

Cat Scratch Disease and Other Zoonotic *Bartonella* Infections

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

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• Diagnosis of Animal Disease and
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Importance

Members of the genus *Bartonella* are maintained in many domesticated and wild animal hosts. *Bartonella henselae*, the best understood species, infects housecats and other members of the Felidae. Additional species of *Bartonella* are found in cats, dogs, livestock, rodents, rabbits and other wild and domesticated animals. In immunocompetent humans, *B. henselae* causes cat scratch disease, which is most often a relatively benign and self-limiting illness. In contrast, *B. henselae* infections are often severe in immunocompromised individuals, and can be fatal without antibiotic treatment. Other species of *Bartonella* have also been linked occasionally to human illnesses, with varying levels of evidence for a causative role. The significance of *Bartonella* spp. as pathogens for animals is currently unclear. The vast majority of infections are asymptomatic, and although these organisms have been implicated occasionally in illnesses, proving a causative role is difficult.

Etiology

Bartonella spp. are fastidious, pleomorphic, Gram negative rods in the family Bartonellaceae, α -2 subgroup of the Proteobacteria. More than 20 species of *Bartonella* have been described in animals. *B. henselae* (formerly *Rochalimaea henselae*) is the major agent of cat scratch disease, and a causative agent for bacillary angiomatosis, peliosis hepatis and possibly other conditions. There is some evidence that genotypes or strains of *B. henselae* might vary in their zoonotic potential. Other *Bartonella* species suggested to be pathogens in people and/or animals include *B. clarridgeiae*, *B. koehlerae*, *B. vinsonii* subsp. *berkhoffii*, *B. vinsonii* subsp. *arupensis*, *B. vinsonii* subsp. *vinsonii*, *B. alsatica*, *B. bovis* (formerly *B. weisii*), *B. elizabethae*, *B. washoensis*, *B. grahamii*, *B. rattimassiliensis* and *B. tribocorum*, and the candidate species *B. tamiiae* and *B. melophagi*. Proving that these organisms are the cause of an illness, rather than an incidental finding, can be difficult, in part due to the frequency of asymptomatic infections in humans and animals. In animals, proposed criteria for possible *Bartonella* involvement include detection of the organism by culture, PCR assay or serology, together with the exclusion of other causes, and response to treatment with a drug that has activity against this organism. If the syndrome is associated with *Bartonella* infection in other species, this is also suggestive. However, diagnosis can still be challenging, and findings should be interpreted with caution.

Two *Bartonella* species, *B. quintana* and *B. bacilliformis*, are maintained in human populations, and cause Oroya fever or trench fever, respectively. Like *B. henselae*, *B. bacilliformis* also causes bacillary angiomatosis and peliosis hepatis. Neither *B. quintana* nor *B. bacilliformis* is known to cause any illness in animals, although *B. quintana* has been detected in animals on rare occasions.

Species Affected

Bartonella species maintained in felids

Domesticated cats and other felids are the reservoir hosts for *B. henselae*. This organism has been detected in cheetahs (*Acinonyx jubatus*), African lions (*Panthera leo*), cougars (*Felis concolor*), bobcats (*Lynx rufus*) and wildcats (*F. silvestris*). It has been found occasionally in other animals including dogs, horses, cattle, feral pigs, seals, whales and porpoises. Armadillos are susceptible to experimental infection, and mice can be infected under some laboratory conditions. Cats are also thought to be the reservoir hosts for *B. clarridgeiae* and possibly *B. koehlerae*. Both organisms have been detected rarely in dogs, and DNA from *B. koehlerae* was found in feral pigs.

Bartonella species maintained in canids

B. vinsonii subsp. *berkhoffii* infects canids including dogs, coyotes (*Canis latrans*), gray foxes (*Urocyon cinereoargenteus*) and island foxes (*U. littoralis*). Both dogs and coyotes have been suggested as reservoir hosts. It was also found in a horse and feral pigs. *B. rochalimae* has been found in dogs and wild canids including red foxes (*Vulpes vulpes*), gray foxes, island foxes, coyotes and a wolf (*C. lupus*), as well as raccoons (*Procyon lotor*) and various rodents such as rats, shrews and gerbils.

