BARTONELLA INFECTIONS IN HUMANS AND ANIMALS: AN UPDATE.

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Conditions Caused by *Bartonella* Species in Humans.

<table>
<thead>
<tr>
<th>Bartonella sp.</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. bacilliformis</em></td>
<td>Carrion’s disease (<em>Oroya fever or verruga peruana</em>)</td>
</tr>
<tr>
<td><em>B. quintana</em></td>
<td>Trench fever, endocarditis, chronic bacteremia, bacillary angiomatosis</td>
</tr>
<tr>
<td><em>B. henselae</em></td>
<td>Cat scratch disease, endocarditis, myocarditis, chronic bacteremia, neuroretinitis, arthritis, status epilepticus, bacillary angiomatosis, peliosis hepatis, prolonged fever, weight loss, glomerulonephritis, osteomyelitis…</td>
</tr>
<tr>
<td><em>B. clarridgeiae</em></td>
<td>CSD? (<em>serological evidence only</em>)</td>
</tr>
<tr>
<td><em>B. elizabethae</em></td>
<td>Endocarditis</td>
</tr>
<tr>
<td><em>B. vinsonii berkholffii</em></td>
<td>Endocarditis</td>
</tr>
<tr>
<td><em>B. grahamii</em></td>
<td>Uveitis</td>
</tr>
<tr>
<td><em>B. vinsonii arupensis</em></td>
<td>Fever, confusion, underlying valvulopathy</td>
</tr>
<tr>
<td><em>B. washoensis</em></td>
<td>Cardiopathy (myocarditis?)</td>
</tr>
</tbody>
</table>
INSECTS ASSOCIATED or POSSIBLY ASSOCIATED WITH THE TRANSMISSION OF \textit{Bartonella} spp.

<table>
<thead>
<tr>
<th>SPECIES</th>
<th>INSECT VECTOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{B. bacilliformis}</td>
<td>Sand flies (\textit{Lutzomyias} sp.)</td>
</tr>
<tr>
<td>\textit{B. quintana}</td>
<td>Human body louse (\textit{Pediculus humanus corporis})</td>
</tr>
<tr>
<td>\textit{B. henselae}</td>
<td>Cat flea (\textit{Ctenocephalides felis}); Ticks?</td>
</tr>
<tr>
<td>\textit{B. clarridgeiae}</td>
<td>Cat flea (\textit{Ctenocephalides felis})??</td>
</tr>
<tr>
<td>\textit{B. koehlerae}</td>
<td>Cat flea (\textit{Ctenocephalides felis})??</td>
</tr>
<tr>
<td>\textit{B. vinsonii vinsonii}</td>
<td>Vole ear mite (\textit{Trombicula microti})</td>
</tr>
<tr>
<td>\textit{B. vinsonii arupensis}</td>
<td>Deer tick? (\textit{Ixodes scapularis})??</td>
</tr>
<tr>
<td>\textit{B. vinsonii berk Hoffii}</td>
<td>Ticks ?? (\textit{Rhipicephalus sanguineus, Dermacentor variabilis, Amblyoma americanum, Ixodes scapularis, Ixodes pacificus})??</td>
</tr>
<tr>
<td>\textit{B. bovis}</td>
<td>Biting flies??, ticks??</td>
</tr>
</tbody>
</table>

\textit{Bartonella bacilliformis} infections: Carrion Disease (Oroya fever and Verruga peruana).

- Endemic in South America, mainly Andean river valleys of Peru, (especially Rimac and Santa Eulalia river valleys), Ecuador and Colombia. Recent outbreaks discovered near Cuzco, Peru. Foci lie at right angles to the prevailing winds and at altitudes of 700 to 2500 meters where the sandfly \textit{Lutzomyia verrucarum} lives.

- No animal reservoir known. Humans can be bacteremic for months (up to 10\% of the population in endemic areas).

- \textit{Oroya fever}: acute, progressive and severe anemia. 40\% lethality.

- \textit{Verruga peruana}: 1-2 months after acute illness or commonly without previous acute form. Miliary or nodular or deep-seated lesions.
Verruga Peruana

Verruga Peruana
*Lutzomyia Verrucarum* female

*Bartonella Bacilliformis* vector

Trench Fever

caus**ed by:**

*Bartonella quintana*

transmitted by the human body louse

*Pediculus humanus corporis*
**Trench Fever, caused by *Bartonella quintana***

- Worldwide distribution. More than 1 million soldiers during WWI infected with *B. quintana* developed trench fever.
- Symptoms: incubation: 15-25 days. Fever with recurrence (= 5-day or quintan fever), headache and pain in the legs.
- Humans only known reservoir. Asymptomatic carriers reported in homeless people in Europe and USA.
- Vector: Human body louse (*Pediculus humanus* var. *corporis*). Can transmit disease 5-10 after feeding on infected persons. Infective for life, *B. quintana* replicates actively in louse intestines. Transmission likely through lice feces, infectious for up to 1 year.
Bacillary Angiomatosis

Cutaneous Lesion

Source: Dr. Jane Koehler, UCSF
Bacillary Angiomatosis

Source: Dr. F. A. Murphy

Bartonella Henselae

Source: Dr. Jane Koehler, UCSF
High rate of *Bartonella henselae* infection in HIV-positive outpatients in Johannesburg, South Africa.

- Non-random survey of outpatients attending HIV clinics in Johannesburg, South Africa.
- 188 patients sampled, of whom 19 (10.1%) were PCR positive for *B. henselae*.
- Only 1 patient had a suspected diagnosis of bacillary angiomatosis. 13 of the 19 were tested serologically and 8/13 (62%) were seropositive (1:64 or higher).
- By comparison, 2 (1%) of 204 blood cultures from HIV positive patients were positive for *B. henselae* (Clarridge et al., J. Clin. Microbiol. 1995;33:2107-2113).

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**Cat Scratch Disease (*Bartonella henselae*)**

**Epidemiology:** Cats are the main reservoir (28% of US pet cats sero +). Cats can be bacteremic for months. Stray cats, young cats more likely to be bacteremic. No vertical/horizontal transmission. Fleas are main vector from cat to cat. Cat to humans: mainly scratch, likely inoculation of infective flea feces at time of scratch. Flea transmission to humans possible, not clearly demonstrated. Recent suggestion of possible tick transmission.

**Symptoms:** 1 week after scratch: papule/vesicule at inoculation site, 2-3 weeks: lymphadenopathy, fever,
Complications: Parinaud’s syndrome, granulomatous lesions, retinitis, endocarditis, encephalitis (1 lethal case).

**Diagnosis:** in humans, mainly serology; in cats: blood culture/PCR

**Treatment:** No benefit in classical forms. In severe cases, Doxycycline, Erythromycin, Rifampin, Azithromycin: 15-21 days.
CAT-SCRATCH DISEASE

Figure 2. The primary inoculation papule of cat-scratch disease occurs three to 10 days after injury. The lesion has usually disappeared by the time symptoms develop. (Photograph courtesy of Churchill Livingstone, Inc.)

