatment with azithromycin resulted in resolution of the muscle and joint pain within 7 days. The symptoms of myositis have not recurred during the 3 months post azithromycin therapy period.

Family Member of a Veterinarian:

Case 2: Henoch-Schenlein Purpura

After attending a *Bartonella* lecture, a New York City veterinarian called this laboratory to discuss the possibility that his 17-month-old son, who had a persistent red rash on his right forearm, may have Henoch-Schenlein purpura, a cutaneous rash that can be caused by several bacteria, one of which is *Bartonella*. The cat, that had continually licked the boy's right hand, tested positive for *Bartonella*. The veterinarian arranged for his pediatrician to test his son for *Bartonella*. The boy's test was indeterminate for *B. henselae* antibody. The rash resolved without antibiotic therapy.

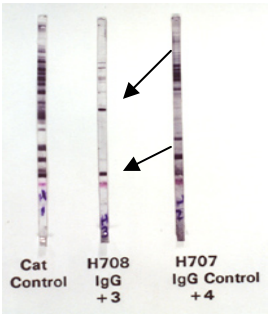
Veterinary Hospital Employees:

Case 3: Vet Tech: Chronic Uveitis

The son of a Long Island veterinarian, who worked in his father's practice, developed a chronic iritis and uveitis for 4 years which was preceded by a long-term lymphadenopathy. Despite numerous diagnostic tests, the etiology of the uveitis could not be determined. After reading the "Cats and *Bartonella*, Information for Cat Owners" brochure from this

laboratory he called us to discuss the possibility that *Bartonella* might be the etiologic agent for his uveitis. We agreed to test him, for experimental purpose only, for *Bartonella* antibodies by our western immunoblot test with the understanding that he would have our results confirmed by a licensed human *Bartonella* test. We found strong IgG antibody (see Figure below) to *Bartonella* that was confirmed by his physician (*B. henselae* 1:128). Azithromycin therapy resolved the chronic uveitis within 1 month.

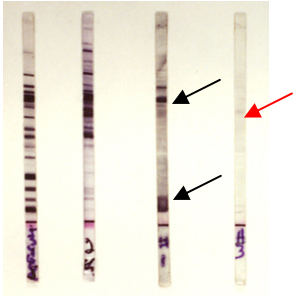
Western Blot for *Bartonella* Antibody



Case 4: Vet Tech: Cat Scratch Disease

A 28-year-old female veterinary technician working in Florida was scratched on the right arm by a 3-month-old kitten. Approximately 5 weeks later she developed a painful swelling in the right axillary lymph node. The technician called our laboratory to arrange to test the kitten for *Bartonella*. In addition, we agreed to test her, for experimental purpose only, for *Bartonella* antibodies by our western immunoblot Fe*Bart*® Test with the understanding that she would have our results confirmed by a licensed human *Bartonella* test. The kitten was strongly positive (+4) indicating infection. The technician was positive for IgG and IgM antibodies to *Bartonella* by our western blot test (see Figure below). Her antibody status was confirmed and her lymphadenopathy resolved within 1 month without therapy.

Western Blot for *Bartonella* Antibody



Cat Control | Kitten | IgG | IgM Vet Tech

Cat Owners:

Case 5: Vet Tech: Conjunctivitis & Skin Nodule

A 33-year-old New Jersey veterinary technician received a scratch to her right hand. Several days later two raised non-erythematous nodules occurred and persisted for several weeks. Four weeks later she developed persistent chronic conjunctivitis (Figures 1 & 2). We found her positive by western blot however, a confirmatory antibody tested for *B. henselae* by her physician was negative. The reason for this discrepancy may be due to the fact that our western blot detects antibody to all 5 feline *Bartonella* whereas the human test was specific for antibodies to *B. henselae*. The technician may have been infected with *B. clarridgeiae* and not *B. henselae*. No azithromycin was given and the signs persist.

