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Bartonella henselae Prevalence in Domestic Cats in California: Risk Factors and Association between Bacteremia and Antibody Titers

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The isolation of *Bartonella henselae*, the agent of cat scratch disease, from the blood of naturally infected domestic cats and the demonstration that cats remain bacteremic for several months suggest that cats play a major role as a reservoir for this bacterium. A convenience sample of 205 cats from northern California was selected between 1992 and 1994 to evaluate the *B. henselae* antibody and bacteremia prevalences and to determine the risk factors and associations between bacteremia and antibody titers. *B. henselae* was isolated from the blood of 81 cats (39.5%). Forty-two (52%) of these bacteremic cats were found to be infected with ≥1,000 CFU/ml of blood. Impounded or former stray cats were 2.86 (95% confidence interval [CI] = 1.94, 4.22) times more likely to be bacteremic than the pet cats. Young cats (<1 year old) were more likely than adult cats to be bacteremic (relative risk = 1.64; 95% CI = 1.19, 2.28). Bacteremic cats were more likely than nonbacteremic cats to be infested with fleas (relative risk = 1.64; 95% CI = 1.38, 1.96). No association between *B. henselae* infection and feline immunodeficiency virus antibody prevalence was observed. Eighty-one percent of the cats (166 of 205) tested positive for *B. henselae* antibodies, and titers were higher in bacteremic than in nonbacteremic cats. Multiple logistic regression analysis indicated that younger age and seropositivity for *B. henselae* antibodies were associated with bacteremia. Serological screening for *Bartonella* antibodies may not be useful for the identification of bacteremic cats (positive predictive value = 46.4%), but the lack of antibodies to *B. henselae* was highly predictive of the absence of bacteremia (negative predictive value = 89.7%). Seronegative cats may be more appropriate pets for immunocompromised individuals who are at increased risk for developing severe *B. henselae* disease.

Cat scratch disease (CSD) was first described in France by Debré et al. (6) in 1950, yet the causative bacterial agent of CSD remained obscure until 1992, when *Bartonella* (formerly *Rochalimaea*) *henselae* (2) was implicated in CSD by serological and microbiological studies (7, 20). *B. henselae* has been linked to bacillary angiomatosis (BA) in immunocompromised humans (11, 12, 22), bacillary peliosis (24, 27), and relapsing bacteremia and endocarditis (14, 23), as well as to CSD (7, 20, 29). The most common of these syndromes in the United States is CSD, a persistent necrotizing inflammation of the lymph nodes in immunocompetent humans. According to Jackson et al. (8), there were an estimated 24,000 cases of CSD among humans in 1992, some 2,000 of whom were hospitalized.

Exposure to cats was one of the several criteria used in the diagnosis of the disease, but the exact role of the cat as a vector or reservoir of the infectious agent causing CSD was not clear (10, 16). Cats, especially young kittens, were suspected of playing a major role in the transmission of the infectious agent (3). Two epidemiological studies, one on the risk factors associated with BA (26) and the other on the risk factors associated with CSD (29), found a statistical relationship between traumatic contact with cats and the development of CSD or BA. In the study conducted by Tappero et al. (26), persons who had been scratched or bitten by cats were nearly four times more likely to develop BA or bacillary peliosis than those who had not. In their study of CSD in Connecticut, Zangwill et al. (29) found that patients with CSD were 15 times more likely than controls to own a kitten, 27 times more likely to be scratched or bitten by a kitten, and 29 times more likely to have at least one kitten with fleas.

The isolation of *B. henselae* from the blood of naturally infected cats (11, 19) and the demonstration that cats remain bacteremic for several months (11) suggest that cats play a major role as a reservoir for the bacterium. In a study to determine the prevalence of *B. henselae* bacteremia in cats from the San Francisco Bay Area, Koehler et al. (11) reported a prevalence of 41% (25 of 61) from blood samples from impounded and pet cats. They also found that younger cats were more likely to have a positive culture than older cats. A serological and epidemiological study of banked cat sera collected between 1980 and 1985 in Baltimore, Md. (4), indicated a *Bartonella* antibody prevalence of 14.7% (87 of 592). The prevalence of *Bartonella* antibodies increased significantly with cat age and weight and also was associated with seropositivity to *Toxoplasma gondii*. *B. henselae* antibody prevalence was also higher among feral cats (44.4%).