Cat Scratch Disease

Vesicle at inoculation site
Cat Scratch Disease

Cat Scratch Disease
Cat Scratch Disease: Analysis of 130 seropositive cases

- In Japan, cases occurred mainly in Fall and Winter.
- 80% were < 18 years old.
- Regional lymphadenopathy in 85% (110/130) of the patients:
  neck (33%), axillary (27%), inguinal (18%)
- Main symptoms were: fever, headache and malaise (77%)
  Typical syndrome: 80% (103/130);
  Atypical: 20% (27)
  - fever of unknown origin (37%);
  - neuroretinitis (22%), encephalopathy (15%),
  - hepatosplenic granuloma (11%) and Parinaud’s
    oculoglandular syndrome (7.5%).
- Fever of unknown origin or lasting > 14 days in 27 cases (21%),
  of which 11 (41%) lacked lymphadenopathy.
Cat Scratch Disease
Optic Neuritis Due to *Bartonella henselae* Infection

A 14-year-old girl presented with worsening headaches, unilateral decreased visual acuity (20/20 [right eye] and 5/200 [left eye]), and ocular pain in the left eye. A retinal examination showed bilateral optic-disk elevation with edema, lipid exudates that formed a macular star, and an area of choroiditis surrounded by serous fluid. IFA titers of antibodies against *Bartonella henselae* were 1:160 or more for IgM and 1:512 or more for IgG. The patient owned a cat but did not recall a specific scratch. Source: Herz & Lahay. N. Engl. J. Med. 2004; 350:e1.

*Bartonella henselae* infection associated with neuroretinitis, central retinal artery and vein occlusion, neovascular glaucoma, and severe vision loss.

A 21-year-old man had no light perception in the left eye secondary to concurrent central retinal artery and vein occlusion believed to have resulted from infection with *Bartonella henselae*. Forty days later, he developed neovascular glaucoma in the left eye. Source: Gray et al. Am J Ophthalmol. 2004; 137: 187-189.

One month after presentation, color fundus photograph of the left eye reveals optic disk edema, dilated and tortuous retinal veins, intraretinal hemorrhages in all four quadrants, and retinal pallor.
*Bartonella henselae* infection associated with neuroretinitis, central retinal artery and vein occlusion, neovascular glaucoma, and severe vision loss.


Left: Fluorescein angiogram reveals absent retinal arterial fluorescence with background choroidal fluorescence.

Right: minimal filling of the superior juxtapapillary vasculature

*Ctenocephalides felis*
Persistent *Bartonella* bacteremia in humans.

**B. bacilliformis**

5 to 10% of people in an endemic area of Peru were found to be bacteremic without evidence of clinical signs (Weiman and Pinkerton, 1937, Proc. Soc. Exp. Biol. Med. 37:596-598).

**B. quintana**

Experimentally infected volunteers bacteremic for as many as 300 to 443 days after onset of Trench fever (Swift, 1920, Arch Inter. Med. 26:76-98). Asymptomatic carriers described in the 1940s.

In a recent urban outbreak in Marseilles, France, 14% of 71 homeless persons were bacteremic for *B. quintana*, and of those bacteremic patients 80% were afebrile (Brouqui et al., N. Engl. J. Med. 1999;340:184-189).

**B. henselae**

A few human cases of persistent bacteremia in immunocompetent persons have been reported (reviewed by Koehler, 2000).

### Rheumatic manifestations related to *Bartonella* infection in humans

<table>
<thead>
<tr>
<th>Symptoms/ syndromes</th>
<th>Agent</th>
<th>PCR/Serol</th>
<th>Source</th>
</tr>
</thead>
</table>
Role of *Bartonella henselae* in the etiology of Henoch-Schonlein purpura.


Henoch-Schonlein purpura (HSP) is a vasculitis with an immune pathogenesis mediated by IgA. Its etiology remains obscure.

One case with evidence of exposure to kittens and a high titer (for *B. henselae*).

Serosurvey performed on series of cases and controls. *B. henselae* antibodies in 12/18 (67%) of cases versus 8/57 (14%) controls (p < 0.0001).

Vertebral Osteomyelitis due to *Bartonella henselae* in Adults: A report of two cases.


• Two adults, one HIV positive, had osteomyelitis
  28 yr-old male with fever, sweats, and upper quadrant abdominal pain, low back pain (Gardner and had a 3 mo-old kitten). Bone biopsy showed multiple foci of polymorphonuclear infiltration and medullar hyperplasia. PCR + and sero+ with *B. henselae*.
  30 yr-old HIV+ man with fever, myalgia, backache and sweats was infected with *B. henselae*. Had been scratched by a kitten. Was seropositive for *B. henselae*.

• Bone involvement is rare (about 0.1% (2/1443) to 0.3% (5/1852) of cases. Only 23 cases of CSD with bone involvement published, 4/23 in adults. Locations: spine (10 cases), limbs (5 cases), pelvis (2 cases), sternum (2 cases) and skull (2 cases), unknown (2 cases).
Subacute *Bartonella* Infection in Swedish Orienteers Succumbing to Sudden Unexpected Cardiac Death or Having Malignant Arrhythmias.


During the period 1979-92, an increasing number of sudden cardiac deaths occurred in young Swedish, male elite orienteers.

Myocarditis in 16 victims and in 4 cases also fatty infiltration mimicking arrhythmogenic ventricular cardiomyopathy (ARVC). Tissues from 5 cases tested for *Bartonella* by PCR targeting gltA gene.

*Bartonella* DNA detected in the heart of 4 deceased and lung of a fifth one. Sequences were close to *B. quintana* in 2 cases and identical to *B. henselae* in 3 cases. Four of the 5 cases and 2 additional cases with ARVC had *Bartonella* antibodies.

Molecular Epidemiology of *Bartonella* Infections in patients with bacillary angiomatosis-peliosis.


• Of the 49 patients with bacillary angiomatosis/peliosis,
  26 (53%) were infected with *B. henselae*, and
  23 (47%) were infected with *B. quintana*.

• Subcutaneous and lytic bone lesions were strongly associated with *B. quintana*, whereas peliosis hepatis was associated exclusively with *B. henselae*.

• Patients with *B. henselae* infection were identified throughout the study period and were epidemiologically linked to cat and cat flea exposure (P<0.004), whereas those with *B. quintana* were clustered and were characterized by low income (P=0.003), homelessness (P=0.004), and exposure to lice (P=0.03).
Molecular Epidemiology of *Bartonella* Infections in patients with bacillary angiomatosis-peliosis.


**Bacillary Angiomatosis-Peliosis site according to *Bartonella* species**

<table>
<thead>
<tr>
<th>Site*</th>
<th><em>B. quintana</em> (N=23)</th>
<th><em>B. henselae</em> (N=26)</th>
<th>P Value (Fisher’s exact test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>21</td>
<td>19</td>
<td>0.15</td>
</tr>
<tr>
<td>Lymph node</td>
<td>1</td>
<td>12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bone</td>
<td>8</td>
<td>0</td>
<td>0.001</td>
</tr>
<tr>
<td>Liver or</td>
<td>0</td>
<td>6</td>
<td>0.02</td>
</tr>
<tr>
<td>Liver and spleen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subcutaneous mass</td>
<td>8</td>
<td>1</td>
<td>0.008</td>
</tr>
</tbody>
</table>

* 24 patients had *Bartonella* infection at multiple sites
Molecular Epidemiology of *Bartonella henselae* Infection in HIV-infected patients and their cat contacts using pulsed field gel electrophoresis and genotyping.


