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NEWSLETTER

Recent *Bartonella* Publications:

Evelyn E. Zuckerman, Editor **Winter 2008** **Vol. 7, Number 1**

In This Issue:

In the winter 2008 issue of the NVL Newsletter we will review important recent animal and human *Bartonella* publications. There are 1,835 *Bartonella* scientific articles at the time of this writing including several articles, describing psychotic and fatal neurological complications.

Bartonella in Animals:

Kangaroos:

Kangaroos and prairie dogs are the most recent animals to join the growing list of animals that are chronic carriers of *Bartonella*. There are presently more than 20 *Bartonella* species distributed among: humans, cats, cougars, dogs, foxes, wolves, horses, cattle, sheep, squirrels, voles, mice, rats, rabbits, guinea pigs, raccoons, bats, sea turtles, and porpoises. Arthropod vectors that transmit *Bartonella* among and between animals are: fleas, ticks, keds, biting flies, sand flies, and lice. Although *Bartonella* has not yet been found in mosquitoes, it seems probable that they will also be added to the list of *Bartonella* vectors in the future.

***Bartonella australis* sp. Nov. from Kangaroos, Australia. Fournier, P-E., Taylor, C., Barrassi, L., Smith, G., and Raoult, D. Emerging Inf Dis, 13:1961, 2007.**

Only 2 *Bartonella* species, *B. henselae* and *B. quintana*, had been found in Australia until this discovery. Three *Bartonella* isolates were cultured from the blood of 5 *Macropus giganteus* grey kangaroos from central coastal Queensland, Australia. This is the first *Bartonella* isolated from kangaroos or from any marsupial. The new *Bartonella* species is related more closely to *B. elizabethae* and *B. tribocorum* which are often found in rodents. It will be interesting to determine if any *Bartonella* diseases are found in people who handle or care for kangaroos.

Eastern grey kangaroo

Prairie Dogs:

Temporal and Spatial Patterns of *Bartonella* Infection in Black-tailed Prairie Dogs (*Cynomys ludovicianus*). Bai, Y., Kosoy, M.Y., Ray, C., Brinkerhoff, R.J., and Collinge, S.K. Microb. Ecol. 56:373, 2008

Bartonella were cultured from 20 black-tailed prairie dog colonies in Boulder County, CO from 2003-2005. *Bartonella* were found in all colonies and the overall prevalence was 23.1% but varied from 4.8% to 42.5% in various colonies. The prevalence in prairie dogs was lower than in other rodent species. The public health significance of *Bartonella* in prairie dogs remains to be elucidated.

Prairie dog colony

Bartonella in Humans:

Almost all human publications concerning cat scratch disease (bartonellosis) begin with the following general statement "Cat scratch disease is typically a self-limiting illness which does not require antibiotic therapy." Although this is true for ~80% of CSD cases, more severe sequelae are being reported each year. *Bartonella* infections of humans are not "usually self-limiting" as the following publications will demonstrate. Both neurological and cardiovascular effects of *Bartonella* infection can be life-threatening.

A Case of Fatal Disseminated *Bartonella henselae* Infection (Cat Scratch Disease) with Encephalitis. Fouch, B., and Coventry, S. Arch Pathol Lab Med, 131: 1591, 2007.

A 6-year-old, previously healthy, Hispanic boy presented with left axillary lymphadenopathy. He had exposure to a dog and cat, but not to kittens. Cephalexin and ibuprofen therapy were instituted for presumed CSD. He quickly developed fever, vomiting, and abdominal pain followed by severe headaches and several seizures. His condition continued to deteriorate by hospital day 4 with mental status changes, seizures and finally respiratory arrest. Blood cultures were sterile and head computed tomography revealed diffuse cerebral edema with effacement of basilar cisterns. The patient died and the family gave permission for an autopsy.

The axillary lymph node was negative for *Bartonella* organisms by special stain but was positive by PCR assay. Examination of the brain was negative by PCR and for *Bartonella* organisms. Extensive evaluation for other infectious etiologies was also negative. The brain had inflammatory infiltrates, perivascular cuffing and small microglial nodules. There was evidence of widespread necrotizing granulomas in the spleen. Serology for *B. henselae*, IgG 1:128 and IgM <1:16, was interpreted as "equivocal." **Editor's Note: These serologic data are interpreted by some laboratories as positive. The lack of IgM but 1:128 IgG titer indicates chronicity even though, after antibiotic therapy, the patient presented with acute illness and died within 4 days of hospitalization.**

Bivalvular *Bartonella henselae* Prosthetic Valve Endocarditis. Vikram, H., Bacani, A.K., DeValeria, P., Cunningham, S.A., & Cockerill, F.R., III. J Cl Micro, 45:4081-4084, 2007.