Figure 1

Chronic conjunctivitis & scleral injection

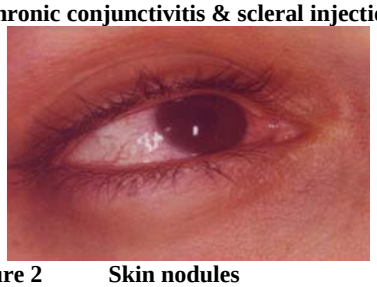
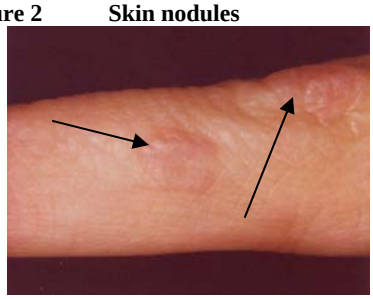


Figure 2 Skin nodules



Case 6: Cat Owner: Cat Scratch Disease

A 27-year-old married New Jersey women called us to test her cats for *Bartonella* after her physician diagnosed her with CSD and told her to "get rid of your cats." She had 3 cats, all from shelter backgrounds, in the household. The owner's history was alarming in that she was originally misdiagnosed with breast cancer due to a lump in her breast. She had been scratched on her right forearm by one of her cat's hind claws. Four months later she developed fever, aches and fatigue along with pain in her right axilla. An abscess developed in the axilla along with a lump and tenderness in her right breast. Two weeks of Ampicillin did not improve her condition and she was diagnosed with breast cancer by ultrasound. Fortunately she sought a second opinion from an infectious disease specialist who quickly diagnosed cat scratch disease. Treatment with doxycycline for 2 months was successful. Two of the 3 cats were strongly positive for *Bartonella* on our test and the 3rd cat was a +2, questionable. All 3 cats were treated successfully with azithromycin. The woman tested positive by our western blot test and by a licensed human test while her husband tested negative. This case illustrates that invasive diagnostic test procedures, such as biopsies, may be needed in CSD cases to rule out more severe illnesses.

Case 7: Cat Owner: Bacillary Angiomatosis

A homeless HIV-infected drug addict presented to a NYC hospital with fever and red lumps on his face and chest after adopting a healthy 16-week-old stray kitten from the street. The kitten was heavily infested with fleas. We were asked to test the kitten for *Bartonella*. The kitten was strongly positive +4 by our test. In addition, the patient was also strongly positive for *Bartonella* on our test and was confirmed by a licensed human test. The patient was treated with erythromycin for 4 weeks and the fever and skin lesions resolved completely.

Case 8: Child: Cat Scratch Disease

A 6-year-old boy was admitted to a NYC hospital with fever and axillary lymph node enlargement. He reported having a 2-year-old cat but there was no history of a scratch or bite. The owners reported seeing no fleas on the cat but it had been adopted as a stray. Red papules developed on the boy's arm followed by development of axillary lymphadenopathy. We tested the boy and found antibody to *Bartonella*, which was confirmed by a licensed human test. We then asked the parents if we could test the cat but were told "the grandmother's Pit Bull ate the cat last week."

Case 9: Child: Cat Scratch Disease

A 5-year-old boy, living in Michigan, was diagnosed clinically and by serology with CSD. We were called to test the 8 cats in the household. We found 7 of the 8 cats to be strongly positive (see Figure below).

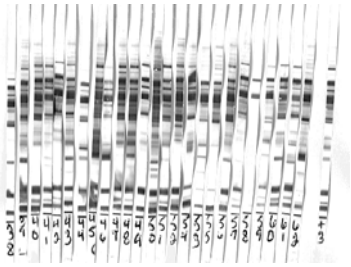
Western Blot for *Bartonella* Antibody

The authorities were threatening to remove the children from the household due to the numerous cats and the CSD occurrence. After we stated that the cats could be treated to remove the *Bartonella* infection the family was permitted to keep the cats and their children. All of the cats were treated with azithromycin.

Case 10: Cat Owner: Cat Scratch Disease

Twenty-four of 25 cats (Figure below), living in an Ohio household, where a person developed CSD and one cat had uveitis, were strongly positive for *Bartonella*. The danger to humans in such a household is significant.

Western Blot for *Bartonella* Antibody



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5. Eskow, E. et al.: Archives of Neurology 58: 1357-1363, 2001.
6. Massei, F. et al. European Journal of Pediatrics 159: 416-419, 2000.