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Bartonella species found in ungulates

Cattle are the reservoir hosts for *B. bovis* (formerly *B. weisii*). This organism has been found in a few cats and dogs, and some asymptomatic horses were seropositive. *B. chomelii* has been detected in cattle, *B. melophagi* in sheep, and *B. capreoli* and *B. schoenbuchensis* in deer. *B. capreoli* was also isolated from elk (*Cervus elephas*), and *B. schoenbuchensis* from a cow.

Bartonella species found in rodents and rabbits

Bartonella spp. reported to have rodent reservoir hosts include *B. vinsonii* subsp. *arupensis*, *B. vinsonii* subsp. *vinsonii*, *B. birtlesii*, *B. doshiae*, *B. peromysci*, *B. phoceensis*, *B. rattimassiliensis*, *B. talpae*, *B. taylorii*, *B. tribocorum*, *B. grahamii*, *B. elizabethae*, *B. queenslandensis* and *B. washoensis*, as well as newly proposed species such as *B. japonica* sp. nov. and *B. silvatica* sp. nov. The species *B. vinsonii* subsp. *arupensis*, *B. elizabethae*, *B. grahamii*, *B. taylorii* and *B. washoensis* have also been detected in a few dogs, while many cats in Sweden are seropositive for *B. elizabethae*. The reservoir host for *B. tamiae* is not known, although rats have been proposed, and this organism caused illness in experimentally infected laboratory mice.

B. alsatica has been found in rabbits.

Bartonella in other animals

Bartonella species or their DNA have also been detected in other mammals such as North American river otters, kangaroos, wild badgers (*Meles meles*) and bats.

Zoonotic potential

B. henselae, mainly acquired from housecats, is a zoonotic pathogen. This organism is the major cause of cat scratch disease, but *B. clarridgeiae* and *B. koehlerae* have been implicated in rare cases. Other species that have been implicated in rare clinical cases or suggested as human pathogens include *B. alsatica*, *B. vinsonii* subsp. *berkhoffii*, *B. vinsonii* subsp. *arupensis*, *B. vinsonii* subsp. *vinsonii*, *B. elizabethae*, *B. washoensis*, *B. grahamii*, *B. rattimassiliensis*, *B. tribocorum*, *B. tamiae* and *B. melophagi*.

Geographic Distribution

B. henselae occurs worldwide in cats. Based on serological surveys, *B. vinsonii* subsp. *berkhoffii* also appears to be present worldwide.

Transmission

Bartonella henselae

B. henselae is transmitted between cats by cat fleas (*Ctenocephalides felis*), probably via flea feces. This organism is reported to survive for 3 days in flea feces. Cats can also be infected experimentally by intravenous or intramuscular injection of feline blood, suggesting that iatrogenic spread (including transmission through blood transfusions) might be possible. Transmission was not

observed when cats were in contact, but fleas were absent, indicating that casual contact and the sharing of food or water dishes are not significant sources of exposure. In one experiment, *B. henselae* was not spread by sexual contact (bacteremic females and uninfected males) or vertically to kittens. Once a cat has been infected, bacteremia can last for weeks to months, and the number of bacteria in the blood can fluctuate greatly during this time. Intermittent *B. henselae* or *B. clarridgeiae* bacteremia was reported to persist for almost 15 months in some experimentally infected cats, and for as long as 3 years in naturally infected cats (although it is possible that these cats were reinfected).

Little is known about *B. henselae* in other species, but its DNA was detected in oral swabs from dogs, and in dog fleas (*Ctenocephalides canis*) removed from dogs.

Other species of Bartonella

Fleas are thought to be important vectors for many other *Bartonella* species, including many that are associated with rodents. Organisms that have been detected in the cat flea, in addition to *B. henselae*, include *B. clarridgeiae*, *B. koehlerae* and *B. quintana*. Other arthropods such as flies, keds, lice, sandflies, and ticks are also proven or potential vectors for some *Bartonella* species. DNA from rodent-associated *Bartonella* spp. has been detected in several species of lice that parasitize these animals. *B. henselae* and *B. schoenbuchensis* were found in deer keds (*Lipoptena mazamae* and *L. cervi*), and these arthropods are thought to be vectors for *B. schoenbuchensis*. Sheep keds (*Melophagus ovinus*) might be important in transmitting *B. melophagi*. *Bartonella* DNA has also been found in various species of flies, bat bugs (*Cimex adjunctus*) and mites on rodents and bats. It should be noted that evidence of infection does not, by itself, prove that an arthropod is a vector for an organism. The relevance of ticks as vectors for *Bartonella* is controversial. The possibility of tick-borne transmission was suggested by circumstantial or anecdotal evidence, such as rare case reports of *Bartonella* infections diagnosed soon after a tick bite. Some *Bartonella* spp. have been detected in ticks, mainly by PCR, and laboratory studies suggest that they might act as vectors, although this does not prove they are epidemiologically important.