This is a case report of a life-threatening *Bartonella henselae* endocarditis involving prosthetic mitral and aortic valves. A 43-year-old male was diagnosed with culture-negative endocarditis of the mitral and aortic valves in 1999. He was given an aortic homograft and porcine mitral valve followed by 6 weeks of antimicrobial therapy. An etiology for the endocarditis was never established and he remained in good health after the surgery until 2005. In August 2005 he developed severe fatigue and intermittent fevers. Blood cultures were sterile. By November 2005 he progressed to increasing fatigue, persistent fevers and crescentric glomerulonephritis- acute renal

insufficiency. *Bartonella* serology was not performed. One month later, thickened leaflets and vegetations were noted on the aortic and mitral valves. *Bartonella* serology was then performed and the results were *B. henselae* IgG 1:1,024, *B. quintana* IgG 1:16,384 and, corresponding IgM titers were negative (<1:20). The patient then reported acquiring a kitten 6 months prior to the onset of his symptoms and having been scratched and bitten on a regular basis. He did not recall seeing fleas on the kitten. At surgery the aortic homograft leaflets were found to be destroyed and the porcine mitral valve had multiple vegetations. The damaged valves were replaced with St. Jude mechanical valves and PCR analysis demonstrated *Bartonella henselae* in the vegetations.

Postoperatively the patient was treated with a regime of gentamicin, doxycycline, vancomycin, and ceftriaxone. Gentamicin was given for 2 weeks and he remained on doxycycline for 1 year. He was advised to avoid contact with cats and remains well 18 months after surgery. A review of the literature found a total of 6 other cases of *Bartonella* prosthetic valve endocarditis. The 3 cases that had valve replacement surgery survived, whereas 2 of the 3 patients who did not have valve replacement surgery died. This case demonstrates the importance of considering infectious endocarditis (including *Bartonella*) in the differential diagnosis of glomerulonephritis despite the sterile blood cultures.

Editor's Note: This case highlights the necessity for veterinarians to alert their immunosuppressed clients- heart valve replacement patients, cancer therapy patients, organ transplant patients and HIV-infected people to the potential risk of *Bartonella* from cats. Veterinarians should counsel their immunosuppressed clients to have their cats tested and to avoid contact with cats whose *Bartonella* status is unknown.

Stroke as a Manifestation of Acute *Bartonella henselae* Endocarditis. Schneer, S., Marcoviciu, D., Beilin, V., Goffman, M., and Dicker, D. Harefuah, 146:902, 2007.

A 37-year-old male was hospitalized due to low grade fever and weakness. He was diagnosed with infective endocarditis caused by *B. henselae*. His mitral valve was severely damaged and he experienced a cerebrovascular event (stroke) caused by septic emboli. The patient had severe neurological damage due to his stroke and his mitral valve was replaced. The authors conclude that "there should be a high index of suspicion for the presence of this pathogen (*B. henselae*) in cases presenting with signs of infection associated embolic events."

Editor's Note: Dr. Charla Jones, Veterinary Cardiology and Medicine Service, Austin, TX, has treated many *Bartonella* infected cats, and a few dogs, with heart valve disease, cardiomyopathy and aortic thrombi which are analogous to the previous report and this case.

***Bartonella tamiae* sp. Nov., a Newly Recognized Pathogen Isolated from Three Human Patients from Thailand. Kosoy, M., *et al*., J Clin Micro, 46:772-775, 2008.**

Three strains of a novel *Bartonella* species (B. tamiae) were cultured from human patients in Thailand. The human disease spectrum and animal host reservoir(s) are unknown.

Do *Bartonella* Infections Cause Agitation, Panic Disorder, and Treatment-Resistant Depression? Schaller, J.L., Burkland, G.A., and Langhoff, P.J. MedGenMed, 9:54, 2007.

This report is a very important observation of the unrecognized psychiatric and depressive illnesses caused by *Bartonella*. Three patients developed acute onset personality changes, agitation, depression, and panic attacks. Initial *Bartonella* clinical signs of CSD- skin papules, regional lymphadenopathy, fever, and an angiomatosis rash were not recognized as indicating *Bartonella* infections. After unsuccessful psychiatric therapy, these patients were tested for *Bartonella* infections.