*B. henselae* was isolated from 12 HIV-infected individuals with bacillary angiomatosis/peliosis hepatis and from their 15 domestic cat contacts.

Three of the 4 patients with *B. henselae* genotype I infection, but none of the 8 genotype II patients had hepatosplenic vascular proliferative lesions ($p=0.018$).

Four of the 5 human-cat pairs had closely-related PFGE fingerprints and concordant results by 16S rDNA typing, strongly suggesting that human infection was caused by the cat contact.
**Bartonella henselae infection in HIV-patients and their cats.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Genotype</th>
<th>Bacillary angiomatosis-peliosis lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Skin</td>
</tr>
<tr>
<td>A</td>
<td>I</td>
<td>+</td>
</tr>
<tr>
<td>B</td>
<td>II</td>
<td>N.D.</td>
</tr>
<tr>
<td>C</td>
<td>I</td>
<td>+</td>
</tr>
<tr>
<td>D</td>
<td>II</td>
<td>-</td>
</tr>
<tr>
<td>E</td>
<td>II</td>
<td>+</td>
</tr>
<tr>
<td>F</td>
<td>I</td>
<td>+</td>
</tr>
<tr>
<td>G</td>
<td>II</td>
<td>+</td>
</tr>
<tr>
<td>H</td>
<td>I</td>
<td>+</td>
</tr>
<tr>
<td>I</td>
<td>I</td>
<td>+</td>
</tr>
<tr>
<td>J</td>
<td>II</td>
<td>+</td>
</tr>
<tr>
<td>K</td>
<td>II</td>
<td>-</td>
</tr>
<tr>
<td>L</td>
<td>II</td>
<td>N.D.</td>
</tr>
</tbody>
</table>

a= hepatomegaly and/or splenomegaly; b= granulomatous hepatitis

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**Molecular Epidemiology of Bartonella henselae Infection in HIV-infected patients and their cat contacts using PFGE and genotyping.**

**Similarity %**

![Graph showing similarity percentage with PFGE bands](image)

Pt 12 (II)  Pt 8 (I)
Pt 13 (II)  Pt 14 (II)
Pt 10 (I)  Pt 3 (I)
Pt 7 (II)  Pt 6 (II)
Pt 4 (II)  Pt 9 (II)
Pt 5 (II)  Pt 11 (II)

![PFGE image](image)
Limited Diversity among Human Isolates of *Bartonella henselae*.


A study of 59 Australian/New Zealand isolates of *B. henselae* revealed a limited diversity among those of human origin (n=28). Human isolates from all over eastern Australia were type I, whereas feline isolates were more likely to be type II, with less congruity of inheritance between 16S and *gltA* alleles. It was similar to previous results from the Netherlands (Bergmans et al., 1996) and Germany (Arvand et al., 2001; Sander et al., 1999).

It is suggestive that human isolates of *B. henselae* come from a limited subset of strains.

Evidence of Rodent-Associated *Bartonella* and *Rickettsia* Infections among Intravenous Drug Users from Central and East Harlem, New York City.


Cohort of 204 injection drug users (IDUs) from Central and East Harlem, New York City (1997-1998). Tested for seven rickettsial (*R. akari, R. rickettsii, R. prowazekii, R. typhi*), or *Bartonella* sp. (*B. elizabethae, B. henselae*, and *B. quintana*) antigens.

Highest prevalence with *B. elizabethae* (46%), 10% reacted with *B. henselae* and 2% with *B. quintana* and 9% reacted to *Rickettsia akari*.

Harlem IDUs are commonly exposed to two rodent-associated zoonotic agents.
Serosurveys of *Bartonella henselae* infection in humans in Japan.

Kumasaka et al., 2001 Rinsho Byori., 49 (9):906-910.


Kikuchi: Testing by IFA for *B. henselae* in 48 CSD suspects, 159 patients with cardiovascular diseases (CVD) and 129 healthy Vet. Students.

- **CSD suspects:** 19 (39.6%) had IgG and 4 (8.3%) had IgM
- **Patients with CVD:** 5 (3.1%) IgG +
- **Vet. Students:** 14 (10.9%) had IgG and 1 (0.8) had IgM

Most sero+ persons had had contacts with cats. In CSD suspects: females>> males and young>> old.

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**BARTONELLA SPECIES INFECTING CATS**

<table>
<thead>
<tr>
<th>Species</th>
<th>Distribution</th>
<th>Vector</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. henselae</em></td>
<td>Worldwide</td>
<td>Cat flea (<em>Ctenocephalides felis</em>) (Koehler et al., 1994; Chomel et al., 1996)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Ticks?</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>USA:</strong> two human cases (Lucey et al., 1992)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>U. K. : Seropositivity associated with</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>B. burgdorferi</em> seropositivity (n=71, r=0.43, P&lt;0.001) (Barnes et al., 2000).</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Bartonella</em> positive UK ticks reported.</td>
</tr>
<tr>
<td><em>B. claridgeiae</em></td>
<td>Worldwide</td>
<td>Cat flea (more likely) (Raoult, person. comm.)</td>
</tr>
<tr>
<td><em>B. koehlerae</em></td>
<td>California</td>
<td>Cat flea (likely) (Droz et al., 1999)</td>
</tr>
<tr>
<td><em>B. bovis</em></td>
<td>USA (Utah, Illinois)</td>
<td>Unknown. Cat flea?? (Regnery et al., 2000)</td>
</tr>
</tbody>
</table>
### Bartonella sp. bacteremia prevalence in domestic cats from Western Europe

<table>
<thead>
<tr>
<th>Location</th>
<th>N</th>
<th>B. henselae</th>
<th>B. clarrig.</th>
<th>B. h./ Total (%)</th>
<th>B. c.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Denmark</strong></td>
<td>93</td>
<td>1</td>
<td>20 (95)</td>
<td>0</td>
<td>21 (22.6)</td>
</tr>
<tr>
<td>(Shelter/pet cats, Chomel et al., Vet. Res., 2002)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>100</td>
<td>0</td>
<td>13*</td>
<td>0</td>
<td>13 (13)</td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>193</td>
<td>1</td>
<td>18 (90)</td>
<td>1</td>
<td>20 (10.4)</td>
</tr>
<tr>
<td><strong>Netherlands</strong></td>
<td>113</td>
<td>6 (24)</td>
<td>10 (40)</td>
<td>4 (16)</td>
<td>5 (20) 25 (22)</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>94</td>
<td>17 (34)</td>
<td>18 (36)</td>
<td>15 (30)</td>
<td>50 (53)</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>436</td>
<td>11 (15)</td>
<td>36 (50)</td>
<td>2 (2.8) 15 (21)</td>
<td>8 (11) 72 (16.5)</td>
</tr>
<tr>
<td><strong>Greece</strong></td>
<td>39</td>
<td>2 (15)</td>
<td>3 (16)</td>
<td>50 (13)</td>
<td></td>
</tr>
<tr>
<td>(Stray cats, Athens, Chomel et al., unpublished data)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