The objectives of our study were (i) to determine the risk factors associated with *B. henselae* bacteremia and seropositivity in a convenience sample of cats from various sources (pets, impounded cats, clinic cats, feral cats) in northern California

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and (ii) to determine the relationship between the *B. henselae* antibody titer and the level of bacteremia in infected cats. Such a study is of importance for assessing the relationship between bacteremia and antibody prevalence in order to develop a diagnostic strategy in selecting infection-free cats as pets, especially for immunocompromised individuals.

MATERIALS AND METHODS

Animals. Two hundred five cats from northern California were enrolled in the study between June 1992 and September 1994. The cats were from four subgroups belonging to two different cat populations: the Davis pet cat group (68 cats), the San Francisco pet cat group (44 cats), the Davis impounded cat group (49 cats), and the Sacramento former stray cat group (44 cats) (see Table 1). One hundred twelve cats were pets. Sixty-eight pet cats either were owned by veterinary students (31 cats) or were brought in by clients for elective procedures at the School of Veterinary Medicine Teaching Hospital (37 cats). Most of these 68 cats were from Sacramento and Yolo counties and will be referred to as the Davis pet cat group. The 44 remaining pet cats were brought to a veterinary clinic in the San Francisco Bay Area. Although the bacteremia findings for some of these 44 San Francisco Bay Area cats were reported previously (11), we included them in the present study to determine the seropositivity of these cats and the relationship of seropositivity with bacteremia. Ninety-three cats were either impounded cats (49 cats, including 15 cats for which bacteremia data were reported previously [11]) brought to the School of Veterinary Medicine Teaching Hospital for spaying or neutering or former stray cats (44 cats, referred to as the Sacramento former stray cat group) belonging to one owner who maintains an indoor colony of a variety of cats that she found in her neighborhood or that have been injured. All of the cats were physically examined by experienced veterinarians at the time that blood samples were drawn. When possible, a total volume of 2.5 ml of blood was taken from the jugular or saphenous vein of each cat. Blood (1.5 ml) was collected in a pediatric lysis-centrifugation tube (Wampole Laboratories, Cranbury, N.J.) for isolation of *B. henselae* and also in a serum separation tube for serological testing. For the Davis and San Francisco pet cat groups and the Sacramento former stray cat group, the owners filled out questionnaires concerning age, sex, neutering history, the cat's environment and length of ownership, the initial source of the cat and its age when it was acquired, the presence of flea infestation, and the presence of other cats or dogs in the household. For the Davis impounded cat group, limited descriptive data (estimated age, sex, and flea infestation) were recorded by one of the investigators at the time of blood sampling. All impounded cats were assumed to be outdoor and stray cats. The questionnaire and the protocol for collecting the blood from the cats were reviewed and approved by the University of California, Davis, Animal Care and Use Committee (protocol 5737).

Blood culture. The pediatric lysis-centrifugation tubes were centrifuged at $1,800 \times g$ for 75 min at room temperature, and the pellet was resuspended in 120 μl of inoculation medium (11). The resuspended blood pellet was plated onto heart infusion agar (BBL, Becton Dickinson, Cockeysville, Md.) containing fresh 5% rabbit blood, and the plate was incubated at 35°C in 5% CO_2 for 3 weeks. Cultures were examined daily for bacterial growth. The number of colonies observed was recorded as the number of colony-forming units per milliliter of blood.

Identification of isolates from cat blood as *B. henselae*. Identification of the isolate as *B. henselae* was based on the phenotypic characteristics, and the species was confirmed by PCR-restriction fragment length polymorphism analysis of a fragment of the citrate synthase gene (18).