Case 1: A 41-year-old minister underwent dramatic personality changes after returning from a camping trip to North Carolina where he had removed 3 *Ixodes* deer ticks from his leg and shoulder. Five weeks later he complained of fever and painful lymphadenopathy of his right axillary lymph node. He tested negative for the Lyme disease agent at the CDC but was serologically positive for *B. henselae* (IgG 1:256). He developed serious agitation, panic attacks, and major depression and was diagnosed by his psychiatrist as having bipolar disorder. High doses of psychotic drugs and antidepressants had minimal effect and the patient had episodes of throwing objects during periods of agitation. After consulting an infectious disease physician he was treated with azithromycin and rifampin for 8 weeks. Finally, when his lymphadenopathy resolved, his psychiatric and aggression signs returned to normal.

Case 2: A medical student presented with an "unusual rash" on her thighs, measuring 2-4 by ½ inches which was diagnosed by a dermatologist as angiomatosis. Cushing's syndrome, Kaposi's sarcoma and HIV infection were ruled out as the cause. She complained of panic attacks, profound restlessness, depression, and information processing limitations that began around the time of the appearance of her rash. Treatment with psychotic drugs and antidepressants had minimal effect. She had major risk factors for *Bartonella* infection including recent adoption of kittens from a shelter, numerous flea bites, and allowing the kittens to sleep in her bed. She explained that her cats routinely licked her hands, mouth and often gently scratched and bit her when playing. Although the authors did not report performing PCR or serology for *Bartonella*, the patient's nurse practitioner had seen a case of CSD and suggested that the patient had *Bartonella*-induced bacillary angiomatosis. Based on this clinical assumption, the patient was treated with azithromycin for 8 weeks. Despite a recurrence after 6 months, which was treated for an additional 3 months, she recovered fully and all psychiatric symptoms resolved.

Case 3: A Midwestern businessman began to have new adult-onset social anxiety, panic attacks, generalized anxiety disorder, and major depression all of which began several months after returning from a camping and hunting trip in Florida. Shortly after returning from the trip he experienced "flu" and fever for about 9 days. He also developed 3 raised papules under his left arm. He reported no rashes, tick attachments, flea exposure or dog or cat contact. However, his camping partner did have a tick bite and was treated for Lyme infection due to an oval pink rash. Treatment with psychotic drugs and antidepressants had minimal effect. Although he tested negative for Lyme disease by western blot and *Bartonella* by PCR, he was seropositive for *Bartonella* IgG at 1:128. After failing treatment with doxycycline (100 mg BID) for 3 weeks he was treated with rifampin (300 mg BID) and trimethoprim-sulfamethoxazole (160 mg/800 mg BID) for 1 month. The patient rapidly returned to approximately 85% normal.

Conclusion: Patients with *Bartonella* induced psychiatric disorders generally require higher doses of antidepressants, benzodiapines, or the use of antipsychotic drugs to function normally. The psychotic signs and depression resolved after treatment for their *Bartonella* infections. The authors stated: "The presence of *Bartonella*-induced psychiatric symptoms should not be surprising. First, psychiatric disorders are brain disorders, and *Bartonella* is documented as causing many diverse neurologic brain disorders. Second, *Bartonella* infections are associated with RBCs, which allow small *Bartonella* bacteria (a fraction of the RBC size) to enter the brain's vascular system. These *Bartonella*-infected RBCs probably cause psychiatric morbidity due to brain pathology, as indicated by the fact that some *Bartonella* patients have neurologic disorders, such as seizures, hemiplegia, ischemic strokes, transverse myelitis, and multiple granulomatous lesions, as well as meningitis and encephalitis.[1-3]"

Editor's Note: This is a very important paper which infers that *Bartonella* may be responsible for some psychiatric and depressive disorders. Such conditions should be investigated in people with frequent contact with cats such as shelter workers, cat breeders, cat "collectors", veterinarians and veterinary hospital personnel.

Musculoskeletal Manifestations of Cat Scratch Disease. Bickels, M.E., *et al*., Clin Infect Dis, 45:1535, 2007.

Musculoskeletal manifestations (MMs) were studied, over an 11 year period in Israel, in 913 people with CSD. MMs were defined as myalgia, arthritis, arthralgia, tendonitis, osteomyelitis, and neuralgia. 96 of 913 (10.5%) of CSD patients developed MMs. Myalgia and arthropathy occurred most often and usually was chronic in duration. Seven patients had symptoms for more than 1 year and 5 developed chronic disease. The authors conclude that MMs are more common than previously reported and affect 10% of CSD patients. MMs occurred more often in patients older than 20 years of age and arthropathy was more common in females. Osteomyelitis, the most well known MM of CSD, is in fact, the least common.