### Bartonella henselae serosurveys in domestic cats from Europe

<table>
<thead>
<tr>
<th>Country</th>
<th>Shelter/stray</th>
<th>Pet</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Netherlands</strong></td>
<td>56/113 (50%)</td>
<td>28/50 (56%)</td>
<td>Bergmans et al., J. Clin. Microbiol., 1997</td>
</tr>
<tr>
<td><strong>Denmark</strong></td>
<td>23/49 (47%)</td>
<td>19/43 (44%)</td>
<td>Chomel et al., Vet. Res., 2002</td>
</tr>
<tr>
<td><strong>France</strong></td>
<td>N. D.</td>
<td>179/436 (41%)</td>
<td>Gurfield et al., Vet. Microbiol., 2001</td>
</tr>
<tr>
<td><strong>U. K.</strong></td>
<td>33/79 (42%)</td>
<td>28/69 (41%)</td>
<td>Barnes et al., Vet. Rec., 2000</td>
</tr>
<tr>
<td><strong>Austria</strong></td>
<td>N. D.</td>
<td>32/96 (33%)</td>
<td>Allerberger et al., Eur. J. Pediatr., 1995</td>
</tr>
<tr>
<td><strong>Germany</strong></td>
<td>N. D.</td>
<td>107/713 (15%)</td>
<td>Haimerl et al., J. Med. Microbiol, 1999</td>
</tr>
<tr>
<td><strong>Switzerland</strong></td>
<td>N. D.</td>
<td>61/728 (8%)</td>
<td>Glaus et al., J. Clin. Microbiol., 1997</td>
</tr>
<tr>
<td><strong>Sweden</strong></td>
<td>N.D.</td>
<td>3/292 (1%)</td>
<td>(73/292 (25%) B. elizabethae)</td>
</tr>
<tr>
<td><strong>Portugal</strong></td>
<td>N.D.</td>
<td>1/14 (7%)</td>
<td>Hjelm et al., Scand. J. Infect. Dis. 2002</td>
</tr>
<tr>
<td><strong>Greece</strong></td>
<td>32/39 (82%)</td>
<td>N.D.</td>
<td>Childs et al., Vet. Rec., 1995</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chomel et al., unpublished data</td>
</tr>
</tbody>
</table>

Between October 1999 and February 2000, 691 blood samples were tested for presence of *Bartonella* spp. from 615 animals.

<table>
<thead>
<tr>
<th>Species</th>
<th>Number tested</th>
<th>Number of samples</th>
<th>Number of Pos. animals</th>
<th>Number of pos. samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cats</td>
<td>360</td>
<td>395</td>
<td>34</td>
<td>30 * B. henselae (II)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 * B. henselae (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2 co-infection</td>
</tr>
<tr>
<td>Dogs</td>
<td>211</td>
<td>239</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Horses</td>
<td>27</td>
<td>39</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cattle</td>
<td>17</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Bartonella* sp. bacteremia prevalence in domestic cats from South-East Asia

<table>
<thead>
<tr>
<th>Location</th>
<th>N</th>
<th>B. henselae</th>
<th>B. clarridg.</th>
<th>B. h./B. c.</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I I/II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>690</td>
<td>43 1 0 5</td>
<td>1 5</td>
<td>1 50 (7.2)</td>
<td>(Pet cats, Maruyama et al., J.Vet. Med. Sci., 2000)</td>
</tr>
<tr>
<td>Thailand</td>
<td>275</td>
<td>48 (+4) 13 6</td>
<td>13 (9+4) (4)</td>
<td>76 (27.6)</td>
<td>(Stray cats/pet cats, Maruyama et al., Am. J. Trop. Med. Hyg., 2001)</td>
</tr>
<tr>
<td>Philippines</td>
<td>31</td>
<td>13 (+4) 0 0 6</td>
<td>19 (61)</td>
<td></td>
<td>(Stray cats, Chomel et al., Am. J. Trop. Med. Hyg., 1999)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>14</td>
<td>6 (type not specified) 3 0 9 (64)</td>
<td>(Stray cats, Jakarta, Marston et al., Clin. Diagn Lab Immunol., 1999)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Bartonella sp. bacteremia prevalence in domestic cats from the U.S.A., Australia and New Zealand**

<table>
<thead>
<tr>
<th>Location</th>
<th>N</th>
<th>B. henselae I</th>
<th>B. henselae II</th>
<th>B. clarrigd.</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA/East</td>
<td>70</td>
<td>NA</td>
<td>NA</td>
<td>7 (10)</td>
</tr>
<tr>
<td>(Shelter/pet cats, Kordick et al., Antimicrob. Agents Chemother., 1997)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA/East</td>
<td>52%</td>
<td>48%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA/West</td>
<td>16%</td>
<td>84%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td>77</td>
<td>35%</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>(pet: 16%, 3/18; feral: 40%, 24/59 (Sydney, Branley et al., Pathology, 1996)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>342</td>
<td>13.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Zealand</td>
<td>48</td>
<td>17%</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

**Bartonella henselae bacteremia or seroprevalence in domestic cats from Africa and the Middle East**

<table>
<thead>
<tr>
<th>Location</th>
<th>N</th>
<th>Bacteremia</th>
<th>Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>171</td>
<td>N.A.</td>
<td>23%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Zimbabwe: 24% (28/119)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R. S. Africa: 21% (11/52)</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>3.2%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Bloemfontein, R.S.A.)</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>25</td>
<td>8%</td>
<td>N.A.</td>
</tr>
<tr>
<td>(Kelly et al., Lancet, 1998)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Israel</td>
<td>114</td>
<td>N.A.</td>
<td>39.5%</td>
</tr>
<tr>
<td>(Baneth et al., Vet. Microbiol., 1996)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egypt</td>
<td>42</td>
<td>N.A.</td>
<td>12%</td>
</tr>
<tr>
<td>(Childs et al., Vet. Rec., 1995)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Acquisition of the cat scratch disease agent *Bartonella henselae* by cat fleas (Siphonaptera:Pulicidae).

- Fleas fed a concentration of $1 \times 10^5$ cfu/ml in blood were examined using IFA assay and PCR.
- Bacteria were present in the gut at 3 h, and persisted up to 9 days after infection.
- Qualitatively, the density of *B. henselae* was greater in the flea gut at day 9, indicating that replication was occurring in the gut.
- *B. henselae* was also detected in the feces of the infected fleas 9 d after infection and produced viable colonies upon inoculation onto heart infusion agar/rabbit blood plates.

Experimental infection of domestic cats with *Bartonella henselae* by inoculation of *Ctenocephalides felis* feces.

- Caged cat fleas were fed on 3 cats injected with $5 \times 10^7$ cfu ID and 3 cats injected with saline. Fleas were fed for 4 d, feces collected at days 2 and 4.
- Four groups of 5 cats were made:
  - **Group 1**: 50 *B. henselae*-exposed fleas were caged and allowed to feed on 5 cats for 6 days.
  - **Group 2**: flea feces collected from the 3 bacteremic cats were combined and each cat received ID 45 mg of feces suspended in 1 ml saline.
  - **Group 3**: 5 cats were fed 50 *B. henselae*-exposed fleas and 45 mg of feces from *B. henselae*-exposed fleas.
  - **Group 4**: controls (using fleas & feces from saline-injected cats).
Experimental infection of domestic cats with *Bartonella henselae* by inoculation of *Ctenocephalides felis* feces.