DNA extraction. Bacterial DNA was extracted from each *B. henselae* isolate from cat blood by a standard protocol (28). The extracted DNA was then used as a template for amplification of a fragment of the citrate synthase gene.

PCR-restriction fragment length polymorphism analysis. An approximately 400-bp fragment of the citrate synthase gene was amplified by using previously described primers and methods (18). Control samples included DNA from a strain isolated from a naturally infected cat, confirmed previously to be *B. henselae* by 16S rRNA gene sequencing (11), and a sample with no DNA template.

PCR products were purified (Wizard PCR Preps; Promega, Madison, Wis.) and were digested overnight with *Taq*I at 65°C. The digested fragments were separated in a 3% MetaPhor agarose gel (FMC Bioproducts, Rockland, Maine) by standard electrophoretic techniques. Fragment sizes were estimated by comparison with a 100-bp ladder (GIBCO Bethesda Research Laboratories, Gaithersburg, Md.), and the banding pattern was compared with that of the *B. henselae* type strain (ATCC 49882; American Type Culture Collection). The identities of some of the isolates were also confirmed by the amplification and sequencing of all or part of the 16S rRNA gene (11).

***B. henselae* indirect immunofluorescence antibody test.** Previously prepared whole-cell preparations of *B. henselae* (strain U-4; University of California, Davis) were used as antigen, according to the method described for testing sera from humans with CSD (20). The only difference was the use of a specific cat cell line, FCWF (*Felis catus* whole fetus). Forty microliters of antigen was dotted onto each well of 12-well polytetrafluoroethylene-coated slides (Cel-line Associates, Newfield, N.J.), which were incubated overnight. The slides were washed twice in phosphate-buffered saline (PBS). The slides were then air dried, fixed in acetone, air dried again, and then stored at −20°C until they were used. Feline sera were diluted 1:64 in PBS and were added to the test wells. The slides were then incubated for 20 min at 37°C and were washed for 5 min in PBS. Fluorescein-conjugated goat anti-cat immunoglobulin (whole-molecule immunoglobulin G; Cappel, Organon Teknika Corp., Durham, N.C.) was diluted 1:800 in 0.01 M PBS with 0.001% Evan's blue, and the mixture was applied to each well. The slides were incubated for 20 min at 37°C and were washed again in PBS for 5 min prior to interpretation with a fluorescence microscope (magnification, ×400). The intensity of bacillus-specific fluorescence was scored subjectively from 1 to 4, and a fluorescence score of ≥2 at a dilution of 1:64 was considered to be a positive result (4). Sera were screened at 1:64 dilution, and any serum sample positive at that dilution was titrated in serial twofold dilutions to the endpoint. A double-blinded reading of each slide was performed by the same two readers.

Other serological tests. The presence of antibodies against *T. gondii* was tested for by indirect agglutination with a commercially available latex agglutination test (Toxo-MT Eiken; Eiken Chemical Co. Ltd., Tokyo, Japan). A titer of ≥64 was considered indicative of previous exposure, according to the manufacturer's indications.

Detection of feline immunodeficiency virus (FIV) antibody and feline leukemia virus (FeLV) antigen by an enzyme-linked immunosorbent assay method was performed as described previously (15, 21). Briefly, for FIV antibody testing (21), cat serum diluted 1:100 in Tris-buffered saline (TBS; 0.15 mol of NaCl per liter, 50 mmol of Tris [pH 7.60] per liter) containing 2% low-fat milk powder and 0.5% Tween 20 supplemented with 20% normal goat serum was added to individual wells for 30 min (100 μl per well). After four washes in TBS, peroxidase-labeled goat anti-cat immunoglobulin G (Kirkegaard & Perry Laboratories, Inc., Gaithersburg, Md.) diluted 1:1,000 in TBS was added to the plate for 30 min (100 μl per well). After washing the plates four times in TBS, substrate (TMB, citric acid, and peroxidase) was added. The optical density of each well was then estimated at 405 nm with a Multiscan spectrophotometer (Flow Laboratories, Irvine, Scotland, United Kingdom).

