

Cat Scratch Disease and Other *Bartonella henselae* Infections

Cat Scratch Fever, Benign Inoculation Lymphoreticulosis, Benign Inoculation Reticulosis, Regional Granulomatous Lymphadenitis, Parinaud's Oculoglandular Syndrome, Bacillary Angiomatosis

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Etiology

Cat scratch disease

Cat scratch disease is, in most cases, caused by *Bartonella henselae*, a fastidious, pleomorphic, gram-negative rod. *B. henselae* was formerly called *Rochalimaea henselae*. *B. henselae* belongs to the family *Bartonellaceae*. This family, which was once thought to belong to the order Rickettsiales, has been removed from that order. There are two major serotypes/genotypes of *B. henselae*: type I (Houston I) and type II (BA-TF/Marseille). Strain variations are thought to exist within these serotypes. *B. clarridgeiae*, also found in cats, has been implicated in a case of cat scratch disease in a veterinarian. *Afipia felis*, formerly thought to cause this disease, has been eliminated as a significant cause.

Other human diseases caused by Bartonella henselae

B. henselae causes bacillary angiomatosis and peliosis hepatis, mainly in immunocompromised individuals. Bacillary angiomatosis is also caused by *B. quintana*, a non-zoonotic pathogen carried by humans. *B. henselae* can cause endocarditis in people with pre-existing valve disease. *B. henselae* can cause fever of unknown origin in humans.

Other Bartonella species implicated in human or animal disease

Other species of *Bartonella* may also be emerging human and/or animal pathogens. All *Bartonella* species are very closely related and may cross-react in serologic assays.

Some *Bartonella* spp. cause disease in their natural host (e.g. *Bartonella quintana* in humans). Other members of this genus typically cause prolonged asymptomatic bacteremia in their reservoir hosts. Species isolated from asymptomatic cats include *B. henselae*, *B. clarridgeiae*, *B. koehlerae* and *B. weissii*. *Bartonella* species have also been found in asymptomatic dogs, coyotes, foxes, rodents, rabbits, elk, deer, bighorn sheep and domestic cattle. *Bartonella* spp. found in animals and implicated in human disease include:

- *B. vinsonii* subsp. *berkhoffii* has been isolated from healthy dogs and coyotes. It has also been implicated in cases of canine granulomatous lymphadenitis, granulomatous rhinitis, liver disease, endocarditis, fever of unknown origin, and sudden death. This species may cause endocarditis in people with pre-existing valve disease.
- *B. vinsonii* subsp. *arupensis* has been isolated from the blood of a cattle rancher with fever and heart valve disease. This organism can also be found in rodents.
- *B. elizabethae*, found in rodents, may cause endocarditis in humans.
- *B. washoensis* has been implicated in human cardiac disease. Rodents are probably the reservoir host.
- *B. grahamii*, found in rodents, may cause human uveitis.

Geographic Distribution

B. henselae occurs worldwide. *B. henselae* type I is more common in the eastern U.S., where it represents approximately half of all isolates, than in the western states. Type II is the dominant serotype in Europe, and type I in Asia.

Transmission

B. henselae is probably transmitted between cats by cat fleas (*Ctenocephalides felis*). Experimental studies have shown that fleas, or the intradermal inoculation of flea feces, can spread the infection between cats. Transmission is reduced or absent when fleas are controlled. *B. henselae* has also been isolated from ticks but the role of this organism is unknown. Whether *B. henselae* can be spread among cats by other routes is unknown. Oral inoculation of infectious flea feces did not transmit the infection. In one experiment, *B. henselae* was not spread by sexual contact or vertically to kittens.

Transmission to humans is not completely understood. Cases of cat scratch fever are usually reported in people who have been scratched, bitten or licked by cats. It is possible that the source of infection is cat claws or teeth contaminated by flea feces. It has also been suggested, but not proven, that fleas may be able to transmit *B. henselae* directly to humans. In Parinaud's oculoglandular syndrome, a form of cat scratch fever that affects the eye, the site of inoculation is thought to be the eyelid or conjunctiva.

This syndrome may occur when patients rub their eyes after contact with a cat.

Cases of cat scratch disease have also been reported after exposure to squirrels, dogs, goats, crab claws and barbed wire. Some of these cases could be due to other species of *Bartonella*.