Transmission of zoonotic Bartonella to humans

Although some details of transmission are not completely understood, people mainly seem to acquire *B. henselae* in scratches and bites from cats. More than 90% of clinical cases occur in people who have been in contact with cats, most often kittens, and the majority of these patients report having been scratched, bitten or licked. In most cases, *B. henselae* probably enters the body through a scratch contaminated by flea feces. Organisms in feline saliva may be transmitted to people in bites, or abrasions that are licked by the cat. It is still unproven whether the bacteria in feline saliva come from the cat's blood, or from flea feces ingested while grooming. However, one recent

study found that *Bartonella* DNA was more likely to occur in oral swabs from bacteremic than nonbacteremic cats.

Entry of *B. henselae* through the eyelid or conjunctiva (e.g., after rubbing the eyes) is thought to account for Parinaud oculoglandular syndrome. The authors of one article speculated that cases of hepatosplenic involvement without lymphadenopathy might be caused by ingesting the organism. The possibility of transmission directly from fleas to humans (e.g., through flea bites) has also been proposed, but there is no evidence that this is possible. A few cases of cat scratch disease have occurred after exposure to inanimate objects such as thorns and splinters, or after bites or scratches from animals other than cats, such as monkeys and dogs. (It is possible that some wounds might have been contaminated later by *B. henselae*.) In a few cases, there is no history of animal contact, and the source of the organism is uncertain.

Infections with organisms other than *B. henselae* are poorly understood, although bites or scratches were implicated in some cases. One infection with *B. vinsonii* subsp. *berkhoffii* was diagnosed after a bite from a dog, and another after a bite from a coyote. A veterinarian became infected with this organism after injury by a needle that passed through canine tissues. Illness associated with *B. alsatica* was reported in a woman who had been scratched while butchering a wild rabbit. In most cases, only circumstantial evidence was available to support the route of transmission.

There is no evidence that zoonotic *Bartonella* can be transmitted from person to person by casual contact. This organism However, *B. henselae* was cultured from human RBC units that had been inoculated with this organism and stored at 4°C for 35 days, suggesting the possibility of transmission in blood transfusions.

Disinfection

Disinfectant susceptibility does not seem to have been published for *Bartonella* species; however, there is no indication that these organisms are unusually resistant to inactivation. In many cases, bacteria can be disinfected with commercial disinfectants, 70% ethanol, 1% sodium hypochlorite and 2% formaldehyde, as well as phenolic disinfectants, 2% aqueous glutaraldehyde and peracetic acid (0.001% to 0.2%). Physical methods of inactivation are moist heat of 121°C (249.8°F), held for 15 to 30 minutes, and dry heat of 160-170°C (320-338°F) for 1-2 hours.

Infections in Animals

Incubation Period

Cats are usually asymptomatic, but some cats inoculated with *B. henselae* developed cutaneous lesions at the inoculation site within 2 days, and/or fever after 2 to 16 days.

Clinical Signs

The importance of *Bartonella* spp. as pathogens in animals is still unclear. Most infections appear to be asymptomatic. Some experimental infections, case reports and studies have suggested possible links to disease, but other studies have been unable to substantiate a role for *Bartonella*. Investigations are complicated by the high prevalence of infections in healthy animals, the uncertainties in diagnostic testing for these organisms, and the possibility of co-infection with other microorganisms.

Cats

Naturally-infected cats with *B. henselae* bacteremia are usually asymptomatic. In experimental studies, most cats inoculated with this organism remained asymptomatic or had only mild clinical signs such as inoculation site reactions, mild nonspecific febrile illness, transient mild behavioral or neurological signs, mild transient anemia, eosinophilia or reproductive disorders. In a recent study, fever and inappetence occurred in some cats exposed to *B. henselae*-infected fleas, but not in cats inoculated intravenously with *B. henselae*. One flea-exposed cat, which may not have mounted an adequate immune response to the infection, became severely ill and myocarditis was found at necropsy. No clinical signs have been reported in cats inoculated with *B. koehlerae* or *B. rochalimae*.