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NEWSLETTER

Feline *Bartonella* Diseases: Pathogenesis and Description

Evelyn E. Zuckerman, Editor **Summer 2003** **Vol. 2, Number 3**

In This Issue:

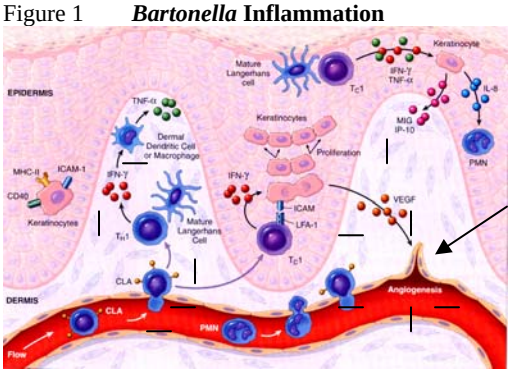
The summer 2003 issue of the NVL Newsletter will review the pathogenesis and the spectrum of feline *Bartonella* diseases.

Bartonella Pathogenesis

Feline *Bartonella* are Gram-negative bacilli that possess pili which are hair-like structures found on the bacteria's surface. *Bartonella* have a strong tendency to stick or clump together in tissues and in culture and to stick to, and penetrate, RBCs and endothelial cells. The ability to adhere to each other, and to the membranes of RBCs and endothelial cells, leads to the wide and varied tissue pathogenesis observed in cats, dogs and people. Pili and a protein called deformin are probably responsible for the sticky properties.[1]

The wide tissue tropism of *Bartonella* is due to the adhesion to endothelial cells which are the constituents of capillaries. *Bartonella* proteins stimulate endothelial cells (Figure 1) to proliferate causing neovascularization or angiogenesis. Thus, *Bartonella* induce chronic lymphocytic plasmacytic granulomatous inflammatory reactions in highly vascular tissues throughout the infected animal's body. These tissues are: oral and respiratory mucosa, ocular tissues, the gastro-intestinal tissues, the skin, and organs such as the liver, spleen and lymph nodes. In fact, since capillaries are found in all tissues, all tissues are susceptible to the inflammatory effects of *Bartonella*. The tissue reactions are apparent to the cat owners and veterinarians in the mucosa of the mouth, eye and respiratory tract or evidenced in the GI tract by chronic vomiting or diarrhea.

Figure 1 ***Bartonella* Inflammation**



Legend: The black rods (--) represent *Bartonella* in the skin or mucosa. The bacteria induce angiogenesis (arrow) and an outpouring of inflammatory cytokines which recruit inflammatory cells such as lymphocytes, plasma cells and macrophages.

Feline *Bartonella* Diseases:

Feline *Bartonella* diseases are characterized by chronic inflammation of vascular tissues.[2-16] Inflammatory reactions often occur concurrently in multiple sites such as the oral and respiratory tissues, ocular and oral tissues or in other combinations. Although numerous pathogenic organisms can cause inflammatory diseases in various tissues, it appears that *Bartonella* is the cause of about 50% of the following conditions:[14,16]

Feline *Bartonella* Diseases:

Oral Disease:
- Gingivitis
- Stomatitis
- Oral Ulcers
- Submandibular lymphadenopathy

Respiratory Diseases:
- URI
- Rhinitis
- Sinusitis

Ocular Disease:
- Uveitis
- Chorioretinitis
- Conjunctivitis

Intestinal Diseases:
- Inflammatory bowel disease
- Diarrhea (chronic)
- Vomiting (chronic)

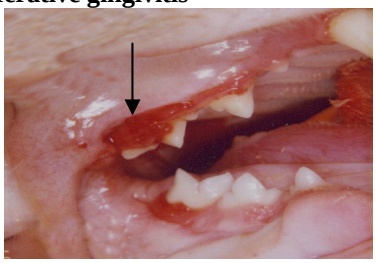
Other Diseases:
- Lymphadenopathy
- Fever of unknown origin
- Hepatic peliosis
- Bacillary angiomatosis
- Valvular heart disease (murmurs)

Experimentally induced feline diseases include: fever, lymphadenopathy, renal disease, neurological signs, anemia, reproductive failure, cardiac lesions and cholangitis.[6-8,12,13] We and others have described chronic inflammatory diseases associated with *Bartonella* infections in pet cats.[2,4,7,14,16] It should be noted that many of these diseases, identical to those seen in cats, were first found to be caused by feline *Bartonella* in humans.