**Foil et al., J. Med. Entomol., 1998;35:625-628.**

<table>
<thead>
<tr>
<th>CAT GROUPS</th>
<th>No. /No.</th>
<th>Bacteremic/Exposed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1:</strong> (infected-fleas deposited)</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td><strong>Group 2:</strong> (flea feces injected ID)</td>
<td>5*/5</td>
<td>*3/5 after 1 week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*2/5 after 2 weeks</td>
</tr>
<tr>
<td><strong>Group 3:</strong> (fed fleas/flea feces)</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td><strong>Group 4:</strong> (controls)</td>
<td>0/5</td>
<td></td>
</tr>
</tbody>
</table>

Experimental infection of domestic cats with *Bartonella henselae* by inoculation of *Ctenocephalides felis* feces.

**Finkelstein et al., J. Med. Entomol., 2002;39:915-919.**

- *B. henselae* can multiply in the cat flea.
- *Bartonella henselae* can persist in flea feces in the environment for at least 3 days.
Clinical symptoms associated with natural *Bartonella henselae* infection (antibodies) in domestic cats.

Japanese cats: Lymph node swelling:  
*B. henselae* +: 13.6%,  
*B. henselae* & FIV +: 42.9%  
Gingivitis:  
*B. henselae* +: 27.3%,  
*B. henselae* & FIV +: 71.4%  

Swiss cats: Seroprevalence: 8.3% (61/728 cats)  
No difference in prevalence between healthy (7.2%) and sick cats (9.2%).  
In sick cats: increased frequency of stomatitis (p=0.0117) and a variety of diseases of the kidneys and the urinary tract (p=0.0337).  
There was an increased prevalence of *B. henselae* in cats positive for feline coronavirus (p=0.0185) or feline spumavirus (p=0.0235)  
(Glaus et al., 1997; J. Clin. Microbiol. 35:2883-2885.)

Vegetative endocarditis associated with natural *Bartonella* infection in domestic cats.  

Between 1990 and 1997, vegetative endocarditis diagnosed in six neutered cats aged between 3 and 9 years.  
Diagnosis made using echocardiography (5 cases) or at necropsy (1 case).

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Breed</th>
<th>Valve Affected</th>
<th>Culture/Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3</td>
<td>FN</td>
<td>DSH</td>
<td>aortic, mitral</td>
<td>ND</td>
</tr>
<tr>
<td>B</td>
<td>9</td>
<td>FN</td>
<td>DSH</td>
<td>aortic</td>
<td><em>Bartonella</em> spp.</td>
</tr>
<tr>
<td>C</td>
<td>6</td>
<td>MN</td>
<td>Persian</td>
<td>aortic, mitral</td>
<td><em>Bartonella</em> spp.</td>
</tr>
<tr>
<td>D</td>
<td>8</td>
<td>MN</td>
<td>DSH</td>
<td>aortic, ? Mitral</td>
<td>ND</td>
</tr>
<tr>
<td>E</td>
<td>6</td>
<td>MN</td>
<td>DSH</td>
<td>mitral, aortic</td>
<td>Streptococcus</td>
</tr>
<tr>
<td>F</td>
<td>6</td>
<td>FN</td>
<td>Tonkinese</td>
<td>tricuspid</td>
<td>Gram + cocci</td>
</tr>
</tbody>
</table>

No confirmation of *Bartonella* by PCR, only based on cultural aspect.
Experimental infection and re-infection of SPF cats with various strains and species of *Bartonella*.


<table>
<thead>
<tr>
<th>Primary Infect. Strain</th>
<th># bacteremic cats/ # inoculated cats</th>
<th>Challenge Strain</th>
<th># bacteremic cats/# inoculated cats</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. henselae</em> type I</td>
<td>3/3</td>
<td><em>B. hens. Type I</em></td>
<td>0/3</td>
</tr>
<tr>
<td>(feline type I strain)</td>
<td></td>
<td>(Houston I strain)</td>
<td></td>
</tr>
<tr>
<td><em>B. henselae</em> type I</td>
<td>9/9</td>
<td><em>B. hens. Type II</em></td>
<td>3*/9</td>
</tr>
<tr>
<td><em>B. henselae</em> type II</td>
<td>6/6</td>
<td><em>B. hens. Type I</em></td>
<td>6/6</td>
</tr>
<tr>
<td><em>B. henselae</em> type I</td>
<td>4/4</td>
<td><em>B. clarridgeiae</em></td>
<td>4/4</td>
</tr>
<tr>
<td><em>B. henselae</em> type II</td>
<td>4/4</td>
<td><em>B. clarridgeiae</em></td>
<td>4/4</td>
</tr>
<tr>
<td><em>B. clarridgeiae</em></td>
<td>4/4</td>
<td><em>B. hens. Type I</em></td>
<td>3/4</td>
</tr>
<tr>
<td><em>B. clarridgeiae</em></td>
<td>2/2</td>
<td><em>B. hens. Type II</em></td>
<td>2/2</td>
</tr>
<tr>
<td><em>B. koehlerae</em></td>
<td>2/2</td>
<td><em>B. hens. Type I</em></td>
<td>2/2</td>
</tr>
<tr>
<td><em>B. Koehlerae</em></td>
<td>2/2</td>
<td><em>B. hens. Type II</em></td>
<td>2/2</td>
</tr>
</tbody>
</table>

* Small number of colonies: mean 8.5 CFU/ml (range: 2.6 – 17 CFU/ml)

Cross protection against re-infection by *Bartonella henselae* type II

In a cat primarily inoculated with *Bartonella henselae* type I

![Graph showing cross protection against re-infection by Bartonella henselae type II](graph.png)
### Experimental infection and re-infection of SPF cats with various strains and species of *Bartonella*.  

<table>
<thead>
<tr>
<th>Bartonella species/Type (# cats)</th>
<th>Median days to reach peak bacteremia (range)</th>
<th>Median duration (days) of bacteremia (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. PRIMARY INOCULATION</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>B. henselae</em> type I (n = 16)</td>
<td>25 (14 - 48)</td>
<td>80 (37 - 357)</td>
</tr>
<tr>
<td><em>B. henselae</em> type II (n = 10)</td>
<td>18 (14 – 52)</td>
<td>181 (49 – 582)</td>
</tr>
<tr>
<td><em>B. clarridgeiae</em> (n = 6)</td>
<td>36 (28 – 36)</td>
<td>284 (140 – 363)</td>
</tr>
<tr>
<td><em>B. koehlerae</em> (n = 4)</td>
<td>36 (14 – 36)</td>
<td>74 (70 – 78)</td>
</tr>
<tr>
<td>Overall (n = 36)</td>
<td>28 (14 – 52)</td>
<td>98 (37 – 582)</td>
</tr>
<tr>
<td><strong>B. CHALLENGE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>B. henselae</em> type I (n = 11)</td>
<td>28 (22 – 48)</td>
<td>62 (14 – 77)</td>
</tr>
<tr>
<td><em>B. henselae</em> type II (n = 7)</td>
<td>28 (14 – 35)</td>
<td>70 (37 – 203)</td>
</tr>
<tr>
<td><em>B. clarridgeiae</em> (n = 8)</td>
<td>22 (22 – 36)</td>
<td>138 (43 – 405)</td>
</tr>
<tr>
<td>Overall (n = 26)</td>
<td>27 (14 – 48)</td>
<td>63 (14 – 405)</td>
</tr>
</tbody>
</table>