Similarly, it has been difficult to demonstrate that *Bartonella* causes illness in naturally infected cats. Rare case reports have attributed endocarditis and other diseases in individual cats to *B. henselae* or other *Bartonella* species. Three studies suggested possible links between *B. henselae*, (or seropositivity to this organism) and an increased risk of gingivostomatitis, but three other studies could detect no association. One group reported that seropositive cats were more likely to have various unspecified urinary tract diseases. A newer study found a weak association between seropositivity, but not bacteremia, and idiopathic lower urinary tract disease, and no correlation with urolithiasis or chronic kidney disease. A possible association between *B. henselae* and uveitis has also been proposed, but two newer studies were unable to substantiate this link. One retrospective study suggested that *Bartonella* infections might be associated with neurological signs in some cats, but two other studies found no evidence for this.

Dogs

No clinical signs other than transient fever were reported in dogs inoculated with *B. vinsonii* subsp. *berkhoffii*. Two dogs inoculated with *B. rochalimae* also remained asymptomatic, other than inflammation at the inoculation site. *Bartonella* spp. have been suggested as possible etiologic agents in some case reports, particularly for endocarditis, but also for febrile lymphadenitis, liver disease, joint involvement and other diverse conditions. In one intriguing report, a dog infected with *B. vinsonii* subsp. *berkhoffii* developed a condition resembling human

bacillary angiomatosis after treatment with immunosuppressive drugs for pancytopenia, and the lesions responded rapidly to drugs effective against *Bartonella*. As with cats, the number of case reports is limited, and it is difficult to establish a causative role.

Livestock

The effect of *Bartonella* infections in livestock, if any, is unknown. One report suggested that *B. bovis* may have been the cause of endocarditis in two older cows, while a study of a dairy herd found that this organism had no apparent effect on health or reproductive success. Involvement of *B. henselae* was postulated in a few case reports in horses, and some horses that were inoculated with this organism developed injection site reactions and mild to moderate limb edema, as well as other mild clinical signs.

For further information

Further details on these and other studies in cats, dogs, cattle, horses and rodents can be found in the following document [“*Bartonella* Infections in Animals: Clinical Signs”](#).

Post Mortem Lesions

Various lesions including endocarditis, granulomatous lesions, and bacillary angiomatosis, as well as vasculitis and necrosis in an aborted equine fetus, were reported in naturally infected animals with syndromes attributed to *Bartonella*. Lymphadenomegaly, inoculation site lesions and myocarditis were seen in some cats experimentally infected with *B. henselae* or *B. clarridgeiae*.

Diagnostic Tests

Culture of blood or other tissues is the most definitive method to detect *Bartonella* infections; however, these organisms cannot always be isolated from infected animals. They may be easier to culture from some hosts (e.g., *B. henselae* in cats) than others. Even in cats, several attempts may be needed to detect bacteria in the blood, as bacteremia can be intermittent. *Bartonella* spp. are fastidious, and isolation requires specialized media such as fresh chocolate agar or brain–heart infusion agar enriched with blood. Visible colonies of *B. henselae* usually develop in 9 days to 6–8 weeks. Some new media introduced in research laboratories or reported in the literature may improve isolation of *Bartonella* spp., especially in species other than the reservoir hosts. Genotypes of *B. henselae* can be identified by multilocus sequence typing or multiple locus variable number tandem repeat analysis. Genotyping is usually available only in specialized laboratories, and is mainly used for epidemiological studies.

PCR assays are commonly used to detect *Bartonella* spp. in research, and may be available in some laboratories. One sensitive technique employs isolation in a *Bartonella* α -Proteobacteria growth medium (BAPGM) based enrichment culture, followed by multiplex real-time PCR. Contamination with flea feces on the skin, or other sources

of *Bartonella* organisms or DNA, can cause false positive results in PCR tests and culture. In research laboratories, immunocytochemical and immunohistochemical methods can be used to detect *Bartonella* spp. in lesions.