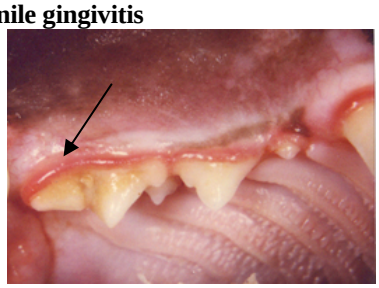
Bartonella references can be obtained at:
www.nlm.nih.gov/

The following are a group of photographs of *Bartonella* diseases of pet cats.

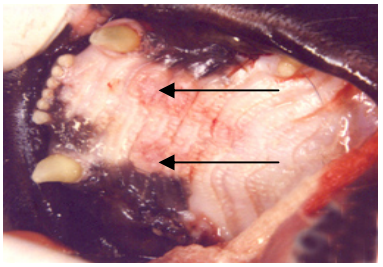
Proliferative gingivitis



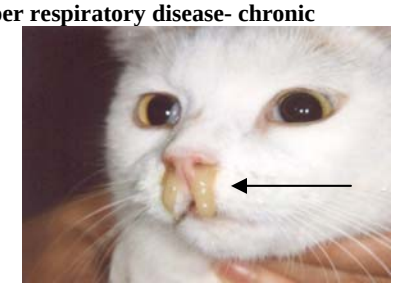
Juvenile gingivitis



Oral ulcers

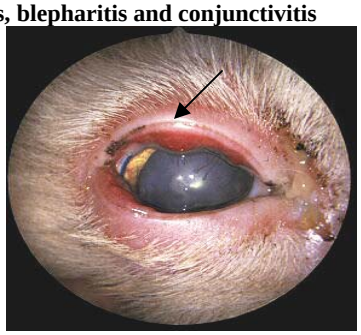


Upper respiratory disease- chronic

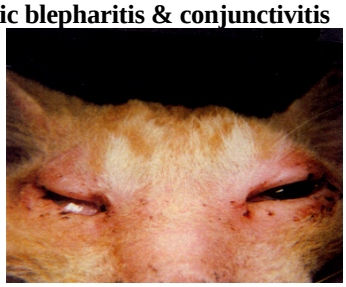


Rhinitis- chronic 1.5 years

Uveitis, blepharitis and conjunctivitis

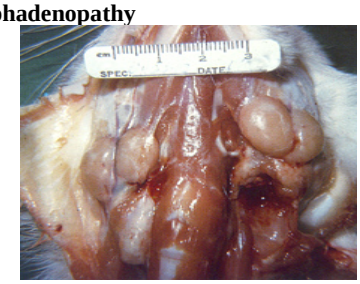


Chronic blepharitis & conjunctivitis

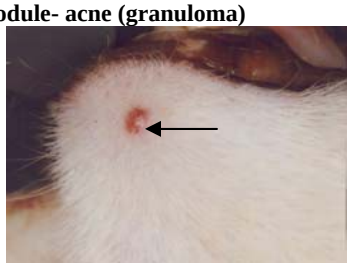


Chronic conjunctivitis

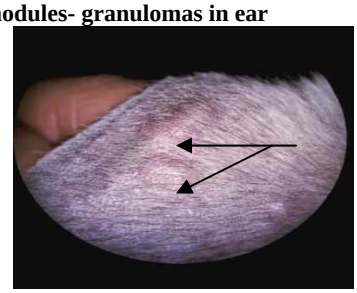
Lymphadenopathy



Skin nodule- acne (granuloma)



Skin nodules- granulomas in ear



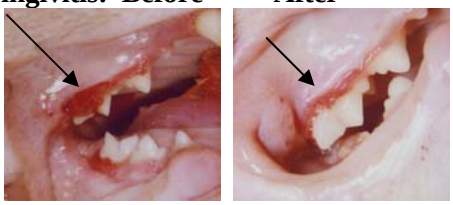
Diarrhea- chronic

Therapy

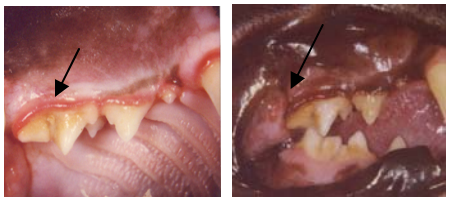
Therapy of feline *Bartonella* diseases is relatively easy. We recommend oral azithromycin-10mg/kg once daily for 21 days. We have reported successful therapy results in approximately 80% of cats with *Bartonella* diseases.[5,15,17] Therapy failures may be explained by the possibility that the presence of *Bartonella*, in these cats, may represent only coincidental infections and may not be the cause of the clinical disease.