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NEWSLETTER

Have a Heart or Broken Heart
Bartonella and Cardiovascular Diseases

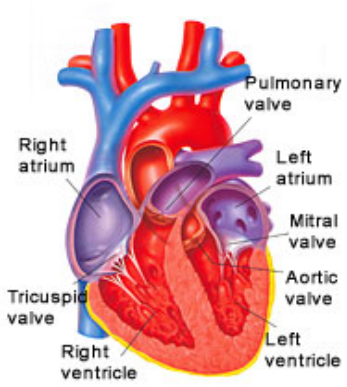
Evelyn E. Zuckerman, Editor **Spring 2008** **Vol. 7, Number 2**

In This Issue:

In the spring 2008 issue of the NVL Newsletter we will discuss the *Bartonella*-induced cardiovascular disease of cats, dogs, and humans. This is one *Bartonella* disease entity where there is clear evidence that *Bartonella* does cause disease in all 3 species.

***Bartonella* cardiovascular diseases are life-threatening in all 3 species.**

"A good heart is worth gold."
William Shakespeare



Cardiovascular Diseases Caused by *Bartonella*

The main cell target for *Bartonella* infection is the endothelial cell which lines capillaries and the cardiovascular system.[1-2] *Bartonella* attach to and penetrate endothelial and other cells which protects the bacteria from immune attack and stimulates the formation (angiogenesis) of new blood vessels.[1,2] Thus, it is not surprising that some of the *Bartonella*-induced diseases occur in the cardiovascular system, especially in the heart.

Bartonella-induced Cardiovascular Diseases

Vasculitis
Heart Disease:
- **Endocarditis (valvulitis)**
- **Myocarditis**
- **Pericarditis**

Thromboembolism (stroke)

"If I can stop one heart from breaking I shall not live in vain."
Emily Dickinson

Human *Bartonella* Cardiovascular Diseases

As for all of the *Bartonella* disease discoveries, the human has served as the "animal model" for cardiovascular diseases of animals.[3-6] There have been numerous reports of *Bartonella*-induced cardiovascular diseases in people and similar diseases have now been reported in other species including dogs, cats, and cattle.[7-17] Of the 23 species of *Bartonella*, 7 have been found to cause infective endocarditis (IE) in people: *B. quintana*, *B. henselae*, *B. elizabethae*, *B. vinsonii* subsp *berkhoffii*, *B. vinsonii* subsp. *arupensis*, *B. koehlerae*, and *B. alsatica*.[18] All but 2 of these *Bartonella* are found in our pet cats and dogs. One to 15% of all cases of IE in people are caused by these zoonotic *Bartonella* which are hard to detect by routine blood cultures because of their fastidious nature. Thus, the most widely used method for the laboratory diagnosis of infection is serology.[18]

IE, a microbial infection of the endocardial surface, affects native and prosthetic heart valves, chordae tendineae and the mural endocardium.[18] About 85% of the cases involve the aortic valve. IE may cause extracardiac signs including fever, heart murmur, petechiae of skin, nails (Figure 1), conjunctiva, and oral mucosa and glomerulonephritis, and liver dysfunction.[6]

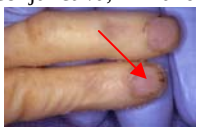


Figure 1

Severe complications include emboli to the CNS (stroke), spleen, liver, and kidneys. Several studies found that combined medical (prolonged antibiotics) and surgical (valve replacement) therapy is required.[19, 20]

The following case report encompasses many important points for the diagnosis and therapy of *Bartonella* infections and diseases and supports many of our previous recommendations.

"A wounded heart can with difficulty be cured."
Johann Wolfgang von Goethe

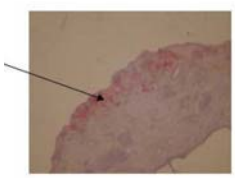
From Cat Scratch Disease to Endocarditis, the Possible Natural History of *Bartonella henselae* Infection.

F. Gouriet, Lepidi, H., Habib, G., Collart, F., and Raoult, D.
BMC Inf Dis. 7:30, 2007

There are many reports that *Bartonella* cause a typical IE which is easily diagnosed using the Duke IE criteria[21] and usually present with valvular vegetations that are detected by electrocardiography. These patients often have a pre-existing cardiac valve lesion, most often from rheumatic fever in childhood (group A *Streptococci*). Although they are exposed to cats, most do not have a history of cat scratch disease (CSD). This is the first case report describing a patient who suffered from CSD and subsequently developed the sequelae of *B. henselae*-induced IE.