Disinfection

The disinfectant susceptibility of *B. henselae* does not seem to have been published; however, the closely related organism *Bartonella bacilliformis* is susceptible to common disinfectants including 70% ethanol, 1% sodium hypochlorite and 2% formaldehyde.

Infections in Humans

Incubation Period

The incubation period in humans is usually 3 to 10 days, but may be as long as 20 days.

Clinical Signs

Catch scratch disease

In immunocompetent people, *B. henselae* causes cat scratch disease, a mild to severe, self-limiting infection. The initial skin rash, seen in 25-90% of patients, consists of one or more small erythematous papules, pustules, macules, vesicles or ulcers at the site of inoculation. One to four weeks later, one or more lymph nodes become enlarged; soon afterward, the skin lesions disappear. The affected lymph nodes are usually painful or tender, and the skin over the nodes is warm, reddened and indurated. Occasionally, the nodes may suppurate. The lymphadenopathy usually lasts for a few weeks to a few months, but in some patients the lymph nodes have remained enlarged for up to 2 years. Other common symptoms are a fever, malaise and fatigue. The fever usually disappears within 2 weeks but fatigue may persist for weeks or months. Less often, there may be headaches, anorexia, vomiting, nausea, weight loss, splenomegaly, generalized pain or a sore throat.

Complications and atypical presentations are reported to occur in 5-16% of patients.

- Parinaud's oculoglandular syndrome occurs in 2-6% of patients. This syndrome is characterized by non-purulent unilateral conjunctivitis, conjunctival granuloma and periauricular lymphadenopathy. It usually resolves without permanent damage.
- Encephalitis has been reported in 1-7% of patients with cat scratch disease. It usually occurs 2 to 6 weeks after the classic symptoms.

- Cranial or peripheral nerve involvement may include myelitis, optic neuritis with transient unilateral blindness, facial nerve paresis or transient peripheral neuropathies. Patients with myelitis can be extremely weak, with abnormal reflexes, sensory loss and sphincter dysfunction.
- In people with existing heart valve abnormalities, *B. henselae* bacteremia can result in endocarditis.
- Disseminated disease occurs in less than 1% of patients. The usual signs are a persistent spiking fever, hepatosplenomegaly and abdominal pain.
- Other reported complications include transient non-specific maculopapular or nodular rashes, thrombocytopenic purpura, osteolytic lesions, arthritis, synovitis and pneumonia.

Cat scratch disease is usually a self-limiting infection, and the complications generally resolve without sequelae. Patients with CNS disease may take up to a year to recover.

Bacillary angiomatosis and bacillary peliosis

B. henselae can cause bacteremia and systemic disease in immunocompromised individuals, particularly people with AIDS. This organism has been found in patients with fever of unknown origin. It also causes bacillary angiomatosis (epithelioid angiomatosis), a vascular proliferative disease of the skin and/or internal organs.

Bacillary angiomatosis can occur in immunocompetent persons, but is most often an AIDS-related disease. The most apparent symptoms are one to hundreds of cutaneous papules and nodules, which may resemble granulomas, Kaposi's sarcoma (violaceous nodules), or lichenoid violaceous plaques. They vary in size from pinhead-sized to 10 cm in diameter. Subcutaneous nodules resembling a common abscess may also be seen. In addition, bacillary angiomatosis can involve the internal organs, including the heart, brain, liver, spleen, larynx, lymph nodes and gastrointestinal tract. The symptoms vary with the organ(s) affected and may include neurologic signs, bone pain, weight loss or symptoms related to massive visceral lymphadenopathy.

Peliosis hepatis is a rare condition, caused by *B. henselae* as well as other pathogens, drugs and toxins. It is characterized by multiple blood-filled cysts and sinusoidal dilatation in the liver. The symptoms of peliosis hepatis may include fever, nausea, vomiting, diarrhea and hepatosplenomegaly. In some cases, it may be an incidental finding at necropsy. Peliosis hepatis can be seen in some patients with bacillary angiomatosis.

Communicability

B. henselae infections do not seem to be transmitted person-to-person by casual contact.

Diagnostic Tests

Most cases of cat scratch disease are diagnosed by the history and physical examination. *B. henselae* infections can be confirmed by culture of the organism, PCR or serology. Isolation of *B. henselae* is difficult, but may be accomplished using specialized media. This organism takes 9 to 45 days to grow. PCR can differentiate *B. henselae* from *B. quintana*, the other cause of bacillary angiomatosis.