Therapy Results:

Gingivitis: Before After



Before After



Respiratory Disease:

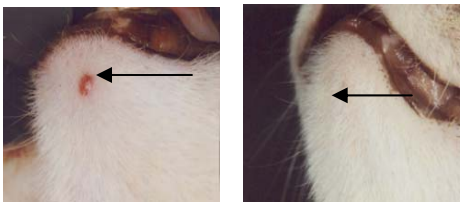
Before After

Conjunctivitis:

Before After

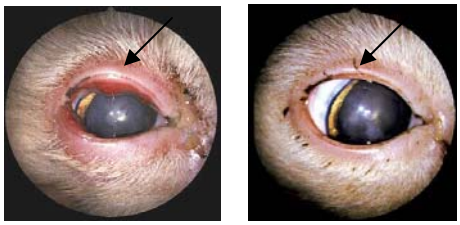
Skin Nodule:

Before After



Uveitis & Conjunctivitis:

Before After



Case photographs courtesy of:

Jan Corbishley, B.S. Oradell Animal Hospital, Paramus, NJ: gingivitis, respiratory disease & skin nodule- chin.

Dr. Jack Broadhurst, Cat Health Clinic, Pinehurst, NC: Blepharitis & conjunctivitis and chronic diarrhea.

Dr. Kerry Ketring, All Animal Eye Clinic, Cincinnati, OH: uveitis & ear skin nodules.

Dr. Larry Kantrowitz, Oradell Animal Hospital, Paramus, NJ: rhinitis.

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16. Hardy, WD, Jr., Zuckerman, E., & Corbishley, J. Serological evidence that *Bartonella* cause gingivitis and stomatitis in cats. American Veterinary Dental Society Meeting, Savannah, GA, October 2002.
17. Hardy, WD, Jr., Corbishley, J., & Zuckerman, E.E. Azithromycin therapy of *Bartonella*-infected cats with gingivitis and stomatitis. American Veterinary Dental Society Meeting, Savannah, GA, October 2002.

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NEWSLETTER

Bartonella and Skin Diseases

Evelyn E. Zuckerman, Editor **Fall 2003** **Vol. 2, Number 4**

In This Issue:

The fall 2003 issue of the NVL Newsletter will discuss the association of *Bartonella* and skin diseases in cats and humans and a diabetes therapy alert. Human *Bartonella*-induced skin lesions often occur at the site of a scratch or bite of a cat.[1,2] In this regard, *Bartonella clarridgeiae* was first shown to be a human pathogen when it was isolated from a veterinarian who developed a cat scratch disease skin lesion at the site of a cat scratch.[1, 3]

Bartonella and Skin Diseases

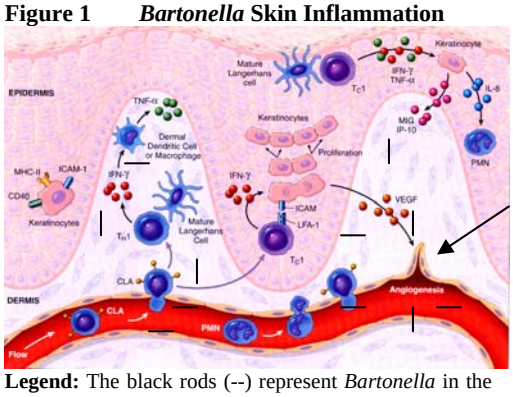
Cats:

Pathogenesis:

Bartonella stick or clump together in tissues and stick to, and penetrate, RBCs and endothelial cells. The ability to adhere to each other, and to the membranes of RBCs and endothelial cells, leads to the wide and varied tissue pathogenesis observed in cats, dogs, and people. Pili, hair-like structures found on the bacteria's surface, and a protein called deformin, are probably responsible for the sticky properties.[4]

The wide tissue tropism of *Bartonella* is due to the adhesion to endothelial cells which are the constituents of capillaries. *Bartonella* proteins stimulate endothelial cells (Figure 1) to proliferate causing neovascularization or angiogenesis. Thus, *Bartonella* induce chronic lymphocytic plasmacytic granulomatous inflammatory reactions in any tissue, including the skin.