A 41 year-old man was hospitalized with mitral valve regurgitation. He had a history of a car accident and developed destructive nosocomial *Staphylococcus aureus* endocarditis of the mitral valve. A bioprosthesis was inserted and failed but was reinserted. Now, 17 years later, there was a systolic murmur and regurgitation through the mitral valve again. Three blood cultures were sterile and he had valve replacement again. Histology, culture, and PCR analysis of the resected prosthetic valve showed the presence of *B. henselae* (Figure 2). Serum tested retrospectively for *B. henselae* IgG by western blot was positive with a titer of 1:200.

A.



B.

Figure 2 A) Immunohistochemical detection of *B. henselae* (arrow) in the resected mitral valve. B) Resected lymph node showing inflammatory granuloma. Reproduced with permission.

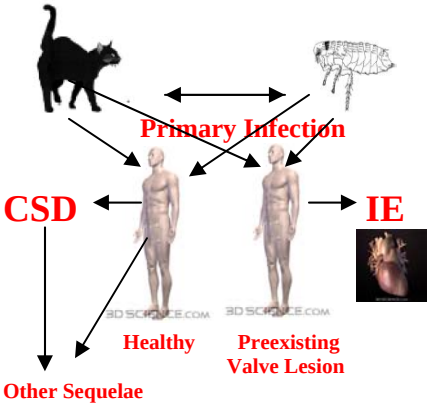
Retrospectively, it was discovered that 6 months earlier the patient was diagnosed with suspected lymphoma of the inguinal lymph node. Histology of the resected node showed necrotizing lymphadenitis suggestive of CSD. The patient was not a cat owner but reported a scratch from a stray cat in a single contact one month before the development of inguinal lymphadenopathy. There was no indication in the report of any antibiotic therapy at that time.

Seroprevalences of antibodies to *B. henselae* in healthy people have ranged from 3 to 6%.[22] This suggests that many *B. henselae* primary infections are asymptomatic. Patients with valvular lesions, who are asymptomatically infected and bacteremic, may be susceptible to eventually developing IE.

These authors state: "While antibiotic treatment is not currently recommended for patients with CSD,[23] treatment might be indicated in patients who have valve lesions as this might prevent IE as has been reported for patients with Q fever.[24] IE is a life threatening disease and it is critical that a diagnosis be made as soon as possible. We suggest that patients with CSD and valvular heart disease should be tested within a year for serological, blood culture or DNA detection of continued *B. henselae* infection. If these tests are positive, early antibiotic treatment may be indicated to prevent IE."

Editor's Note: This is a very important article which discusses the sequelae that can occur after CSD has resolved. It is the recommendation of our laboratory that all people with CSD be treated for at least 1 month with azithromycin in order to prevent any sequelae that may occur after regression of the CSD syndrome. Sequelae may be neurological, vascular (IE), arthropathy, and ocular-chorioretinitis. It seems imprudent not to treat to prevent the sequelae that occur in about 20% of people who have recovered from CSD.

Bartonella Pathogenesis



Adapted from reference 18.

"The heart of a wise man should resemble a mirror, which reflects every object without being sullied by any." Confucius

Dog *Bartonella* Cardiovascular Diseases

Like the human cardiovascular diseases, canine cardiovascular diseases are not common. They include: endocarditis, myocarditis, and possibly cardiomyopathy (Table 1). There are numerous reports documenting *Bartonella*-induced cardiovascular diseases.[7-17] As with people, IE in dogs involves the aortic valve most often (~70%) and about 70% of the cases have joint signs-arthropathy. Unlike most humans with *Bartonella* IE, dogs don't have to have preexisting valvular lesions to allow *Bartonella* to attach at an injured valve site. We found 17% (39/224) of dogs with heart disease seropositive for *Bartonella*.

Histologic changes in *Bartonella*-induced endocarditis include chronic lymphocytic and histiocytic cell infiltrates, mineralization, and endothelial cell and vascular proliferation which is typical of *Bartonella*-induced inflammation in any tissue. *Bartonella* within the endothelial and endocardial cells was noted in one study.[14] *Bartonella* may get to the endocardium or valvular endothelium by direct invasion from the blood stream or they may migrate through small blood vessels at the base of the valve.[14] In fact, both possibilities may occur.