Serological tests for *B. henselae* include immunofluorescent antibody, ELISA and immunoblotting (Western blotting). The demonstration of intraocular *Bartonella*-specific antibody helps substantiate the involvement of this organism in cases of uveitis. False-positive test results appear to be common in all serological assays, and authors recommend the use of serology in conjunction with blood culture or PCR testing. Some infected cats and dogs do not have antibodies to *Bartonella*, although the organism can be identified in blood and/or tissues by culture or PCR.

Treatment

Treatment is usually recommended only for animals that are ill, although it may be considered in other circumstances (e.g., in a young, bacteremic cat living with a highly susceptible individual). Antibiotic resistant isolates of *Bartonella* spp. have occasionally been reported.

Routine treatment of asymptomatic, bacteremic cats is not recommended as a method of zoonosis prevention. No treatment regimen is proven to be consistently effective in eliminating *B. henselae* bacteremia in cats, although some antibiotics have apparently been successful in individual animals. Documenting clearance of the organism is difficult, because bacteremia fluctuates. Routine treatment might also promote the generation of antibiotic-resistant strains. Animals that have eliminated the organism may be reinfected with other *Bartonella* species, and sometimes by different genotypes or strains of the same organism.

Prevention

Flea control decreases the risk that *B. henselae* will be transmitted between cats. When using cats as blood donors, the possibility of transmission from infected animals should be considered. Infection with many *Bartonella* species is not well understood; however, arthropods are thought to be involved in all cases, and vector control should decrease transmission.

Morbidity and Mortality

Clinical cases do not seem to occur frequently in animals, but asymptomatic infections are common, especially in reservoir hosts.

Cats and other Felidae

B. henselae is very common in asymptomatic cats, particularly in warm, humid regions where fleas are more prevalent. Studies using a variety of tests reported seroprevalence rates of 4% to 68% in the U.S., Philippines, eastern Australia, Brazil, Ireland, Italy and Turkey, and 1% or less in Sweden and Norway. More than 80% of the cats in some animal shelters may have antibodies to this organism. *B. henselae* bacteremia is also common in cats;

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in various locations, its prevalence varied from 3% to more than 40%, and was as high as 70-72% in some populations by PCR. Young cats are more likely to be bacteremic than older animals (although older cats are more likely to be seropositive), and feral cats are more likely to be infected than pet cats. Antibodies to *B. henselae* are also common in other captive and wild Felidae.

B. clarridgeiae is thought to be less common in cats than *B. henselae*, although not all studies agree. This organism accounted for approximately 10% of the isolates from bacteremic cats in the U.S., and 30% in France and the Philippines. Similarly, 21% of cats in the U.S. had *B. clarridgeiae* DNA in the blood, and 35% had DNA from *B. henselae*. However, one study found that cats in animal shelters in both Michigan and California were more likely to have antibodies to *B. clarridgeiae* than *B. henselae*. Exposure to other *Bartonella* species may be frequent in some locations. A survey of cats in Sweden reported that 25% were seropositive for *B. elizabethae*. *B. koehlerae* is thought to be rare in cats.

Canidae

The prevalence of *B. vinsonii* subsp. *berkhoffii* varies widely in dogs, with higher levels more likely to occur in tropical than temperate regions. Reported seroprevalence rates ranged from 1% to 12% in surveys from the U.S., Israel, Greece, Turkey, and Reunion Island, and were as high as 65% in some areas of sub-Saharan Africa. Up to 93% of the dogs in some kennels may have antibodies to this organism. Exposure rates may also differ between other populations, with one study reporting higher seroprevalence in stray dogs compared to pets in Turkey, and another study reporting a higher incidence in rural shepherd and farm dogs compared to urban strays. Antibodies to *B. henselae* have also been found in 3-35% of dogs in various surveys.

Some wild canids may also be exposed frequently to *Bartonella*. Antibodies to *B. vinsonii* subsp. *berkhoffii* were detected in approximately 10% to 76% of some fox or coyote populations in parts of the U.S., and antibodies to *B. rochalimae* in 33% to 43% of foxes.