Serologic assays include an indirect immunofluorescence assay and enzyme-linked immunosorbent assay (ELISA). Cross-reactions occur with other species of *Bartonella*. Cross-reactions have also been reported with other organisms including *Chlamydia* spp. and *Coxiella burnetti*. A rise in titer or the presence of IgM suggests a recent infection.

Histopathology of the lymph nodes, and sometimes liver or spleen, is suggestive but not diagnostic. The lesions of cat scratch fever and bacillary angiomatosis differ; cat scratch fever is characterized by stellate abscesses, and vascular proliferation is seen with bacillary angiomatosis.

Skin testing, using crude lymph node antigens, was used in the past. It is now an uncommon test; it was abandoned due to fears of transmitting other infectious agents such as the hepatitis viruses.

Treatment

Most cases of cat scratch disease in immunocompetent individuals are self-limiting. Treatment is usually supportive and symptomatic. Severely affected lymph nodes are occasionally excised. Although *B. henselae* is sensitive to a number of antimicrobials *in vitro*, antibiotics are not consistently effective for cat scratch disease. They may be recommended by some authorities, particularly if the lymph nodes are severely affected, the course of disease is prolonged, or organs other than the lymph nodes have become involved.

In contrast, bacillary angiomatosis caused by *B. henselae* usually responds well to antibiotics. Numerous antibiotics, including erythromycin, doxycycline, rifampin, aminoglycosides, cefoxitin, cefotaxime, mezlocillin, trimethoprim-sulfamethoxazole and ciprofloxacin may be effective.

Prevention

Prevention depends on avoiding bites and scratches from cats, particularly kittens. Rough play with kittens should be discouraged, and any bites or scratches should immediately be washed with soap and water. Allowing the cat to lick the skin, particularly open wounds, should also be discouraged. Hand washing after contact with a cat may be helpful. Flea control may also be a preventative measure, but this is not certain.

Declawing does not appear to affect transmission but keeping the nails clipped is suggested by some sources. Preliminary data suggest antimicrobials may be able to clear the bacteremia in cats; however, it is not known whether these cats are susceptible to reinfection or recrudescence.

Morbidity and Mortality

An estimated 22,000 to 24,000 cases of cat scratch disease are thought to occur in the U.S. each year. Prevalence rates ranging from 1.8 to 9.3 cases per 100,000 persons have been reported. In the U.S., 3.6% to 6% of the general population has antibodies to *B. henselae*. Two studies reported seroprevalence rates of 7% and 51% in veterinarians in the U.S. and Europe, respectively. Any age can be affected, but most cases occur in children, who are more likely to be scratched or bitten. The incidence of disease is seasonal in temperate but not tropical areas, with the peak incidence from August to October in northern temperate regions.

Cat scratch disease in immunocompetent individuals is usually self-limiting and benign; however, the symptoms may last for 1 to 5 months and occasionally longer. Most people, including those with neurologic involvement, recover fully and deaths are extremely rare. Reinfection is infrequent.

Complications and disseminated diseases such as bacillary angiomatosis are more likely to develop in people who are immunocompromised. Bacillary angiomatosis usually responds well to antibiotics, but can be fatal if left untreated.

Infections in Animals

Species Affected

Cats and other felids are thought to be the only reservoir hosts for *B. henselae*. Organisms have been isolated from domestic cats, cheetahs and mountain lions. Antibodies have been found in domestic cats, Florida panthers, mountain lions, bobcats and cougars. Symptomatic infections have been reported only in some experimentally infected cats. However, there have been suggestions that *B. henselae* may be involved in some chronic feline diseases.

B. henselae has not, to date, been isolated from naturally infected animals other than the Felidae. *B. henselae* DNA was recently found in liver lesions (peliosis hepatis) in a dog, but bacterial isolation was not done. Armadillos are susceptible to experimental infection. Mice can also be infected under some conditions.

Incubation Period

In experimentally infected cats, cutaneous lesions may appear at the inoculation site within 2 days. Fever was first seen 2 to 16 days after inoculation. Whether symptoms occur in naturally infected cats is not yet known.

Clinical Signs

There is currently no firm evidence that *B. henselae* causes disease in any animal species; however, some experimental infections and serologic studies have suggested possible links to disease.