Figure 1 *Bartonella* Skin Inflammation



Legend: The black rods (--) represent *Bartonella* in the blood, skin, or mucosa. The bacteria induce angiogenesis (arrow) and an outpouring of inflammatory cytokines which recruit inflammatory cells such as lymphocytes, plasma cells, and macrophages.

BARTONELLA-INDUCED SKIN DISEASES:

Human:
Cutaneous bacillary angiomatosis
Cutaneous rash- Henoch-Schenlein purpura
Cutaneous granuloma annulare

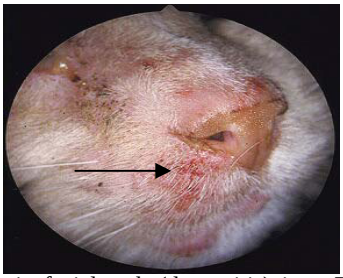
Feline:
Cutaneous papules- "acne"
Cutaneous granulomas
Dermatitis- rash

The skin reactions are apparent to the cat owners and veterinarians as rashes, red raised papules "acne", and granulomas (Figures 2-9). We found 105 of 204 (52%) cats with skin conditions were infected with *Bartonella* (Table 1).[5-7] Many of the infected cats with skin conditions also had concurrent inflammatory disease in other sites such as gingivitis, uveitis, conjunctivitis and URI.

Table 1
***Bartonella*-Associated Skin Diseases in Cats**

Disease	# Tested	# Positive	% Positive	> X Healthy
Healthy	620	122	20%	X
Dermatitis-rash	123	63	51%	2.5X
Papules "Acne"	39	18	46%	2.3X
Granulomas	42	24	57%	2.8X
Totals	204	105	52%	2.6X

Figure 2



Chronic facial rash (dermatitis) in a *Bartonella* infected cat with chronic uveitis. The uveitis and facial skin rash resolved completely with azithromycin therapy.[8, 11]

Dr. Kerry Ketring:
All Animal Eye Clinic, Cincinnati, OH

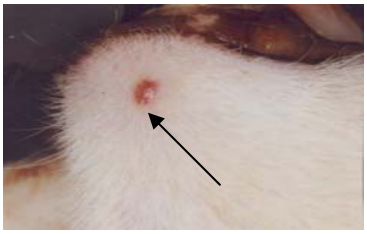
Figure 3a Before Therapy

Chronic facial rash (dermatitis) in a cat with chronic conjunctivitis and blepharitis.

Figure 3b After Therapy

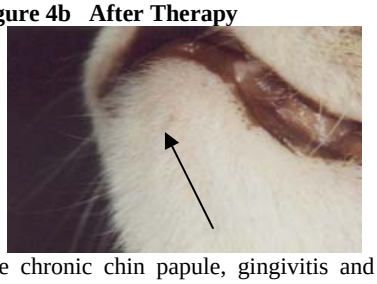
The skin rash and eye inflammation resolved completely with azithromycin therapy.[9-11]
Dr. Jack Broadhurst,
Cat Health Clinic, Pinehurst, NC

Figure 4a Before Therapy



Chronic chin papule "acne" in a young cat who also had gingivitis and chronic URI.

Figure 4b After Therapy

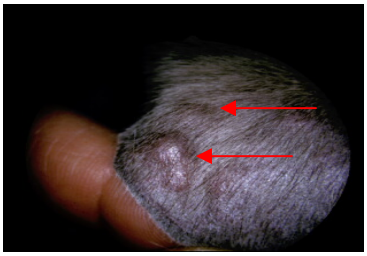


The chronic chin papule, gingivitis and URI completely resolved after azithromycin therapy. **Jan Corbishley, R.V.T.: Oradell Animal Hospital, Paramus, NJ**

Figure 5 Papule

Cutaneous papule in a 6 month old kitten who also had chronic gingivitis. This lesion is similar to the papule seen, at the scratch or bite site, in many people with CSD. We isolated 1000 *Bartonella* per ml from the blood of this cat. The gingivitis and skin lesions completely resolved with azithromycin therapy.