Detection of the FeLV p27 antigen was performed by a sandwich technique (15). Briefly, the wells were coated with monoclonal antibodies specific for FeLV p27. Bound antigen was detected by adding anti-FeLV p27 monoclonal antibody conjugated to horseradish peroxidase (1 h at 37°C).

Statistical analysis. For univariate analyses, nonparametric tests (chi-square, Fisher's exact test) were used to test for associations between culture positivity and putative explanatory factors, such as age, sex, origin, and flea infestation. Similar tests were performed to test for associations between seropositivity and the same explanatory factors. The Mantel-Cox test was used to assess trends in risk across ordinal exposure categories. Multivariate logistic-binomial regression was used to assess the effect of putative risk factors for bacteremia and seropositivity to *B. henselae* while controlling for random effects associated with the clustered sample data. Analyses were performed by using Epi Info (5) and EGRET (Statistics and Epidemiology Research Corporation, 1994).

RESULTS

Description of cat population. Of the 205 cats, 56.6% were females and 61% of the cats were spayed or neutered. The ages of the cats ranged from 4 months to 20 years (mean, 4.5 years; median, 3 years). One hundred fifty-one cats (73.7%) were ≥1 year of age. Pet cats (mean age, 5.97 years) were older than impounded cats (mean age, 2.7 years), because cats <1 year old accounted for 13.4% of the pet cats and 42% of the impounded cats. Twenty-one cats (10.2%) were declawed; 11 of them (52%) were owned by veterinary students. Most of the declawed cats (19 of 21) were ≥3 years of age.

Sixty-three percent of the 205 cats and 82.7% of the 156 owned cats lived mostly or completely indoors at the time of the survey, but more than 50% of the owned cats lived outdoors before adoption. Most of the cats (82%) lived in an urban area, and more than three-fourths of the cats (160 of 205) were reported to have been stray cats at some time. Of the 156 owned cats, 106 cats (68%) had been owned for more than 1 year and 36 cats had been owned for 6 months or less at the time of sampling. Eighty percent (125 of 156) of the owned cats were living in households with other pets, most commonly, cats. Sixty-nine percent (141 of 205) of the cats were reported to be infested with fleas or were carrying fleas at the time of the blood collection. Ten cats (5%) were associated with a human case of CSD or BA.

TABLE 1. *B. henselae* bacteremia and antibody prevalences by origin among 205 northern California cats, 1992 to 1994

Cat origin	No. (%) of cats		
	Total	Bacteremic	Seropositive
Pet			
Davis	68	3 (4.4)	42 (61.8)
San Francisco	44	21[a] (47.7)	38 (86.4)
Impounded, Davis	49	26[a] (53.0)	42 (85.7)
Former stray, Sacramento	44	31 (70.4)	44 (100.0)
Total	205	81 (39.5)	166 (81.0)

[a] Includes bacteremia data published previously (11).

Bacteriological and serological data. *B. henselae* was isolated from the blood of 81 (39.5%) of the 205 cats (Table 1). Similarly, *B. henselae* was isolated from 37% of the 146 cats if data for the 59 cultures of cat blood reported previously (11) are excluded. All isolates were confirmed to be *B. henselae* by *Taq*I PCR-restriction fragment length polymorphism analysis of the citrate synthase gene fragment. Bands were identical to the ones shown by the *B. henselae*-positive control (data not shown). The prevalence of bacteremia ranged from 4.4% in the Davis pet cat group to 70.4% in the Sacramento former stray cat group (Table 1). The number of CFU per milliliter of blood varied from 8 to more than 4,000. Forty-two cats (52%) were found to have a level of bacteremia of ≥1,000 CFU/ml. Seventy-nine percent (33 of 42) of these cats were from the Davis impounded cat group or the Sacramento former stray cat group, and 76% (32 of 42) were reported as being or having been stray cats. Most of the bacteremic cats (38 of 42; 90.5%) were reported to be infested with fleas. Fifty percent (21 of 42) of these cats were less than 1 year old. The prevalence of bacteremia was higher among cats <1 year old than among cats ≥1 year old (Table 2).