### Experimental infection of SPF cats with two different strains of *Bartonella henselae* type I: A comparative study.  

<table>
<thead>
<tr>
<th><em>B. henselae</em> Strain (# cats)</th>
<th>Inoculum (CFU/ml)</th>
<th>Fever Onset (days)</th>
<th>Duration (days)</th>
<th>Bacteremia Duration (mean)</th>
<th>Relapses</th>
</tr>
</thead>
<tbody>
<tr>
<td>feline type I (n=6)</td>
<td>4.8 x 10^7</td>
<td>2-12 (mean: 5.8)</td>
<td>7-14</td>
<td>237 days</td>
<td>5/6 (83%)</td>
</tr>
<tr>
<td>Houston I (n=6)</td>
<td>6.6 x 10^6 to 9.6 x 10^7</td>
<td>0</td>
<td>0</td>
<td>60 days</td>
<td>0/6 (0%)</td>
</tr>
<tr>
<td>P value</td>
<td>p &lt; 0.01</td>
<td></td>
<td></td>
<td></td>
<td>p =0.02</td>
</tr>
</tbody>
</table>
Mean bacteremia level in SPF cats inoculated with *B. henselae* feline type I (n=6) and Houston I (n=6).

**Figure:**

- **Y-axis:** Level of bacteremia (CFU/ml log10)
- **X-axis:** Weeks after inoculation

**Graphical Comparison:**

- Blue line: *B. henselae* feline type I
- Pink line: *B. henselae* Houston I

---

**ARTHROPODS ASSOCIATED or POSSIBLY ASSOCIATED WITH THE TRANSMISSION OF BARTONELLA HENSELAE**

- **Cat flea** (*Ctenocephalides felis*) ([Zangwill et al., 1993; Koehler et al., 1994; Chomel et al., 1996])

- **Ticks?**

  **USA:** Cat-related risk factors for cat scratch disease ([Zangwill et al., 1993]):
  - Ticks on humans: matched Odds ratio: 5.5 (95% Confidence interval: 1.2-25).
  - (21/56 cases, 5/56 controls)
  - Two human cases of *B. henselae* infection after tick bites ([Lucey et al., 1992]).

  **UK:** Four human co-infection Lyme/Bartonella, Bartonella-positive ticks collected on a cat and in household of a case ([Eskow et al., 2001]).

  - Seropositivity associated with *B. burgdorferi* seropositivity (n=71, r=0.43, P<0.001) ([Barnes et al., 2000]).
  - *Bartonella* positive UK ticks reported (Birtles, pers. comm.).
**Bartonella Infection in Dogs and association with tick-borne infections, U.S.A and Israel.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>% seropositive to B. berkoffii</th>
<th>Suspected vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pappalardo et al., 1997</td>
<td>Dog sera</td>
<td>3.6% (69/1920)</td>
<td><em>Dermacentor variabilis</em></td>
</tr>
<tr>
<td></td>
<td><em>R. rickettsii</em></td>
<td>7.8% (11/141)</td>
<td><em>Rhipicephalus sanguineus</em></td>
</tr>
<tr>
<td></td>
<td><em>E. canis</em></td>
<td>36% (54/151)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>B. canis</em></td>
<td>57.1% (4/7)</td>
<td></td>
</tr>
<tr>
<td>Breitschwerdt et al., 1998</td>
<td>12 dogs</td>
<td>4/12 (33%) (serol)</td>
<td><em>Amblyomma americanum</em></td>
</tr>
<tr>
<td></td>
<td><em>E. canis pos.</em></td>
<td>7/12 (58.3%) (DNA)</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>E. chaffeensis pos.</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kordick et al., 1999</td>
<td><em>Ehrlichia +</em></td>
<td>25/27 (93%) (sero)</td>
<td><em>Rhipicephalus sanguineus</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>18/24 (75%) (DNA)</td>
<td><em>Amblyomma americanum?</em></td>
</tr>
<tr>
<td>Baneth et al. 1998</td>
<td>Tick-borne</td>
<td>4/40 (10%)</td>
<td>Not indicated</td>
</tr>
<tr>
<td></td>
<td>Dis. suspects</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
MOLECULAR EVIDENCE OF *BARTONELLA* spp. IN QUESTING ADULT *IXODES PACIFICUS* TICKS IN CALIFORNIA.

<table>
<thead>
<tr>
<th>Origin</th>
<th>Sex</th>
<th>% of ticks with <em>Bartonella</em> infection (n PCR+/n tested)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baird Ranch</td>
<td>Male</td>
<td>0 (0/4)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>0 (0/5)</td>
</tr>
<tr>
<td>Red Fern Ranch</td>
<td>Male</td>
<td>42.9 (3/7)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>57.1 (4/7)</td>
</tr>
<tr>
<td>Windy Hill Open</td>
<td>Male</td>
<td>25.8 (17/66)</td>
</tr>
<tr>
<td>Space Reserve</td>
<td>Female</td>
<td>8.1 (5/62)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>19.2 (29/151)</strong></td>
</tr>
</tbody>
</table>

MOLECULAR EVIDENCE OF *BARTONELLA* spp. IN QUESTING ADULT *IXODES PACIFICUS* TICKS IN CALIFORNIA.

<table>
<thead>
<tr>
<th>Origin</th>
<th># Ticks</th>
<th>PCR-RFLP profile</th>
<th>Closest <em>Bartonella</em> species*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red Fern Ranch</td>
<td>3</td>
<td><em>B. quintana</em>-like</td>
<td><em>B. quintana</em> (97.8%–100%)</td>
</tr>
<tr>
<td>Windy Hill Open</td>
<td>6</td>
<td><em>B. henselae</em>-like</td>
<td><em>B. henselae</em> (97.4%-100%)</td>
</tr>
<tr>
<td>Space Reserve</td>
<td>5**</td>
<td><em>B. bovis</em>-like</td>
<td><em>B. bovis</em> (99.3%-99.6%)</td>
</tr>
<tr>
<td></td>
<td>1***</td>
<td><em>B. vins. berkhoffii</em></td>
<td><em>B. vins. Berkhoffii</em> (98.9%)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Unrecognized</td>
<td><em>B. washoensis</em> (99.3%-100%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>11</td>
<td>Bart. co-infection</td>
<td>unconclusive</td>
</tr>
</tbody>
</table>

*% DNA similarity based on 273 bp of the gltA gene; ** one mixed infection *B. bovis/B. henselae; *** mixed infection *B. vins. berkhoffii/B. henselae*
Concurrent Infection of the Central Nervous System by *Borrelia burgdorferi* and *Bartonella henselae*. Evidence For a novel tick-borne disease complex.


**Subjects:** Two male patients (14 and 36 years old) and 2 female patients (15 and 30 years old) with a history of tick bites and Lyme disease.

**Results:**
- Patients living in Lyme-endemic area of New Jersey, with chronic Lyme disease symptoms (neuroborreliosis).
- Seropositive for *Bartonella henselae*. *B. henselae* DNA detected in patients’ blood.
- DNA of *B. henselae* and *Borrelia Burgdorferi* in CSF.
- *B. henselae* DNA detected in live deer ticks obtained from the households of 2 of these patients.

