TOP 5

TOP 5 *BARTONELLA* SPECIES OF HUMAN SIGNIFICANCE

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Bartonella spp are vector-borne, blood-borne, gram-negative bacteria of emerging global health importance in humans and animals, with new species, reservoirs, and arthropod vectors being identified with increasing frequency.[1] In their reservoir hosts, *Bartonella* spp can cause intraerythrocytic bacteremia and endotheliotropic infections that can last weeks to years without resultant disease.[2] Of the 38 known *Bartonella* spp, at least 17 species or subspecies are known to cause disease in humans,[1] with *B henselae*, *B quintana*, *B bacilliformis*, *B koehlerae*, and *B vinsonii* subsp *berkhoffii* most frequently identified.[2,3]

TOP 5 *BARTONELLA* SPECIES OF HUMAN SIGNIFICANCE

1. *B henselae*
2. *B quintana*
3. *B bacilliformis*
4. *B koehlerae*
5. *B vinsonii* subsp *berkhoffii*

Clinicopathologic differences of the many *Bartonella* spp are not well-documented,[2] and factors such as virulence among species and strains, mode of transmission, host immune response, concurrent disease, and immunosuppression may all contribute to clinical signs and degree of disease manifestation.[3]

Following are the author's top 5 *Bartonella* spp and their significance in humans.

1 *B henselae*

B henselae can be found worldwide,[4] and although cats are its primary reservoir,[5,6] other animals (eg, dogs, raccoons, mongooses) may also be sources of infection.[2] *B henselae* is transmitted among cats through flea feces (*Ctenocephalides felis*) and scratches from nails contaminated with flea feces.[2,4,7,8] *B henselae* transmission to humans from dog bites[2,9] and cat bites and scratches[5,6] appears to be a low-risk source for human infection unless the animal is concurrently infested with fleas or the nails or saliva are contaminated with flea feces.[2] Ticks, spiders, and mites may also play a role in transmission of *B henselae* to animals and humans.[2,10,11] Bacteremia has been identified in various animals[2]; in cats (stray or pet), infection prevalence varies considerably by geographic area.[6] Infection prevalence in cats is highest in warm, moist areas with high flea burdens.[4,5,12] A North American study found seroprevalence rates to be higher in warmer regions as compared with cooler regions.[12] Overall, 27.9% of cats tested in that study were seropositive. Bacteremia in cats can be intermittent,[10] occurs primarily in cats younger than 2 years, and can last a year or longer.[6,7] The seroprevalence rate of *B henselae* in dogs in the southeastern United States has been recorded to be 10% in healthy dogs and 27% in sick dogs.[13] Broader studies have found 2% to 3.8% of dogs to be seropositive for *B henselae*.[14,15]

B henselae infection in humans and animals can be subclinical; this is particularly common in cats due to their coevolution with *B henselae*.[2,7,16] Although association between infection and clinical signs in cats is equivocal,[17] signs can include endocarditis,[2,6] myocarditis,[2,7] fever,[18] lethargy,[3,18] gingivostomatitis,[19] uveitis, conjunctivitis, and others.[3] In dogs, *B henselae* can cause fever, endocarditis, granulomatous hepatitis, peliosis hepatitis, lymphadenomegaly, panniculitis, and vasoproliferative lesions, as well as others.[2,3,5,20]

B henselae is the predominant cause of cat scratch disease (CSD) in humans.[10,21] There are an estimated 500 hospitalizations and 12 000 outpatient cases of CSD each year in the United States.[8] In humans, at the site of inoculation, a cutaneous papule or pustule develops 3 to 10 days after contact with an infected animal and may last 1 to 3 weeks.[4] Accompanying signs may include regional lymphadenopathy, fever,[18] fatigue, malaise, headache, sore throat, and/or rash.[4] More severe signs may include neuralgia, endocarditis, osteomyelitis, Parinaud's oculoglandular syndrome, pneumonia, hepatitis, splenitis, and/or encephalopathy.[4] *B henselae* and *B quintana* are causative agents of bacillary angiomatosis, a neovascular disorder that occurs primarily in immunocompromised individuals and involves the skin, lymph nodes, and a variety of organs.[4,22,23] Although CSD is often self-limiting, *B henselae* can cause chronic or intermittently clinical illness accompanied by persistent bacteremia.[24]