Cats

Naturally-infected bacteremic cats are asymptomatic. Some studies have suggested that *B. henselae* might be pathogenic under some circumstances: In one study, there was a significant increase in the incidence of lymphadenopathy and gingivitis in cats that were seropositive for both feline immunodeficiency virus (FIV) and *B. henselae*, compared to cats with antibodies only to FIV. Another study found a correlation between the presence of antibodies to *B. henselae* and stomatitis or kidney disease.

An association between *B. henselae* and uveitis has been proposed, based on the detection of antibodies to this organism in the serum and aqueous humor of an immunocompetent cat with uveitis. In a follow-up study, anti-*Bartonella* IgG was found in the aqueous humor of 7 of 49 cats with uveitis, and 0 of 49 healthy cats. Four of 9 experimentally infected cats also had IgG antibodies in the aqueous humor. Unexplained cataracts were reported in SPF cats from a commercial vendor within a year after the cats became naturally infected with *Bartonella*. The relationship between the cataracts and the infection is not known, and this association may be coincidental.

Experimental infections have been equivocal: In some experimental infections, all inoculated cats remained asymptomatic. In one experiment, cats developed inflammatory swellings or pustules at the site of inoculation. Several other studies have also reported clinical signs, including transient fever, lethargy, anorexia, myalgia and lymphadenopathy. Transient behavioral or neurologic dysfunction, consisting of disorientation, hypersensitivity to stimuli, lack of responsiveness to environmental stimuli, or increased aggressiveness, have been reported in some studies. Mild transient anemia, eosinophilia, delayed conceptions and reproductive failures have also been seen. Both type I and types II *B. henselae* have caused clinical signs.

Dogs

B. henselae has not been isolated from dogs, and experimentally infected dogs do not become bacteremic. *B. henselae* DNA has been found in the liver of a dog with peliosis hepatis (blood-filled cysts and cavities in the liver), but culture was not done.

Rodents

In some studies, experimentally infected rodents have remained asymptomatic. In rodents inoculated with large numbers of bacteria, the only lesion was granulomatous hepatitis.

Non-human primates

In one experiment, simian immunodeficiency virus (SIV)-infected macaques inoculated with *B. henselae* remained asymptomatic. These monkeys did not become bacteremic or seroconvert. In another experiment, two macaques became febrile and developed subcutaneous pur-

ple-red spots at the inoculation site. The significance of this finding is unclear, as *B. henselae* was not recovered from the regional lymph nodes and the animals did not seroconvert.

Communicability

Serologic studies suggest that 14-70% of cats may carry *B. henselae* at some point in their lives. Kittens are more likely to be infected than adults. Bacteremia can last for months and, in some cats, up to several years. Relapsing bacteremia has been observed in some cats.

Diagnostic Tests

B. henselae can be isolated from the blood and tissues of infected cats, as well as from cat fleas. Isolation of *B. henselae* is difficult, requires specialized media, and has mainly been used in research. The organism takes 9 to 45 days to grow. Serologic assays (indirect immunofluorescence, ELISA, immunoblotting), polymerase chain reaction (PCR) assays, transmission electron microscopy and confocal microscopy have also been used in research.

There can be cross-reactions between *Bartonella* species in serologic assays. In humans, cross-reactions have also been reported with other organisms including *Chlamydia* spp. and *Coxiella burnetti*. Some cats do not have antibodies at the time of bacteremia.

Treatment

Preliminary data suggest that tetracycline can be used to treat asymptomatic *B. henselae* bacteremia in cats; however, it is not known whether these cats are susceptible to reinfection or recrudescence.

Prevention

Prevention is not well understood. Flea control probably decreases the risk of transmission between cats. Some authorities suggest that keeping cats indoors may also be beneficial.

Morbidity and Mortality

From 14% to 55% of cats in the U.S. have antibodies to *B. henselae*. Seroprevalence rates of 40-70% have been reported in warm, humid parts of the world; these high rates are thought to be related to the increased prevalence of fleas. Feral cats are more likely to be seropositive than pet cats. Approximately 30% of captive wild felids are also seropositive. No morbidity or mortality has been reported in natural infections, to date.

Post-Mortem Lesions

Lymphadenomegaly, and histopathologic lesions in a variety of tissues, have been reported in cats experimentally infected with *B. henselae* or *B. clarridgeiae*. The histopathologic lesions included lymph node hyperplasia, splenic follicular hyperplasia, lymphocytic cholangitis, lymphocytic

hepatitis, lymphocytic plasmacytic myocarditis and lymphocytic interstitial nephritis.

