

# Bartonellosis: Current concepts for diagnosis and management

Despite having little effect on cats, various species of *Bartonella* can cause medical problems in humans

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**B**artonella henselae, the causative agent of cat scratch disease (CSD) in humans, has been the focus of intensive scientific inquiry over the previous decade. Substantial research into this organism has been undertaken in both veterinary medicine and human medicine although, until recent years, the bulk of the work has focused primarily on human bartonellosis. This small pleiotrophic bacterium appears to peacefully co-exist with the domestic cat; its potential role as a feline pathogen has not been conclusively demonstrated. If it is a feline pathogen at all, it would appear to be a relatively innocuous one. Unfortunately, such is not the case for human beings. A number of different medical disorders arise in humans as a result of infection with various species of *Bartonella*. These diseases include cat scratch disease, bacillary angiomatosis, bacillary (hepatic) peliosis, trench fever and endocarditis. Because CSD tends to take a relatively benign course in most people, bartonellosis was not considered

a major threat to human health until the human immunodeficiency virus (HIV) gained a foothold in society. Because large segments of our population are immunosuppressed through retroviral infection or because of chemotherapy for cancer or organ transplants and because we now have a greater appreciation for the zoonotic potential of the genus *Bartonella*, we must embrace a changing clinical picture for bartonellosis. It would seem reasonable to consider all cases of human bartonellosis potentially serious.

## ■ Scratching the surface

Of the human diseases associated with *Bartonella* spp., CSD is the most well-known. It was first reported in 1931 but the etiologic agent remained undetermined for decades. For a number of years, *Afipia felis* was considered the most likely agent but supportive evidence for its role could not be found in serologic studies. A breakthrough occurred in 1983 when a small gram-negative bacillus was recognized in lymph nodes from patients with CSD following application of Warthin-Starry silver stain to histologic sections of tissue. Just a few years later, two articles representing inde-

Photo 1:  
Most, but not all,  
cases of cat  
scratch disease  
are associated  
with a cat  
scratch or bite.



Photo: Centers for Disease Control

pendent work appeared in the same 1990 issue of the *New England Journal of Medicine*; each contained revolutionary information related to the causative agent of CSD. One paper described the application of polymerase chain reaction (PCR) technology to bacteria found in bacillary angiomatosis lesions of AIDS patients. Organisms closely related to *Rochalimaea quintana*, the cause of human trench fever, were identified. In the other paper, blood cultures from CSD patients grew out a

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similar gram-negative organism. Strong evidence for the role of *Rochalimaea henselae*, now *Bartonella henselae*, was put forth in each of these landmark reports. Many infectious disease specialists feel that the discovery of *Bartonella henselae* as the cause of CSD will represent one of the most interesting and unique medical discoveries of the 20<sup>th</sup> century.

The purpose of this paper is to review the human and feline health implications associated with bartonellosis.

### ■ Cat Scratch Disease

Although cat scratch disease is the most well-known form of bartonellosis, it represents only one of five distinct clinical syndromes associated with *Bartonella* spp. infection. (The other forms have been previously listed.) The number of reported cases of CSD reported each year varies between resources, ranging from 6,000 to 22,000 new cases annually.

Without a reasonable index of suspicion, physicians may fail to document the epidemiologic features of CSD. In most cases, the initial sign of CSD is a

small, erythematous papule which develops at, or near, the site of a cat scratch (see Photo 1 p. 36). Most lesions occur on the hands, arms or face. Regional lymphadenopathy may develop two or three weeks later; the node is typically tender and obviously swollen. More cases are reported in fall and winter, when cats may come indoors and have closer contact with humans. Children are more often affected than adults, with 60 percent of cases occurring in patients less than 20 years of age. Contact with a cat (especially kittens) is common to the history of most cases, although 20-30 percent have no history of contact with a cat (see Photo 2). A scratch is most commonly reported, but some cases have been associated with a cat bite (see Photo 3, p. 38).

Both immunocompetent and immunodeficient humans may become infected. In the majority of cases, especially with presence of a functional immune system, the course of disease is limited to a few weeks and results in eventual recovery. Treatment of localized disease is controversial because there have been no controlled studies which prove that antibiotic therapy alters the course of disease. In most cases, treatment is limited to symptomatic therapy, such as anti-inflammatory drugs. In immunocompromised patients (such as those with HIV or those receiving cancer chemotherapy or other immunosuppressive therapy), the disease may be much more serious. Instead of remaining limited to cutaneous lesions and regional lymph nodes, the infection may progress to bacteremia and significant systemic involvement.

For those patients that require hospitalization, substantial healthcare costs are dedicated to treatment. In 1992, it was estimated that the annual cost of caring for CSD patients in the United States was \$12 million dollars, with an average hospital stay of four days.