One hundred sixty-six (81%) cats tested positive for *B. henselae* antibodies by immunofluorescence assay (geometric mean titer, 1:310). Seventy-seven cats (37.5%) were bacteremic and had *B. henselae* antibodies. Eighty-nine cats (43.4%) had *B. henselae* antibodies and were not bacteremic, and 4 cats (2%) were bacteremic but did not have specific antibodies. The remaining 35 cats were both bacteriologically and serologically negative. Antibody titers were significantly higher (Mann-Whitney test, $P < 0.0001$) in bacteremic cats (median, 1:512) than in nonbacteremic cats (median, 1:128). Cats <1 year old had a higher antibody prevalence than cats ≥1 year old (Table 2). Ninety-two percent (86 of 93) of the Davis impounded cat and Sacramento former stray cat groups had *B. henselae* antibodies, whereas 71.4% (80 of 112) of the Davis and San Francisco pet cat groups had *B. henselae* antibodies, a statistically significant difference (relative risk [RR] = 1.29; 95% confidence interval [CI] = 1.14, 1.48).

Nineteen cats (9.3%) were positive for FeLV antigen, 60 cats (29.3%) had FIV antibody, and 6 cats (2.9%) had both FeLV antigen and FIV antibody. Seven cats (3.4%) had antibodies against *T. gondii*. Of the 10 cats belonging to humans with CSD or BA, 7 were bacteremic when tested.

Univariate analysis. Among the Davis and San Francisco pet cat groups, the prevalence of bacteremia was 21.4% (24 of 112), whereas in the Davis impounded cat and Sacramento former stray cat groups, cats (57 of 93) were almost three times more likely to be bacteremic than the Davis and San Francisco pet cats (RR = 2.86; 95% CI = 1.94, 4.22). Outdoor cats were more likely than indoor cats to be bacteremic (RR = 1.39; 95% CI = 0.99, 1.94), but that association was not statistically significant.

Young cats (<1 year old) were more likely than adult cats (≥1 year old) to be bacteremic (RR = 1.64; 95% CI = 1.19, 2.28). Among the bacteremic cats, young cats were also 1.7 times more likely than adult cats to have a high degree of bacteremia (≥1,000 CFU/ml of blood) (95% CI = 1.14, 2.54). Bacteremic cats were also more likely than nonbacteremic cats to be infested with fleas (RR = 1.64; 95% CI = 1.38, 1.96). More specifically, bacteremic Davis and San Francisco pet cats were 2.14 times more likely than nonbacteremic Davis and San Francisco pet cats to be infested with fleas (95% CI = 1.6, 2.87). Flea infestation was not a risk factor associated with cats being *B. henselae* seropositive. Conversely, the higher the antibody titer, the more likely that cats were infested with fleas ($P = 0.002$).

Age at the time of acquisition or having previously been a stray cat was not associated with *B. henselae* bacteremia or seropositivity. The presence of FIV antibodies and FeLV antigenemia were not associated with being bacteremic or serologically positive for *B. henselae*. Adult cats (≥1 year old) were more likely than young cats to be serologically positive for FIV (RR = 2.03; 95% CI = 1.07, 3.83), whereas cats <1 year old were more likely than adult cats to be serologically positive for *B. henselae* (RR = 1.17; 95% CI = 1.04, 1.32). No correlation between *B. henselae* antibody prevalence and *T. gondii* antibody prevalence was observed.

Of the bacteremic cats, 95% (77 of 81) were serologically positive, but of the nonbacteremic cats, only 28.2% were serologically negative. Three of the four seronegative but bacteremic cats were adults (2, 6, and 13 years old, respectively) with low levels of bacteremia (16, 21, and 260 CFU/ml of blood, respectively). One of these three cats was also FIV antibody positive. The fourth cat was a 6-month-old kitten with a very high grade bacteremia (≥4,000 CFU/ml of blood). Follow-up sera from these four cats were not available. Among the seropositive cats, fewer than 50% (77 of 166) were bacteremic, but 89.7% of the seronegative cats were not bacteremic. No correlation between serological titers and bacteremia levels was observed (Fig. 1), but cats with antibody titers of ≥1:512 were more likely to be bacteremic (RR = 1.53; 95% CI = 1.10, 2.12).