Figure 6 Granulomas



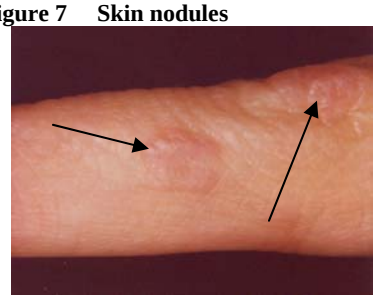
Large cutaneous granulomas in the ear of a cat with chronic uveitis. The uveitis and ear nodules completely resolved with azithromycin therapy.[8]

Dr. Kerry Ketring:
All Animal Eye Clinic, Cincinnati, OH

Human:

Bartonella-induced skin diseases (bacillary angiomatosis, rashes and granulomas) were first described in humans and similar conditions were then recognized in cats.[1-6]

Figure 7 Skin nodules



Two raised non-erythematous papules in a veterinary technician at the site of a cat scratch that persisted for several weeks. She was positive for *Bartonella* antibody.

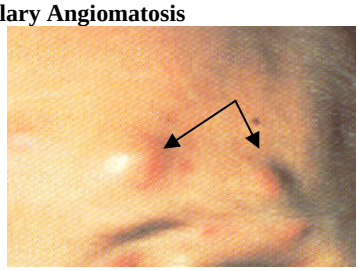
Case 1: Henoch-Schenlein Purpura

The 17-month-old son of a veterinarian developed a persistent red rash on his right forearm which resembled Henoch-Schenlein purpura, a cutaneous rash that can be caused by several bacteria, one of which is *Bartonella*. The family's cat, that had continually licked the boy's right hand, tested positive for *Bartonella*. The boy was indeterminate for *Bartonella* and the rash resolved without therapy.

Case 2: Cat Owner: Bacillary Angiomatosis

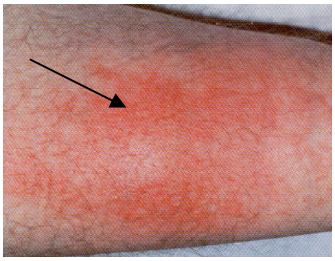
A homeless HIV-infected drug abuser presented to a NYC hospital with fever and red lumps on his face and chest after adopting a healthy 16-week-old stray kitten from the street. The kitten was heavily infested with fleas and was strongly positive for antibody to *Bartonella*. The patient was also strongly positive for *Bartonella* antibody. The skin lesions and fever completely resolved after 4 weeks of erythromycin therapy.

Figure 8
Bacillary Angiomatosis



Bacillary angiomatosis on the face of an HIV infected IV drug abuser who adopted a 16-week old *Bartonella*-infected kitten.

Figure 9 Skin Rash- Dermatitis



Erythematous dermatitis in the pre-tibial area of a *Bartonella*-infected patient.

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Bartonella references can be obtained at:
www.nlm.nih.gov/

Bartonella Therapy Alert Diabetes Mellitus

It has come to our attention, through the very astute observations of Dr. Phillip Raclyn of the Riverside Veterinary Group, New York, NY and Yorktown Animal Hospital, Yorktown Heights, NY, that azithromycin therapy of *Bartonella* infected cats with diabetes mellitus may markedly alter the requirement for insulin maintenance. Dr. Raclyn has treated two *Bartonella*-infected diabetic cats (treated for other *Bartonella*-associated diseases) with 21 days of azithromycin and noted that one cat no longer required insulin to maintain a normal blood glucose level. The second cat went into a hypoglycemic coma while being treated with azithromycin. The cat recovered and presently requires significantly less insulin for blood glucose maintenance.

We theorize that *Bartonella* may be responsible for inducing inflammation of the pancreas in some cats resulting in diabetes mellitus. Thus, when azithromycin therapy removes the *Bartonella*-infection, and resulting pancreatic inflammation, the insulin controlled glucose metabolism may return to normal in some cats. In this regard we have checked our *Bartonella* Fe*Bart*® Test records and found that 63 of 123 (51%) cats with diabetes were infected. Most of these diabetic cats were being tested for another reason, such as gingivitis, URI or another *Bartonella*-associated inflammatory disease.

Inflammation of the insulin producing tissues of the pancreas may cause malfunction resulting in inadequate insulin release and altered glucose metabolism. We would like to obtain follow-up information on azithromycin treated diabetic cats.

****RECOMMENDATION****

The blood glucose levels of *Bartonella*-infected diabetic cats, who are being maintained on insulin, should be monitored closely during azithromycin therapy. Alteration of the insulin maintenance dose may be required.