To date, the mechanism of transfer

of *B. henselae* from cat to human remains elusive. Intradermal inoculation of flea feces is most likely, although it has not yet been proven. Presence of the organism within the oral cavity of cats makes bite wounds another potential route.

### ■ Forms of human bartonellosis

Trench fever, a disease transmitted by the human body louse and caused by *B. quintana*, reached epidemic proportions during World War I as troops were forced into unsanitary and overcrowded conditions. It began to steadily decline after World War II but

Photo 2: Contact with kittens less than 6 months of age is a common epidemiologic finding in cat scratch disease.

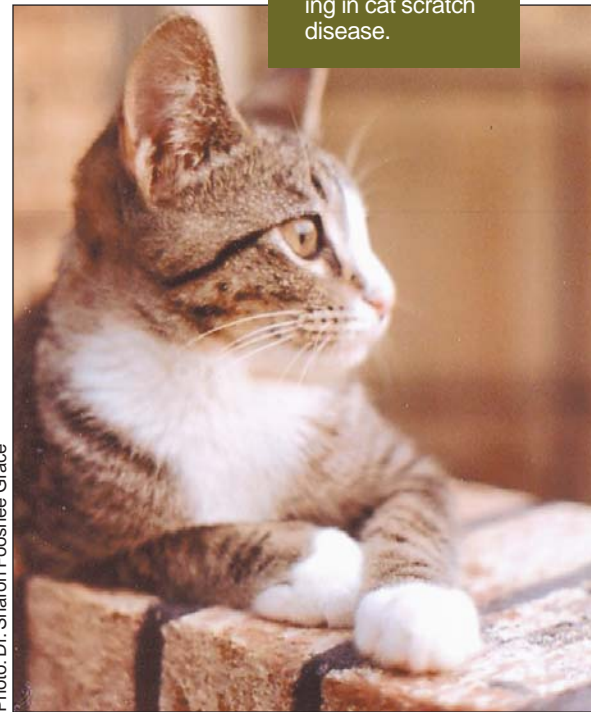


Photo: Dr. Sharon Fooshee Grace

started to re-emerge in the 1980s as greater numbers of people were immunosuppressed because of AIDS or as a result of immunosuppressive medication. More recently, it has been reported among chronic alcoholics and homeless people; researchers have termed this "urban trench fever." This remains an important opportunistic pathogen of immunocompromised humans.

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Bacillary angiomatosis and bacillary (hepatic) peliosis may be caused by *B. quintana* or *B. henselae*. These diseases are most often found in severely immunocompromised people, such as those suffering from the advanced stages of AIDS infection. Bacillary angiomatosis lesions develop when poorly formed blood vessels proliferate and form cysts or lobules. In at least 50 percent of cases, the lesions are cutaneous and appear as an erythematous papule. When similar blood-filled cysts occur in the liver and/or spleen, the disease is called bacillary (hepatic) peliosis. These diseases represent a pathologic response which is very distinct from that of CSD, although physi-

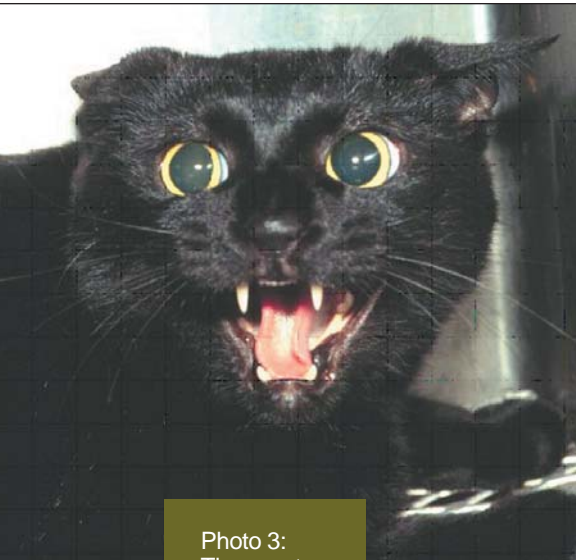


Photo 3: The exact mechanism by which cats transmit *Bartonella* to humans remains unknown.

Photo: Dr. Gary Norsworthy

cians are unsure as to the reason(s). One infectious disease specialist indicated that *Bartonella* spp. might be the only infectious organism capable of producing pure angiogenesis in humans.

In 1993, *Bartonella* was associated with endocarditis in humans for the first time. Three species of *Bartonella* were found capable of inducing vegetative cardiac lesions.

### ■ Feline Bartonellosis

*Bartonella henselae* is the most common species infecting the domestic cat, although

two others may occur (*B. clarridgeiae* and *B. koehlerae*) and co-infection with more than one species is possible. The prevalence of bacteremia in healthy cats is variable but may be quite high (25-41 percent). Bacteremia tends to persist for months, or even years. Interestingly, some cats may be bacteremic in the absence of detectable antibody. Rates of seropositivity are even higher than those for bacteremia, especially in areas which effectively support reproduction of fleas. Despite the fact that CSD is associated with kittens, rates of seropositivity increase with age of the cat. Eight years is the average age for seroreactivity. Seropositivity may occur in the absence of proven bacteremia.