Cat *Bartonella* Cardiovascular Diseases

Bartonella-associated cardiovascular diseases of cats include: endocarditis, myocarditis, cardiomyopathy, and thromboembolism (saddle thrombus). Myocarditis was induced in 8 of 13 experimentally infected cats.[25] However, there is only one documented case of *Bartonella* induced endocarditis in a pet cat.[17] The cat had a grade III/IV systolic murmur, arrhythmia, severe cardiomegaly, high titer of *Bartonella* antibody, was seronegative for other organisms, was blood culture negative and, *Bartonella* was found in the damaged aortic valve at necropsy.

We found 1,052 of 2,205 (48%) of cats with cardiovascular diseases to be seropositive for *Bartonella*. Table 1 gives a summary of the *Bartonella* antibody incidence in cats with major cardiovascular clinical signs. Although *Bartonella* may cause cardiovascular diseases in cats, definitive proof of the extent awaits further studies.

Table 1. Seroprevalence of *Bartonella* in Cardiovascular Diseases*

Disease	Dog	Cat
Vasculitis	2/19 11%	6/11 55%
Murmur	13/66 20%	566/1,184 48%
Endocarditis	9/33 27%	41/69 59%
Myocarditis	6/40 15%	162/342 47%
Arrhythmia	8/30 27%	40/78 51%
Embolism	None	12/18 67%

***Many cats had several clinical signs.**

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For more *Bartonella* references:
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NEWSLETTER

Therapy of *Bartonella* Infection and Disease

Evelyn E. Zuckerman, Editor **Summer 2008** **Vol. 7, Number 3**

In This Issue:

The summer 2008 issue of the NVL newsletter will discuss the therapy of *Bartonella* infected cats. We will present ways to assess *Bartonella* therapy considering various treatment outcomes.

Clinical Aspects of *Bartonella* Therapy

Healthy Cats:

Since healthy cats do not show clinical inflammatory signs, evaluation of the elimination of *Bartonella* infection can only be accomplished using the therapy titration test.

Cats with Inflammatory *Bartonella* Diseases:

Many inflammatory diseases of cats have a polymicrobial etiology. That is, *Bartonella*, other bacteria, fungi and viruses can act together, in various combinations, to cause chronic inflammation in many organ systems. Follow-up evaluations of 7,086 treated cats with inflammatory diseases show that 80% had a greater than 50% improvement and 33% had total resolution of their diseases (Table 1).

Table 1

Clinical Response of 7,086 Cats with *Bartonella* Diseases

% Clinical Improvement	Number of Cats	% of Cats Improved
Excellent 100%	**2,370**	**33%**
Excellent 80-99%	**1,892**	**27%**
Good 60-79%	**735**	**10%**
Fair 50-59%	**712**	**10%**
None <50%	**1,314**	**19%**
Worse	**63**	**1%**
Totals:	**7,086**	**100%**

Tables 2 and 3 present various clinical therapy scenarios that the practitioner may face when treatment of *Bartonella* infected diseased cats results in only partial clinical resolution. The tables give likely explanations for observed therapy outcomes and make recommendations as to further clinical protocols to follow.

Bartonella infected cats with inflammatory diseases can be evaluated for resolution of their clinical signs and for the elimination of *Bartonella* infection using the therapy titration test. The observation of clinical signs does not always correlate with the successful elimination of *Bartonella* infection. For example, a cat with severe gingivitis may show no clinical improvement even though antibiotic therapy has eliminated *Bartonella* infection. In this case, the cause of the gingivitis was not due to *Bartonella* and *Bartonella* was only "in the background" in the cat. Cats that show 50-75% disease improvement, with a titer decrease, also probably have multiple causes of their disease.

Most often, cats with *Bartonella* inflammatory diseases, treated with azithromycin, rifampin, or doxycycline, will show significant clinical improvement of their disease (Table 1 & Figures 1 & 2).[1-4] However, we are often asked by practitioners what to do when a *Bartonella* infected cat with inflammatory disease does not respond fully, or at all, to antibiotic therapy. Tables 2 & 3 present a summary of the various scenarios that may occur when practitioners treat *Bartonella* infected cats with inflammatory diseases.

How to use Table 2: Evaluate the clinical response to therapy of the treated cat and go to the row corresponding to the % improvement observed. Choose the appropriate further therapy in the corresponding columns to the right.