Cattle

Infection with *B. bovis* seems to be common in cattle, especially beef breeds, with some U.S. studies reporting that 80% or more of the beef cattle examined were bacteremic or had antibodies to this organism. Some studies have reported lower infection rates in dairy cattle (e.g., bacteremia in 81-96% of beef cattle and 17% of dairy cattle in California, or 0.2% of dairy cows and 42.5% of beef cattle in Taiwan). Infection rates may, however, vary with the herd, age of the animals, or other factors. In France, *B. bovis* was found in the blood of 59% of the animals in one dairy herd, with the highest prevalence (93%) in heifers. Despite the high prevalence in this herd, there were no adverse effects on reproductive function or health.

Rodents and other small mammals

Bartonella spp. may be common among wild rodents in urban locations, as well as in some other wild animals, such as rabbits. Pet rodents can also be infected. One study detected *Bartonella* spp. in blood samples from 26% of exotic small mammals imported into Japan as pets. The prevalence was much higher in animals that had been captured from the wild (37%), compared to animals from breeders (approximately 3%). In animals bred for the pet trade, *Bartonella* was found only in Siberian chipmunks (*Tamias sibiricus*) from China. Among the pet rodents captured from the wild, bacteremia was common among animals in the families Muridae and Sciuridae, while no organisms were found in animals from the families Octodontidae and Erinaceidae.

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Incubation Period

In cat scratch disease, cutaneous lesions usually develop at the inoculation site within 7 to 15 days after exposure, and lymphadenopathy is typically seen after 1-3 weeks. However, clinical signs have been reported as soon as 3 days and up to 50 days after exposure.

Clinical Signs

B. henselae appears to infect some immunocompetent people without causing clinical signs, and mainly causes cat scratch disease in people who become ill.

Cat scratch disease

In many cases, the first sign of cat scratch disease is the development of one or more small, reddish-brown, erythematous papules, pustules, macules, vesicles or ulcers at the inoculation site. These lesions disappear in 1-3 weeks, and may be mistaken for insect bites; however, they are not usually pruritic. The characteristic solitary lymphadenopathy or (less frequent) regional lymphadenopathy usually develops within a few weeks of exposure. Affected lymph nodes are often painful or tender, and the skin over the nodes can be warm, reddened and indurated. Cellulitis is, however, rare. Occasionally, the nodes may suppurate, especially when they are large. Lymphadenopathy usually lasts for a few weeks to a few months, occasionally up to a year, and rarely longer. Cat scratch disease without lymphadenopathy seems to be unusual in young, healthy patients, but it is reported to be more common in elderly individuals and transplant patients. Other common symptoms in cat scratch disease are a low grade fever, malaise and fatigue. The fever usually disappears within 1-2 weeks but fatigue may persist for weeks or months. Less often, there may be other nonspecific signs such as headache, anorexia, vomiting, nausea, weight loss, generalized pain or a sore throat.

Complications may occur in some patients, with an increased incidence in the elderly and people who are

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immunocompromised. Encephalitis has been reported in as many as 4-5% of patients in some case series. It typically occurs 1-6 weeks after the classic symptoms, but cases without lymph node involvement, as well as cases preceding lymphadenopathy, have been reported. This condition may progress rapidly to seizures, coma with respiratory depression and other severe signs, but patients usually recover completely without permanent damage. Death is possible but very rare. Some patients may have cranial or peripheral nerve involvement, without encephalitis. Neuroretinitis is an uncommon but well-recognized condition in cat scratch disease. It is characterized by the sudden onset of painless visual loss, usually unilateral. Although the condition is temporary and resolves in months, some patients may have residual defects such as mildly decreased visual acuity, or abnormal color vision or contrast sensitivity. Other infrequent to rare complications of cat scratch disease include arthropathy (especially of the knee, wrist, ankle and elbow joints), disseminated disease with granulomatous hepatitis and/or splenitis, anterior uveitis, subretinal masses in HIV-positive patients, endocarditis (most often in people with existing heart valve abnormalities), osteomyelitis often localized to one area, various nonspecific rashes, pulmonary involvement, and other conditions. Fever of unknown origin has also been attributed to *B. henselae*.

An atypical form of cat scratch disease, called Parinaud oculoglandular syndrome, is thought to result from inoculation of the organism into the eye. This syndrome is characterized by no purulent unilateral conjunctivitis and/or conjunctival granuloma, together with preauricular, submandibular, or cervical lymphadenopathy. It usually resolves in several weeks without permanent damage.