B. henselae DNA has been found in blood-filled cysts and cavities (peliosis hepatis) in the liver of a dog. The significance of this finding is unknown.

Granulomatous hepatitis has been reported in experimentally infected rodents.

Internet Resources

- Centers for Disease Control and Prevention (CDC)
<http://www.cdc.gov/healthypets/diseases/catscratch.htm>
- eMedicine.com - Cat scratch disease
<http://www.emedicine.com/emerg/topic84.htm>
<http://www.emedicine.com/PED/topic333.htm>
- eMedicine.com - Bacillary angiomatosis
<http://www.emedicine.com/derm/topic44.htm>
- The Merck Manual
<http://www.merck.com/pubs/mmanual/>
- Unraveling Mysteries Associated with Cat-Scratch Disease, Bacillary Angiomatosis, and Related Syndromes
<http://www.cdc.gov/ncidod/eid/vol1no1/regnery.htm>

References

- Acha PN, Szyfres B (Pan American Health Organization [PAHO]). Zoonoses and communicable diseases common to man and animals. Volume 1. Bacterioses and mycoses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Cat-scratch disease; p. 78-81.
- Aiello SE, Mays A, editors. The Merck veterinary manual. 8th ed. Whitehouse Station, NJ: Merck and Co; 1998. Contagious ecthyma; p 619-620.
- Amersham Health. Peliosis hepatis [online]. The Encyclopaedia of Medical Imaging Volume IV:1. Available at: <http://www.amershamhealth.com/medcyclopaedia/medical/volume%20IV%201/PELIOSIS%20HEPATIS.ASP>. Accessed 12 Oct 2004.
- Anonymous. Epidemiologic notes and reports. Encephalitis associated with cat scratch disease -- Broward and Palm Beach counties, Florida, 1994. Morb Mortal Wkly Rep. 1994;43:909, 915-6.
- Breitschwerdt EB, Kordick DL. *Bartonella* infection in animals: carriership, reservoir potential, pathogenicity, and zoonotic potential for human infection. Clin Microbiol Rev. 2000;13: 428-438.
- Canadian Laboratory Centre for Disease Control. Material Safety Data Sheet – *Bartonella bacilliformis*. Office of Laboratory Security; 1999 Nov. Available at: <http://www.hc-sc.gc.ca/pphb-dgsp/msds-ftss/index.html#menu>. Accessed 9 Oct 2004.
- Centers for Disease Control and Prevention [CDC]. Cat scratch disease (*Bartonella henselae* infection). CDC; 2003 Feb. Available at: <http://www.cdc.gov/healthypets/diseases/catscratch.htm>. Accessed 8 Oct 2004.
- Freidman AD. Catscratch disease. eMedicine.com; 2003 July. Available at: <http://www.emedicine.com/PED/topic333.htm>. Accessed 8 Oct 2004.
- Jacomo V, Kelly PJ, Raoult D. Natural history of *Bartonella* infections (an exception to Koch's postulate). Clin Diagn Lab Immunol. 2002;9:8-18.
- Lex JR. Catscratch disease. eMedicine.com; 2003 Dec. Available at: <http://www.emedicine.com/emerg/topic84.htm>. Accessed 8 Oct 2004.
- Regnery R, Tappero J. Unraveling mysteries associated with cat-scratch disease, bacillary angiomatosis, and related syndromes. Emerg Infect Dis. 1995;1:16-21.
- Swartz RA. Bacillary angiomatosis. eMedicine.com; 2004 Feb. Available at: <http://www.emedicine.com/derm/topic44.htm>. Accessed 12 Oct 2004.
- Yamamoto, K, Chomel BB, Kasten RW, Hew CM, Weber DK, Lee WI. Experimental infection of specific pathogen free (SPF) cats with two different strains of *Bartonella henselae* type I: A comparative study Vet Res. 2002;33:669–684
- de Souza Zanutto M, Mamizuka EM, Raiz R Jr, de Lima TM, Diogo CL, Okay TS, Hagiwara MK. Experimental infection and horizontal transmission of *Bartonella henselae* in domestic cats. Rev Inst Med Trop Sao Paulo. 2001;43:257-61.