Detection of *BARTONELLA* spp. from 228 Pooled Tick Samples by PCR of the *gltA* Gene, California (1996-1997).


<table>
<thead>
<tr>
<th>County</th>
<th><em>Ixodes</em> sp.</th>
<th><em>Tick</em> Species</th>
<th><em>Dermacentor</em> sp.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N. pools*</td>
<td>N Pos. (%)</td>
<td>N. pools</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>N. Pos. (%)</td>
</tr>
<tr>
<td>Shasta</td>
<td>13 Adults</td>
<td>1 (7.7%)</td>
<td>N. A.</td>
</tr>
<tr>
<td>Sonoma</td>
<td>62 Adults</td>
<td>8 (12.9)</td>
<td>N. A.</td>
</tr>
<tr>
<td></td>
<td>10 Nymphs</td>
<td>1 (10.0)</td>
<td>N. A.</td>
</tr>
<tr>
<td>El Dorado</td>
<td>24 Adults</td>
<td>4 (16.7)</td>
<td>1</td>
</tr>
<tr>
<td>Los Angeles</td>
<td>63 Adults</td>
<td>0 (0)</td>
<td>N. A.</td>
</tr>
<tr>
<td>Orange</td>
<td>36 Adults</td>
<td>8 (22.2)</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 (10.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>D. occidentalis</em> 1/12 (8.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>D. variabilis</em>    1/7 (14.3)</td>
</tr>
</tbody>
</table>

* pool = up to 5 ticks/pool
<table>
<thead>
<tr>
<th>Bartonella species</th>
<th>Clinical signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. vinsonii subsp. berkoffi</td>
<td>Endocarditis, Arrhythmias, Myocarditis, Granulomatous Rhinitis and Granulomatous Lymphadenitis.</td>
</tr>
<tr>
<td>B. henselae</td>
<td>Peliosis hepatis, Granulomatous hepatitis, hepatic lesions</td>
</tr>
</tbody>
</table>
| B. henselae & B. elizabethae | Non specific clinical abnormalities  
(severe weight loss, protracted lethargy, anorexia & chronic disease course) |
| B. clarridgeiae         | Endocarditis, hepatic lesions                                                  |
| B. washoensis           | Endocarditis                                                                    |

Materials and Methods:

- **CASES**: 25 dogs with histopathological diagnosis of endocarditis.
- **CONTROLS**: 28 dogs with history of hip dysplasia, no lymphoplasmatic changes on histopathology of cardiac tissue.
- **Histopathology**: H & E, Warthin-Starry silver staining
- **DNA extraction (Qiagen Kits)**
- **PCR/RFLP of citrate synthase (gltA) gene** (TaqI, HhaI, AciI and MseI endonucleases)
- **Partial sequencing of citrate synthase gene**

RESULTS:

- **CASES**: 73.0% (19/26 dogs) PCR Positive
- **CONTROLS**: 3.6% (1/28 dogs) PCR weak Positive
- **Histopathology**: 20% (4/20) had visible organisms with Warthin-Starry silver staining
- **PCR/RFLP of gltA gene and partial sequencing of the gene**: several profiles or sequences, including
  - **B. vinsonii berkhoffii** (2 from Thailand, 1974; 4 from USA (Bethesda, MD, 1978; San Antonio, TX, 1978 and 1986; Puerto Rico, 1987)
  - **B. henselae-like** (mainly Vietnam, 1970-1972)
  - **B. claridgeiae-like** (Type C) (Germany 1988)
  - **B. washoensis** (Type D) (Guam, 1992; Germany, 1995)
  - **2 mixed infections** (Okinawa, 1970; Florida, 1986)

<table>
<thead>
<tr>
<th>Presenting complaint:</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>lameness</td>
<td>8 (44%)</td>
</tr>
<tr>
<td>lethargy</td>
<td>6 (33%)</td>
</tr>
<tr>
<td>anorexia</td>
<td>6 (33%)</td>
</tr>
<tr>
<td>respiratory problems</td>
<td>4 (22%)</td>
</tr>
<tr>
<td>weakness</td>
<td>3 (17%)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve involvement:</td>
<td></td>
</tr>
<tr>
<td>aortic</td>
<td>9 (50%)</td>
</tr>
<tr>
<td>mitral</td>
<td>8 (44%)</td>
</tr>
<tr>
<td>aortic and mitral</td>
<td>1 ( 6%)</td>
</tr>
<tr>
<td>Etiology:</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (33%)</td>
</tr>
<tr>
<td>Bartonella</td>
<td>5 (28%)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>Streptococcus canis</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1 ( 6%)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>1 ( 6%)</td>
</tr>
</tbody>
</table>

18 dogs, all medium to large breed, median weight

<table>
<thead>
<tr>
<th>ID#</th>
<th>Date</th>
<th>Age</th>
<th>Sex</th>
<th>Breed</th>
<th>Valve</th>
<th>&quot;Bartonella&quot; Serol</th>
<th>Cult</th>
<th>PCR</th>
<th>A. pha Serol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6/99</td>
<td>7 y</td>
<td>MN</td>
<td>Bernese</td>
<td>Aortic</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>2</td>
<td>11/99</td>
<td>14 y</td>
<td>FS</td>
<td>Australian</td>
<td>Mitral</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>3</td>
<td>12/99</td>
<td>14 y</td>
<td>FS</td>
<td>Shetland</td>
<td>Aortic</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>4</td>
<td>1/00</td>
<td>9 y</td>
<td>MN</td>
<td>Shepherd</td>
<td>Aortic</td>
<td>Neg</td>
<td>1024</td>
<td>+ (Bc-h)</td>
<td>1:160</td>
</tr>
<tr>
<td>5</td>
<td>3/00</td>
<td>10 y</td>
<td>MN</td>
<td>Labrador</td>
<td>Mitral</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>6</td>
<td>4/00</td>
<td>2.5 y</td>
<td>MN</td>
<td>Boxer</td>
<td>Aortic</td>
<td>2048</td>
<td>+ (B.c.)</td>
<td>+ (B.c.)</td>
<td>1:100</td>
</tr>
<tr>
<td>7</td>
<td>6/00</td>
<td>9 y</td>
<td>MN</td>
<td>German Shep.</td>
<td>Mitral</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>8</td>
<td>6/00</td>
<td>4 y</td>
<td>MN</td>
<td>Red Hound</td>
<td>Mitral</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>9</td>
<td>10/00</td>
<td>8 y</td>
<td>FS</td>
<td>German Shep.</td>
<td>Mitral</td>
<td>32/64</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>10</td>
<td>10/00</td>
<td>5.5 y</td>
<td>M</td>
<td>Labrador</td>
<td>Aortic</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>11</td>
<td>12/00</td>
<td>6 mo</td>
<td>F</td>
<td>Great Dane</td>
<td>Aortic</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>Neg</td>
</tr>
<tr>
<td>12</td>
<td>1/01</td>
<td>7 y</td>
<td>M</td>
<td>Bull Mastiff</td>
<td>Aortic</td>
<td>1024</td>
<td>+ (Bvb)</td>
<td>1:640</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>1/01</td>
<td>6 y</td>
<td>MN</td>
<td>Airedale</td>
<td>Aortic</td>
<td>1024</td>
<td>+ (Bvb)</td>
<td>1:320</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>1/01</td>
<td>12 y</td>
<td>MN</td>
<td>Golden retr.</td>
<td>Mitral</td>
<td>Neg</td>
<td>Neg</td>
<td>NA</td>
<td>1:80</td>
</tr>
<tr>
<td>15</td>
<td>2/01</td>
<td>10 y</td>
<td>MN</td>
<td>Labrador mix</td>
<td>Aortic</td>
<td>4096</td>
<td>+ (Bvb)</td>
<td>1:100</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>3/01</td>
<td>9 y</td>
<td>MC</td>
<td>Shepherd mix</td>
<td>M&amp;A</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>17</td>
<td>4/01</td>
<td>6.5 y</td>
<td>FS</td>
<td>Bull Mastiff</td>
<td>Mitral</td>
<td>256 (Bc)</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>18</td>
<td>5/01</td>
<td>8 y</td>
<td>FS</td>
<td>Golden retr.</td>
<td>Mitral</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
</tbody>
</table>
Bacterial endocarditis and *Bartonella* endocarditis cases: Comparison in humans and dogs.

