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NEWSLETTER

Have a Heart or Broken Heart
Bartonella and Cardiovascular Diseases©

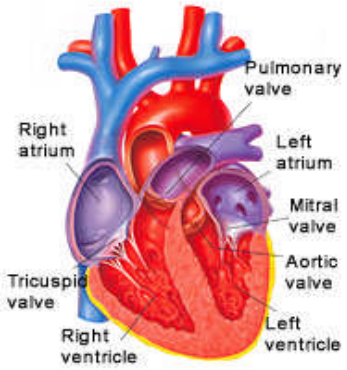
Evelyn E. Zuckerman, Editor **Spring 2008** **Vol. 7, Number 2**

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

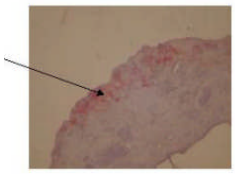
From Cat Scratch Disease to Endocarditis, the Possible Natural History of *Bartonella henselae* Infection.

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.

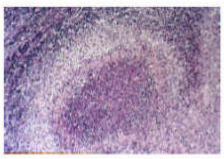


Figure 2 A) Immunohistochemical detection of *B. henselae* (arrow) in the resected mitral valve. B) Resected lymph node showing inflammatory granuloma. Reproduced with permission.

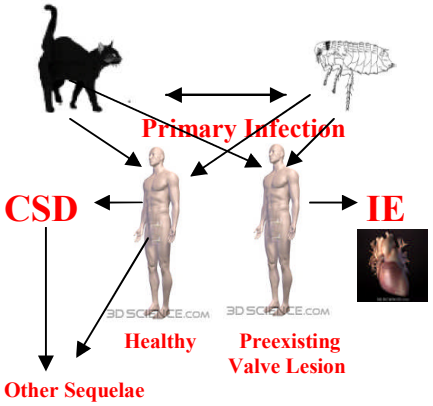
Retrospectively, it was discovered that 6 months earlier the patient was diagnosed with suspected lymphoma of the inguinal lymph node. Histology of the resected node showed necrotizing lymphadenitis suggestive of CSD. The patient was not a cat owner but reported a scratch from a stray cat in a single 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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