Among the 156 owned cats (Davis and San Francisco pet cats and Sacramento former stray cats), cats owned for ≤6 months were more likely to be bacteremic (RR = 1.91; 95% CI = 1.24, 2.93) and seropositive (RR = 1.23; 95% CI = 1.08, 1.4) than cats owned for more than 6 months, but such an associ-

TABLE 2. *B. henselae* bacteremia and antibody prevalences by age among 205 northern California cats, 1992 to 1994[a]

Age (yr)	No. (%) of cats		
	Total	Bacteremic	Seropositive
<1	54	30 (55.5)	49 (90.7)
≥1	151	51 (33.8)	117 (70.5)
1–1.9	20	12 (60.0)	19 (95.0)
2–2.9	21	10 (47.6)	13 (61.9)
3–5.9	44	15 (34.1)	32 (72.7)
≥6	66	14 (21.2)	53 (80.3)
Total	205	81 (39.5)	166 (81.0)

[a] Antibody prevalences indicate those with titers of ≥64.

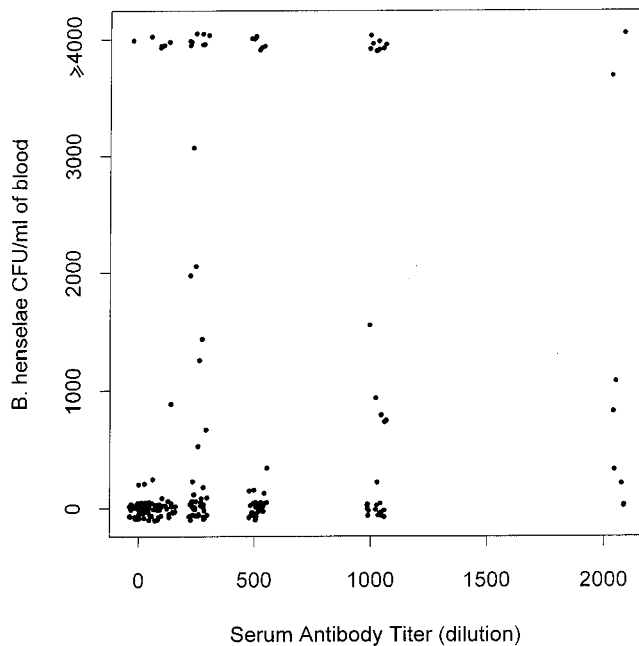

FIG. 1. Relationship (scattergram) of *B. henselae* antibody titer to *B. henselae* bacteremia (CFU per milliliter of blood) in 205 cats from northern California. Each dot represents one cat.

TABLE 3. Multivariate logistic regression ORs and 95% CIs for variables associated with *B. henselae* bacteremia and antibodies in 205 cats from northern California[a]

Outcome and characteristic	OR (95% CI)
Bacteremia	
Age	
≥1 versus <1 yr	0.34 (0.16, 0.73)
<1 yr	1.00
1–2 versus <1 yr	0.89 (0.28, 2.85)
3–6 versus <1 yr	0.17 (0.05, 0.58)
>6 yr versus <1 yr	0.22 (0.06, 0.78)
Immunofluorescence assay antibody titer	
<64	1.00
64–128	1.17 (0.29, 4.63)
256–512	3.84 (1.06, 13.33)
1,024–2,048	5.03 (1.28, 19.75)
Indoor	0.18 (0.06, 0.54)
FIV antibody positive	0.32 (0.14, 0.74)
Flea infestation	1.68 (0.59, 4.77)
B. henselae seropositivity[b]	
Age, ≥1 versus <1 yr	0.29 (0.01, 0.86)
B. henselae-positive culture	3.07 (0.91, 10.34)

[a] Models are adjusted for the presence of other variables listed in the model for each outcome and clustering effects due to sampling.
[b] Immunofluorescence assay titer, ≥64.

ation was not verified when looking at all of the pet cats as a group compared with cats that were not owned. Declawed cats were also less likely than nondeclawed cats to be bacteremic (RR = 0.22; 95% CI = 0.06, 0.86). Such a difference was not observed for the presence of *B. henselae* antibodies.