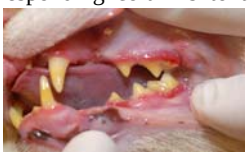

Figure 1
Gingivitis before therapy

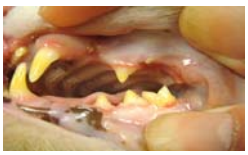

Figure 2
After therapy- 80% improved. See Table 2 rows 5 & 6 for further therapy.

Jan Corbishley, VT, Oradell Animal Hospital, Paramus, NJ

Table 2

Clinical Management of *Bartonella* Inflammatory Diseases

Disease Improvement at End of 21 Days of Azithromycin Therapy	Veterinarian's Decision: Further Therapy Possibilities	Recommendations
1. No improvement	Assume *Bartonella* is **not** eliminated: Re-treat for *Bartonella* with rifampin for 21 days	Submit therapy titration test 6 months after initial 21 days of therapy
2. No improvement	Assume *Bartonella* is eliminated: Treat with other antibiotics- Clindamycin, Amoxicillin, etc. for 2 weeks	Submit therapy titration test 6 months after initial 21 days of therapy
3. 10-49% improved	Assume *Bartonella* is **not** eliminated: Re-treat for *Bartonella* with rifampin for 21 days	Submit therapy titration test 6 months after initial 21 days of therapy
4. 10-49% improved	Assume *Bartonella* is eliminated: Treat with other antibiotics- Clindamycin, Amoxicillin , etc. for 2 weeks	Submit therapy titration test months after initial 21 days of therapy
5. 50-99% improved	Assume *Bartonella* is **not** eliminated: Re-treat for *Bartonella* with rifampin for 21 days	Submit therapy titration test 6 months after initial 21 days of therapy
6. 50-99% improved	Assume *Bartonella* is eliminated: Treat with other antibiotics- Clindamycin, Amoxicillin , etc. for 2 weeks	Submit therapy titration test 6 months after initial 21 days of therapy
7. 100% resolved	No further therapy	Submit therapy titration test 6 months after initial 21 days of therapy
8. 100% resolved but disease recurred	Assume *Bartonella* is eliminated: Treat with other antibiotics- Clindamycin, Amoxicillin , etc. for 2 weeks	Submit therapy titration test 6 months after initial 21 days of therapy
9. 100% resolved but disease recurred	Assume *Bartonella* is **not** eliminated: Re-treat for *Bartonella* with rifampin for 21 days	Submit therapy titration test 6 months after initial 21 days of therapy

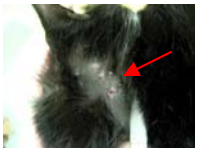

Figure 3
Dermatitis- papules before therapy.

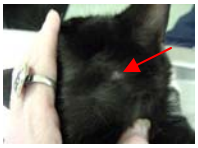

Figure 4
After therapy- 90% improved. If there is a titer decrease-see Table 3 row 6- columns 3 and 4 to the right for interpretation and recommendation.

Dr. Patricia Burke, Tiogue Veterinary Clinic, Coventry, RI.

Bartonella Therapy- 8 Years

During our first 8 years of *Bartonella* testing, we have performed 9,782 therapy titration tests to determine elimination of infection in *Bartonella*-seropositive pet cats 6 months after treatment with: azithromycin (n=9,162), rifampin (n=469) and doxycycline (n=151). A 2 fold titer decrease occurred in 1,119 cats (11.4%) and a 4 fold or greater titer decrease occurred in 7,583 cats (76.5%). Thus, post therapy titer decreases (treatment success) occurred in 87.9% of *Bartonella*-infected cats. 78 of 88 (88.6%) *Bartonella*-seropositive dogs also had post therapy titer decreases (2 fold n=8, 4 fold or greater n=70). Antibiotic therapy of *Bartonella*-seropositive cats and dogs can be effectively monitored using a comparative WB titration test.

Disease Recurrence after Therapy:

Although we do not have accurate statistics for the recurrence of disease following *Bartonella* therapy, we estimate that approximately 15% of cats with inflammatory disease have some degree of recurrence following successful therapy. Most of these cats have a *Bartonella* titer decrease which suggests that the recurrence is due to something other than *Bartonella.*

Table 4
Disease Recurrence and Therapy Titrations: in 103 Cats

Therapy Titer Result	No.	%
Increase titer	8	8%
No titer decrease	14	13%
2 Fold titer decrease	26	25%
4 or > Fold decrease	55	54%

What Does a Positive *Bartonella* Test Mean?

Healthy cat: cat is infected but not showing any inflammatory disease.