<table>
<thead>
<tr>
<th></th>
<th>Humans %</th>
<th>Dogs %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial endocarditis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture neg. infect. endoc.</td>
<td>14 (88/620)</td>
<td>27</td>
</tr>
<tr>
<td>Aortic Valve</td>
<td>43-47</td>
<td>23</td>
</tr>
<tr>
<td>Mitral Valve</td>
<td>47-57</td>
<td>67</td>
</tr>
<tr>
<td>Pre-existing valvular disease</td>
<td>30</td>
<td>unlikely</td>
</tr>
<tr>
<td><strong>Bartonella positive endocarditis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic</td>
<td>88 (29/33)</td>
<td>71.4 (5/7)</td>
</tr>
<tr>
<td>Mitral</td>
<td>12 (4/33)</td>
<td>14.3 (1/7)</td>
</tr>
<tr>
<td>Mixed</td>
<td>6 (2/33)</td>
<td>14.3 (1/7)</td>
</tr>
<tr>
<td>Pre-existing valvular disease</td>
<td>53 (8/15)</td>
<td>unlikely</td>
</tr>
</tbody>
</table>

*Bartonella* spp. identified in 26 positive dogs with endocarditis, A.F.I.P. and U.C. Davis, USA

<table>
<thead>
<tr>
<th>Species</th>
<th>Positive</th>
<th>Culture %</th>
<th>AFIP (N=19)</th>
<th>UCD (N=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. vinsonii</em> subsp. berkoffii</td>
<td>0</td>
<td>31.6 (6)</td>
<td>57 (4)</td>
<td></td>
</tr>
<tr>
<td><em>B. henselae</em>-like</td>
<td>0</td>
<td>42.1 (8)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><em>B. clarridgeiae</em></td>
<td>1</td>
<td>0 (0)</td>
<td>14.3 (1)</td>
<td></td>
</tr>
<tr>
<td><em>B. clarridgeiae</em>-like (type C)</td>
<td>0</td>
<td>5.3 (1)</td>
<td>14.3 (1)</td>
<td></td>
</tr>
<tr>
<td><em>B. washoensis</em> (type D)</td>
<td>1</td>
<td>10.5 (2)</td>
<td>14.3 (1)</td>
<td></td>
</tr>
<tr>
<td>Mixed infection</td>
<td>0</td>
<td>10.5 (2)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>
**Bartonella spp. Valvular Endocarditis in Dogs Necropsied at U.C. Davis (1997-2001).**
(Pasavento et al., in prep.)

- 31 necropsied dogs with valvular endocarditis during the 5-year period.

- Routine blood culture positive for 10 dogs, including *E. coli*, *Pseudomonas aeruginosa*, Beta-hemolytic streptococci and *Staphylococcus* spp.

- *Bartonella* DNA detected by PCR (primers directed at citrate synthase gene) on 12 (38.7%) of these 31 dogs.
  - 2 dogs also blood culture positive for other pathogens
  - 10 dogs blood culture negative.
  
  mean (range) age: 9 (1-16) yrs; 9/12 intact/neutered males
  5/12 had history of polyarthritis or swollen joints.

---

**Detection of Bartonella henselae and B. clarridgeiae DNA in hepatic specimens from two dogs with hepatic disease.**
(Gillepsie et al., JAVMA., 2003;222:47-51.)

- 4-year-old spayed female Basset Hound: 6 month history of recurrent fever, anorexia, weight loss. High hepatic enzyme activity, pyogranulomatous inflammation of the liver. PCR + for *B. henselae*.

- 6-year-old female spayed Doberman Pinscher: High hepatic enzyme activity. Liver biopsy: moderate tpo severe lymphocytic hepatitis. PCR + for *B. clarridgeiae*. 
**Bartonella henselae and B. elizabethae** as Potential Canine Pathogens.


- Four dogs with nonspecific clinical abnormalities, such as severe weight loss, protracted lethargy, and anorexia, in addition to a chronic disease course.

- 3/4 dogs had *B. vinsonii berkhoffii* antibodies.

- Blood: PCR + (16S-23S rDNA) for *B. henselae* in 3 dogs, PCR + for *B. elizabethae* in one dog.

---

**Conditions caused by Bartonella henselae in humans, cats and dogs, and by B. vinsonii berkhoffii in dogs.**

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Humans</th>
<th>Cats</th>
<th>Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic bacteremia</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Lymphadenitis, granulomatous</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>rhinitis and lymphadenitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacillary Angiomatosis/Peliosis</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Endo/Myocarditis, Arrhythmia</td>
<td>++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Prolonged fever</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Lethargy, weight loss, anorexia</td>
<td>?</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Neurological symptoms</td>
<td>++</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>+</td>
<td>?</td>
<td>+/-</td>
</tr>
<tr>
<td>Arthritis, joint pain</td>
<td>+</td>
<td>?</td>
<td>+</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>+</td>
<td>+/-</td>
<td>?</td>
</tr>
<tr>
<td>Uveitis and ocular lesions</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Reproductive disorders</td>
<td>?</td>
<td>+</td>
<td>?</td>
</tr>
</tbody>
</table>
CONCLUSIONS

• *Bartonella* species are a major source of infectious endocarditis in dogs. Localization and type of lesions are very similar in humans and dogs, but dogs present a higher prevalence of *Bartonella* endocarditis and a larger number of *Bartonella* species involved.

• *B. vinsonii* subsp. *berkhoffii* infection is widespread in many parts of the USA and in several countries in Asia and Europe. Infection appears to be more frequent in warm climates. *B. vinsonii* *berkhoffii* infected dogs are more likely to be sero-positive for tick-borne infections, especially *Ehrlichia* spp., and ticks have been found to harbor *Bartonella* spp. DNA, including *B. vinsonii* *berkhoffii*.

• The clinical spectrum of *Bartonella* infection in dogs is expanding and more likely to be not only identical, but also as diverse to what has been observed in humans.