Logistic regression. Univariate logistic regression adjusted for the clustering of samples indicated that age, living outdoors, and being seropositive were risk factors significantly associated with bacteremia. It also indicated that age and being bacteremic were associated with the presence of *B. henselae* antibodies. Cats ≥1 year of age were less likely than cats <1 year old to be bacteremic and to have *B. henselae* antibodies (odds ratio [OR] = 0.34; 95% CI = 0.16, 0.73) and were less likely to be seropositive (OR = 0.29; 95% CI = 0.01, 0.86). The higher the antibody titer, the more likely the cats were to be bacteremic (for titers of ≥1,024, OR = 5.03 and 95% CI = 1.28, 19.75; for titers of <1,024 and >128, OR = 3.84 and 95% CI = 1.06, 13.33; for titers ≤128 and >0, OR = 1.17 and 95% CI = 0.29, 4.63). Bacteremia was less likely to occur in indoors cats (OR = 0.18; 95% CI = 0.06, 0.54), but that habitat was not associated with the presence or absence of *B. henselae* antibodies (OR = 1.07; 95% CI = 0.25, 4.51). Cats that had FIV antibodies were less likely than the FIV antibody-negative cats to be bacteremic (OR = 0.32; 95% CI = 0.14, 0.74). Cats infested with fleas were at higher risk of being bacteremic (OR = 1.68), but the association was not statistically significant (95% CI = 0.59, 4.77) in the regression analysis. Other factors (sex, duration of ownership, age of acquisition, FeLV antigenemia, presence of other pets, or being declawed) were not factors significantly associated with *B. henselae* bacteremia or seropositivity.

Multivariate logistic regression, performed in order to determine independent risk factors, also indicated that cats ≥1 year of age were less likely than cats <1 year of age to be bacteremic and seropositive and that indoor cats were less likely to be bacteremic (Table 3). It confirmed that the higher the antibody titer, the more likely that the cats were bacteremic.

DISCUSSION

Cats have been identified as a major reservoir of *B. henselae* (11). We found that 37% (54 of 146) of the cats tested, or 39.5% (81 of 205) if we included the cats for which microbiological results were reported previously (11), were bacteremic. This percentage is similar to that of the smaller study, in which a prevalence of 41% was reported in the San Francisco Bay Area (11). In the current study, we found a greater variation in the prevalence of bacteremia, ranging from 21.4% in Davis and San Francisco pet cats to 61.3% in Davis impounded cats and Sacramento former stray cats. In North Carolina, Kordick et al. (13) reported *B. henselae* bacteremia in 25% (6 of 24) of healthy cats and 84.2% (16 of 19) of cats involved in cases of CSD. Similarly, 7 of 10 (70%) of our study cats implicated as sources of human cases of CSD or BA were bacteremic. *B. henselae* bacteremia appears to be common in cats in California, providing an extensive reservoir for zoonotic infection. Bacteremia also appears to be more common in cats <1 year old, suggesting that cats are more likely to acquire *B. henselae* infection during the first year of life. This corroborates epidemiological evidence linking exposure of humans to young cats with developing CSD or BA (3, 11, 26, 29). Additionally, the fact that more than 90% of the cats <1 year old in our study had *B. henselae* antibodies also supports infection at an early age. Bacteremia has been reported to last from several weeks to several months (11, 19), with fluctuations in the level of bacteremia by as much as 100-fold with intermittent negative culture (11), but the duration and course of feline *B. henselae* infection remain unknown.