Immunocompetent individuals with cat scratch disease usually recover without antibiotic treatment, and even complications generally resolve without sequelae. Deaths are very rare, with endocarditis usually the most serious concern. Immunocompromised individuals with cat scratch disease can have more severe symptoms, and complications, bacteremia and atypical presentations are more common. Recurrent illness has been described in a few people with severe signs, including a transplant patient.

Bacillary angiomatosis and bacillary peliosis

B. henselae can also cause bacillary angiomatosis (epithelia angiomatosis) and peliosis hepatitis, mainly in people who are immunocompromised.

Bacillary angiomatosis is a vascular proliferative disease of the skin and/or internal organs. It is most often an AIDS-related disease in people with a very low CD4 count. 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 from pinhead-sized to 10 cm in diameter. Subcutaneous nodules resembling a common abscess may also be seen. Bacillary

angiomatosis may also involve various internal organs including viscera, brain, bone, or lymph nodes. The symptoms vary with the organ(s) affected, and can include neurological signs, bone pain, weight loss or symptoms related to massive visceral lymphadenopathy.

Peliosis hepatitis is a rare condition, caused by *B. henselae* as well as other pathogens, drugs and toxins. It is characterized by vascular proliferation in the liver, which can result in multiple blood-filled cysts and sinusoidal dilatation. The symptoms of peliosis hepatitis may include fever, weight loss, abdominal pain, nausea, vomiting, diarrhea and hepatosplenomegaly. In some cases, this condition may be an incidental finding at necropsy. Peliosis hepatitis can occur concurrently with bacillary angiomatosis.

Other zoonotic Bartonella

Illnesses have occasionally been attributed to other *Bartonella* species, with varying levels of evidence for their involvement. Endocarditis has been attributed to a number of species including *B. elizabethae*, *B. koehlerae*, *B. vinsonii* subsp. *berkhoffii*, *B. vinsonii* subsp. *arupensis*, *B. washoensis* and *B. alsatica*. It occurs most often in people with pre-existing abnormalities of the heart valves. A few febrile illnesses occurred in people infected with *B. vinsonii* subsp. *berkhoffii*, *B. washoensis*, *B. rochalimae*, *B. melophagi*, *B. tamiiae* or other species, and *B. alsatica* was linked to regional lymphadenopathy in an elderly woman. Additional details on these cases, as well as further details on cat scratch disease-related complications, are available in the following document [“*Bartonella* Infections in Humans: Clinical Signs”](#).

Diagnostic Tests

Cat scratch disease is often diagnosed by the history and physical examination, with supporting evidence from laboratory tests. Providing definitive evidence for the involvement of *Bartonella* spp. in a medical condition may be difficult. Diagnostic tests for this organism have limitations, and many healthy people are seropositive.

Bartonella spp. can sometimes be cultured from blood or tissues, as in animals; however, conventional blood cultures from immunocompetent patients without systemic disease are often negative for *B. henselae*. PCR assays may also be negative in some people. In serological tests for *B. henselae*, a fourfold rise in titer or the presence of IgM suggests a recent infection. IgM antibodies to *B. henselae* have been reported to persist in humans for less than three months, while IgG may be detected for more than two years. Cross-reactions can occur between species of *Bartonella*, and have also been reported with other organisms such as *Chlamydia* spp. and *Coxiella burnetii*.

Biopsies are not used routinely for cat scratch disease, but they may be employed in some instances (e.g., when neoplasia must be ruled out). Histopathology is suggestive but not diagnostic. Organisms may be detected in tissues with Warthin-Starry silver stain and Brown-Hopps Gram

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stains. *Bartonella* spp. are Gram negative, small, curved, pleomorphic rods. Immunostaining has been used to identify the bacteria, especially in research. Skin testing, using crude lymph node antigens, was employed in the past, but is no longer recommended.

Treatment

Immunocompetent patients

Most cases of cat scratch disease in immunocompetent individuals are self-limiting, and treatment is often supportive and symptomatic. Suppurating nodes may be aspirated to remove pus and reduce the pain, and severely affected lymph nodes or persistent ocular granulomas are occasionally excised. Although *B. henselae* is sensitive to a number of antimicrobials *in vitro*, antibiotics are not consistently effective for cat scratch disease in immunocompetent individuals. Antibiotics (azithromycin) were demonstrated to reduce lymph node size in some patients in one randomized, double blind study, although this drug did not decrease the duration of the illness or have any other effect on clinical signs. Other evidence for antibiotic use in uncomplicated cases is limited or anecdotal, and some studies have demonstrated no benefit.