Transmission between cats requires the participation of an arthropod vector. Evidence is mounting for a possible role of ticks as vectors but, to date, most cases appear to involve the cat flea, *Ctenocephalides felis*. After a flea feeds on a *B. henselae*-infected host cat and ingests a blood meal, the organism is passed in flea excreta. As a cat scratches the skin in response to a flea bite, infectious material is inoculated in and around the claws and nail beds. As the infected cat scratches another cat, *B. henselae* is inoculated intradermally into the naive cat. The organism has also been identified in oral secretions of the cat by PCR amplification of bacterial DNA so oral transmission may yet be proven.

Infected cats typically have no apparent clinical signs of infection (see Photo 4, p. 39). Some recent research has shown that there may be a correlation between the presence of stomatitis and infection with *B. henselae*. Because the organism has been found in the oral cavity, this association will probably result in continued research. Endocarditis and uveitis have also been reported in naturally-occurring infections, but, as mentioned before, clinical signs very rarely occur.

Despite the fact that feline bartonellosis is often subclinical and has no overt

effect on most cats, scientists have not eliminated that possibility that the organism has long-term health implications for the cat. There has been speculation that the continued antigenic stimulation associated with prolonged bacteremia may be detrimental to the immune system, although no specific pathogenic mechanisms have been described to date.

Exposure of cats to *Bartonella* spp. can be demonstrated by detection of antibodies. However, as noted previously, some

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cats with culture-positive bacteremia have been found seronegative for antibodies. Also, because it is unknown how long it takes for cats to become seronegative after infection is cleared, presence of antibodies does not necessarily represent active infection. Blood culture is useful to prove bacteremia, though the organism is fastidious and may take four to six weeks to grow. Negative culture does not eliminate the potential for bacteremia in an individual cat. PCR assay is commercially available and is considered the preferred test at present. PCR can distinguish between infection with *B. henselae* and *B. clarridgeiae*. A blood sample is submitted and the cost for testing an individual cat is not prohibitive.

Although cats may be treated for bartonellosis, it is unclear whether this is necessary or even recommended. Most researchers are unsure whether treatment can result in complete elimination of the organism. Even if it does, the high prevalence of this disease in cats means that re-exposure and re-infection are probably common. In households where an immunosuppressed human resides, it would be reasonable to treat all infected cats and monitor them to be sure that, where possible, the infection is cleared.



Photo: Dr. Sharon Fooshee Grace



Photo 4: While many cats are infected with one or more *Bartonella* spp., clinical signs are not always apparent.

### ■ Conclusion

Clearly, our understanding of both human and feline bartonellosis has grown tremendously in recent years. As new information has become available, our understanding of this unique genus of bacteria has become more refined.

Both physicians and veterinarians can anticipate the results of future research endeavors as we share the common goal of providing improved health-care for our patients.

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Dr. Grace received her DVM degree from Mississippi State University in 1987. She is board-certified by The American Board of Veterinary Practitioners (Canine/Feline) and The American College of Veterinary Internal Medicine. For a number of years, she owned a referral internal medicine practice in Franklin, Tenn. She returned to Mississippi State in 1999 as an associate clinical professor. She is co-author of *The Feline Patient*, published by Lippincott Williams and Wilkins, and a client education series called "Info to Go." Her special interest is feline internal medicine.

### ■ Preventive measures

Because the flea appears to play a pivotal role in cat-to-cat transmission of *Bartonella henselae*, stringent flea control is advisable for prevention of human bartonellosis and to minimize spread of the organism between cats. Tick control should also be implemented because of the possible role these arthropods play in transmission. Declawing infected cats is not necessary because the disease appears to be occasionally transmitted to humans through contact alone, and CSD has been associated with cats that were declawed. As noted above, antimicrobial treatment of infected cats is not guaranteed to clear bacteremia. As such, it should not be considered an effective strategy to prevent CSD in humans. Thorough hand-washing after handling cats should be recommended, particularly for immunosuppressed individuals.

At this time, no vaccine is commercially available to prevent feline bartonellosis. Recent reports suggest significant antigenic variation among various *B. henselae* isolates in the same species. Additionally, when cats were infected with homologous species of *Bartonella* spp., cross protection against other species did not occur. As a result, multiple antigenic variants may be necessary to render a vaccine useful because some cats

are co-infected with more than one strain of *Bartonella*. This continues to complicate research efforts to develop an efficacious vaccine.

Because *Bartonella* spp. can be transmitted between cats by blood transfusion, all donor cats should be screened for bartonellosis before integration into a donor colony.

## Suggested reading

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