Cat with Inflammatory Disease:

1. Cat is infected and *Bartonella* is the sole agent causing the disease or;
2. Cat is infected and *Bartonella* is the partial cause of the disease (polymicrobial disease) or;
3. Cat is infected and *Bartonella* is not the cause of any of the disease- *Bartonella* is "in the background" or;
4. Cat is NOT infected and the positive test (detection of antibody) is an indication of past infection. The cat cleared the infection before the test was taken. This is not common (~5%) as most cats remain infected for years, if not their entire lives.

Table 3 Clinical and Laboratory Evaluation of Inflammatory Diseases and *Bartonella* Therapy

Practitioner's Clinical Evaluation: Disease Improvement	Therapy Titration Test: *Bartonella* Infection Status	Evaluations Based on Clinical Response and Therapy Titration Test	Recommendations
1. No improvement	No titer reduction Still infected	Unsuccessful disease and *Bartonella* therapy	Retreat for *Bartonella*
2. No improvement	Titer reduction Infection eliminated	Unsuccessful disease therapy but successful *Bartonella* therapy. *Bartonella* is not the cause of disease	Retreat for other causative agent(s) with Clindamycin, Amoxicillin, etc. for 2 weeks
3. 10-49% improved	No titer reduction Still infected	Unsuccessful disease and *Bartonella* therapy	Retreat for *Bartonella*
4. 10-49% improved	Titer reduction Infection eliminated	Unsuccessful disease therapy but successful *Bartonella* therapy. *Bartonella* is not the cause of disease	Retreat for other causative agent(s) with Clindamycin, Amoxicillin, etc. for 2 weeks
5. 50-99% improved	No titer reduction Still infected	Partial successful disease therapy but unsuccessful *Bartonella* therapy. *Bartonella* is not the cause of disease	Retreat for *Bartonella*
6. 50-99% improved	Titer reduction Infection eliminated	Partial successful disease therapy and successful *Bartonella* therapy	Retreat for other causative agent(s) with Clindamycin, Amoxicillin, etc. for 2 weeks
7. 100% resolved	No titer reduction Still infected	Successful disease therapy but unsuccessful *Bartonella* therapy. *Bartonella* is not the cause of disease	Retreat for *Bartonella*
8. 100% resolved	Titer reduction Infection eliminated	Successful disease and *Bartonella* therapy. *Bartonella* was the cause of the disease	**CELEBRATE!!**
9. 100% resolved but disease recurred	No titer reduction Still infected	Unsuccessful disease and *Bartonella* therapy	Retreat for *Bartonella*
10. 100% resolved but disease recurred	Titer reduction Infection eliminated	Unsuccessful disease but successful *Bartonella* therapy. *Bartonella* is not the cause of the recurrence	Retreat for other causative agent(s) with Clindamycin, Amoxicillin, etc. for 2 weeks

How to use Table 3: Evaluate the clinical response to therapy of the treated cat and go to the row corresponding to the % improvement observed. In the column to the right, find the therapy titration result and follow the evaluations and recommendations in the last 2 corresponding columns.

Bartonella Re-infection

***Bartonella* treated cats can be re-infected by fleas or ticks after successful therapy. Thus, it is imperative that life-long flea control be instituted. We do not have a test that can determine if a cat has been re-infected. If you suspect that a cat has been re-infected the only option is to re-treat for presumed *Bartonella* infection.**

References:

1. Hardy, W.D., Jr., Zuckerman, E.E., Corbishley, J. *et al.* Successful therapy of *Bartonella henselae* bacteremic healthy pet cats. Annual Meeting, 1nfectious Disease Society of America, New Orleans, September, 1996.

2. Hardy, WD, Jr., Zuckerman, EE, Corbishley, J, Gold, JWM[3], Baron, P, Polsky, B, Gilhuley, K, Kiehn, TE, and Armstrong, DA. Efficacy of high dose, long duration Doxycycline or Azithromycin treatment for *Bartonella* infections in pet cats. Internat Conf Am Soc for Rickettsiology, Big Sky, MT, August, 2001.

3. Hardy, WD, Jr., Corbishley, J., & Zuckerman, E.E. Azithromycin therapy of *Bartonella*-infected cats with gingivitis and stomatitis. Am. Vet. Dental Soc. Meeting, Savannah, GA, October 2002.

4. Ketring, KL, Zuckerman, EE & Hardy, WD, Jr. *Bartonella*: A new etiological agent of feline ocular diseases. JAAHA, 40: 6-12, 2004.