2 *B quintana*

B quintana, and to a lesser extent *B henselae*, was the causative agent of trench fever during World War I and has recently been

the cause of urban trench fever, which occurs predominately among homeless and marginalized populations.[25-28] *B quintana* can be found worldwide and is transmitted among humans via feces of the human body louse (*Pediculus humanus*).[2,26] Humans are considered incidental hosts for all *Bartonella* spp, with the exception of *B quintana*, for which humans are reservoir hosts.[4,17] New findings, however, support the role of *C felis* in transmission and suggest that cats, dogs, and, possibly, the cynomolgus monkey—all accidental hosts—may also serve as sources of infection.[2,3,10,17,29,30] *B quintana* transmission to humans has rarely been associated with cat bites and scratches, and transmission from dogs to humans has never been documented.[10]

B quintana does not appear to cause illness in cats, despite evidence of infection.[3,21,31] *B quintana* infection in dogs is typically subclinical but has been associated with endocarditis.[2,32] Prevalence of these pathogens in cats and dogs is not well-known. A study in Germany demonstrated a *B quintana* seroprevalence rate of 18% in stray cats.[3] In a study in Israel, 2.6% of cats were found to be seropositive only to *B henselae*, 20.2% only to *B quintana*, and 39.5% to both *B henselae* and *B quintana*. In another study in North Carolina, 8.7% of cats were found to be seropositive only to *B henselae*, 7% only to *B quintana*, and 40.4% to both *B henselae* and *B quintana*.[33]

In humans, *B quintana* infection typically results in a self-limiting febrile illness, with fever lasting up to 5 days, fatigue, conjunctival congestion, headache, myalgia, bone pain (particularly shin pain), rash, nystagmus, endocarditis, pericardial effusion, bacillary angiomatosis, and/or bacillary peliosis, particularly in individuals infected with human immunodeficiency viruses.[4,23,26,34] *B quintana* and, rarely, *B henselae* can persist long-term if not treated properly in humans and are known causes of culture-negative endocarditis in humans.[4]

3 *B bacilliformis*

Humans are the only known reservoir of *B bacilliformis*, which is transmitted among humans via the bite of sand flies (*Lutzomyia* spp) located in the Andes mountains, particularly in Peru, Colombia, and Ecuador.[2,5,17,25,35,36] *B bacilliformis* can cause Carrión's disease, a biphasic illness in humans that consists of acute and chronic phases. The acute phase (ie, Oroya fever) is characterized by a wide array of signs (eg, fever, chills, headache, intense myalgia, mental status changes, seizures, profound hemolytic anemia) and has a high fatality rate when untreated. The chronic phase (ie, verruga peruana [ie, Peruvian warts]) appears weeks to months after resolution of the acute phase and is characterized by angioproliferative skin lesions prone to ulceration and bleeding.[4,35] Children and pregnant women may be particularly affected; complications can include fetal death, miscarriage, and/or premature birth.[35]

An animal reservoir of *B Bacilliformis* has not been discovered but may still exist[35]; there have been no documented cases of infection in dogs or cats.[33,36,37]

4 *B koehlerae*

Cats are the primary reservoir of *B koehlerae* transmission to humans,[3,5,6,24] although *B koehlerae* and *B quintana* are less frequently isolated in cats as compared with *B henselae*.[3] Evidence of *B koehlerae* infection has also been found in dogs and the fleas of wild gerbils (*Meriones lybicus*).[2,3,38] *C felis* (and possibly other flea species) is critical in the transmission of *B koehlerae* between animals and humans[2,17]; however, additional arthropod vectors and other documented means of transmission of *Bartonella* spp are emerging.[1]

There are an estimated 500 hospitalizations and 12 000 outpatient cases of cat scratch disease each year in the United States.[8]