Serious, potentially life-threatening complications, such as *Bartonella* endocarditis, are treated with antibiotics. Surgical excision and replacement of the involved valve may also be necessary. Opinions differ on the value of antibiotics for the treatment of non-life-threatening complications that usually resolve on their own.

Immunocompromised patients

Serious *B. henselae* infections in immunocompromised patients, including bacillary angiomatosis, usually respond well to various antibiotics. Patients with uncomplicated cat scratch disease are also treated in most cases, due to the increased risk of severe illness and complications in immunocompromised populations. Prolonged treatment (4-6 months) has been used in patients who relapse.

Prevention

Bites and scratches from cats, particularly kittens, should be avoided. Rough play with kittens is inadvisable, and any bites or scratches should immediately be washed with soap and water. Declawing does not appear to affect transmission, but keeping the nails clipped has been suggested by some sources. Cats should be discouraged from licking a person's skin, particularly eyes, mucous membranes and broken skin. Hand washing after contact with a cat might be helpful.

The ability of cats to transmit *B. henselae* is transient, and authorities do not recommend removing them from the household. The efficacy of antibiotics in eliminating *B. henselae* bacteremia in cats is uncertain. The 2009 Guidelines for Preventing Opportunistic Infections Among HIV-infected Adults and Adolescents note that there is no evidence that routine culture or serological testing of

healthy cats for *Bartonella* provides any benefit for owners. Flea control decreases the risk that household cats will acquire *B. henselae* or transmit it to other cats.

Morbidity and Mortality

Exposure to *Bartonella* spp.

Antibodies to *B. henselae* seem to be relatively common in human populations, often with no apparent history of cat scratch disease. A number of studies, conducted in several countries, found seroprevalence rates varying from less than 1% to 25% or more in the general population. Exposure may be particularly common among children. A study from Italy found antibodies to *B. henselae* in approximately 62% of children and adolescents who presented as outpatients to a clinic for health check-ups or minor illnesses, and who had no symptoms that might indicate bartonellosis. In this study, 8.5% of the participants had high titers, suggesting recent or ongoing subclinical infections. Relatively few surveys have studied exposure to other *Bartonella* species, but antibodies to *B. elizabethae* are reported to be common in Sweden (14% of healthy blood donors) and Thailand (approximately 10% of patients presenting to rural hospitals), as well as among intravenous drug users in the inner city area of Baltimore, Maryland (33%). Antibodies to other *Bartonella* spp. have also been found in some populations.

Illness

Cat scratch disease is not reportable in any country, and the incidence of illness is uncertain. Most clinical cases are thought to involve children, although an increasing number have been identified in adults. In immunocompetent individuals, cat scratch disease is usually self-limiting and benign, although the symptoms may last for 1-5 months and occasionally longer. Significant illness is reported to occur in 5-10% of cases, usually from neurological signs or multisystemic disseminated disease. Nearly all individuals, including those with neurological involvement, recover fully, and deaths are very rare. Endocarditis is usually the most serious complication. Reinfection seems to be infrequent.

In contrast, bacillary angiomatosis and other conditions can be fatal in immunocompromised individuals if left untreated. However, most of these patients recover fully, provided the disease is treated appropriately.

Internet Resources

Centers for Disease Control and Prevention (CDC)
<http://www.cdc.gov/healthypets/diseases/catscratch.htm>

eMedicine.com - Cat scratch disease
http://www.emedicinehealth.com/cat_scratch_disease/article_em.htm <http://emedicine.medscape.com/article/214100-overview>

eMedicine.com - Bacillary angiomatosis
<http://emedicine.medscape.com/article/1051846-overview>

Public Health Agency of Canada.
Pathogen Safety Data Sheets
<http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/index-eng.php>

The Merck Manual
<http://www.merckmanuals.com/professional/index.html>

The Merck Veterinary Manual
<http://www.merckmanuals.com/vet/index.html>

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