CSD = cat scratch disease

OCCUPATIONAL HAZARD

For veterinary staff, *Bartonella* spp pose an occupational hazard.[3,9,49] *B henselae* and *B vinsonii* subsp *berkhoffii* bacteremia have been documented in veterinarians and veterinary nurses who were exposed to arthropods, had frequent contact with cats and/or dogs, and/or experienced scratches or bites (primarily from cats).[9,49] A serosurvey of US veterinarians and veterinary nurses found DNA from at least one *Bartonella* spp in 28% of subjects (*B henselae*, 56%; *B vinsonii* subsp *berkhoffii*, 26%; *B koehlerae*, 22%).[22] Higher rates of headaches and irritability were reported in those found to be positive for *Bartonella* spp.[22] A survey of 89 Spanish veterinarians found 73% of participants to be seropositive for at least one *Bartonella* spp; 11% were positive for *B quintana*, 56% for *B vinsonii* subsp *berkhoffii*, and 37% for *B henselae*.[50] Frequent exposure in the clinic is plausible because *Bartonella* spp has been isolated from blood, bodily fluids, effusions, and other biologic samples from cats, dogs, and humans.[2] Veterinary staff can reduce the risk for infection by practicing good hand hygiene (eg, wearing gloves, frequent handwashing) and by minimizing exposure to fleas and ticks, contact with arthropod feces and animal bites and scratches, and contact with bodily fluids from sick animals, cuts, and needle sticks.[2]

Routine ectoparasite control in pets can reduce risk for transmission of *Bartonella* spp to humans.[2,5,24]

GLOBAL RELEVANCE

Bartonella spp have been found on every continent except Antarctica,[3] and there is considerable belief that their cause of human illness has been significantly underdiagnosed.[3,35,51,52] At least 17 species or subspecies of the 38 known *Bartonella* spp can cause disease in humans.[3] More research is needed to learn about this organism and its epidemiology to manage its global impact.

Infection in cats can lead to subclinical infection and persistent bacteremia[4] or, rarely, epithelioid hemangioendothelioma and systemic reactive angioendotheliomatosis.[2] *B koehlerae* infection in dogs has been associated with endocarditis and splenic disease.[2,20,39,40] A serosurvey of dogs in North America identified a seropositivity rate of 2.4%.[15]

B koehlerae is an uncommon cause of illness in humans[4] but has been associated with regional pain syndrome type I, hallucinations, sensory neuropathy, peripheral visual deficits, endocarditis, and other clinical conditions.[2-5]

5 *B vinsonii* subsp *berkhoffii*

Coyotes, dogs,[41] and foxes are the main reservoirs of *B vinsonii* subsp *berkhoffii*,[2,3] but the subspecies has also been found in cats, deer, horses, humans, a steer, and a red wolf.[2,42,43] A serosurvey of dogs in the United States found a seropositivity rate of 1.5%[14] and a higher rate of 3.6% in clinically ill dogs.[44] Signs in dogs may be subclinical or include anemia, arrhythmias, endocarditis, epistaxis, fever, hemangiosarcoma, myocarditis, splenomegaly, uveitis, and other signs; infection with this subspecies may also cause death.[3,17,45,46]

B vinsonii subsp *berkhoffii* is rare in cats and humans. In cats, signs can include endocardial fibrosis complex, endomyocarditis, and osteomyelitis.[3,42] Reported signs in humans include endocarditis and neurologic symptoms.[2-4,23,47,48] Vectors for transmission include *C felis* and, possibly, ticks and *Pulex* spp fleas.[2] It is probable that *B koehlerae* and *B vinsonii* subsp *berkhoffii* are underrecognized, as testing for *Bartonella* spp other than *B bacilliformis*, *B quintana*, and *B henselae* is rarely performed.[3]

Conclusion

Although new species of *Bartonella* are discovered frequently, the most widespread and well-described in humans and animals is *B henselae*. Many *Bartonella* spp can produce similar clinical signs in a host, but these infections can be subclinical and chronic. Vectors play a significant role in the

epidemiology of all *Bartonella* spp; transmission by other routes, particularly bites and scratches, makes *Bartonella* spp an occupational risk to those working closely with animals, especially those with a flea infestation. The occupational risks for *Bartonella* spp infection in veterinary staff can be reduced through a better understanding of *Bartonella* spp and by adhering to good prevention measures when working with animals (see ***Occupational Hazard***).

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