Flea infestation was found to be more frequent in bactere-

mic cats than in nonbacteremic cats. The association was even stronger when evaluating only pet cats. Similarly, the higher the antibody titer in cats, the more likely they were to be infested with fleas. Because flea infestation was very common in our study cats (90% of the bacteremic cats and 69% of all of the cats), it was not possible to confirm the association between flea infestation and *B. henselae* bacteremia by multivariate analysis. Nevertheless, such data are suggestive of the role of this arthropod vector in the transmission of *B. henselae* among cats, as suggested previously by epidemiological (29) and by microbiological and molecular biological (11) data. A serological study conducted among pet cats throughout North America (9) revealed a higher seroprevalence of *B. henselae* in the pet cat population from warm, humid climates than in the cats from cold, dry climates. Such data could also support the theory that the cat flea is involved in the transmission of *B. henselae*, because this arthropod is more common in warmer climates. Another member of the *Bartonella* genus, *B. bacilliformis*, is transmitted by the sandfly, and *B. quintana*, the agent of trench fever, was transmitted by body lice in World War I (25). Koehler et al. (11) were able not only to identify *B. henselae* DNA by PCR in a single flea but also to demonstrate the presence of live organisms in fleas combed from a bacteremic cat. Experimental infection of cats with infected fleas will be necessary to confirm the role of cat fleas as a vector in the transmission of *B. henselae.*

Although declawing could be suspected as a factor protecting against developing bacteremia according to univariate analysis, multivariate analysis did not sustain the hypothesis, because age was more likely to be a confounding factor. *B. henselae* antibody prevalence was not statistically different for cats whether they were declawed or not; therefore, our data do not support declawing of cats to reduce the risk of *B. henselae* infection.

Five percent (4 of 81) of the bacteremic cats did not have *B. henselae* antibodies. This study was a cross-sectional study; therefore, it was not possible to test these cats a second time. It is possible that the kitten was in an early stage of infection and had not yet developed *B. henselae* antibodies. For the three other cats, one of them may have had a defective immune response associated with the FIV infection, but for the two other cats with low-grade *B. henselae* bacteremia, the reason for the inability to detect *B. henselae* antibodies remains unclear.

Antibody prevalence (81%) was very high in the cat study population when compared with those in other surveys (4, 9, 13). This difference could be related to the population selection, because one group of cats ($n = 44$) heavily infested with fleas belonged to the same owner. All of these cats had antibodies, and the majority of them (70.4%) were bacteremic. Although there was no linear relationship between the antibody titer and the level of bacteremia, serum antibody titration does appear to be useful for predicting the level of bacteremia in cats, because antibody titers of $\geq$512 are more likely to be found in bacteremic cats. The serological test had a positive predictive value of 46.4%, and thus, it is of limited utility in distinguishing between bacteremic and nonbacteremic cats. However, the absence of antibodies to *B. henselae* was highly predictive of the absence of bacteremia (negative predictive value = 89.7%), and therefore, serologically negative cats may be more appropriate pets for the immunocompromised person.

No correlation was observed between *B. henselae* antibody prevalence and *T. gondii* antibody prevalence, although a correlation was reported previously (4). Such a difference could be explained by the very low prevalence of *T. gondii* in our cat population. Both FIV and *B. henselae* infections are more likely to occur in outdoor cats (17). An inverse correlation was observed between *B. henselae* antibody prevalence and FIV antibody prevalence. FIV antibodies are more likely to be found in adult cats (17) at an age when antibodies for *B. henselae* are less prevalent.

On the basis of our data and as suggested previously (1, 11), prospective cat owners who are immunocompromised should preferably acquire an adult indoor cat of known origin rather than a young kitten. Adoption of stray kittens or cats, whose play is likely to result in scratches, should be avoided. Flea control measures should also be undertaken on a regular basis. Culture of cat blood samples still remains the only technique of identifying bacteremic cats, but because culture is difficult and cats can be intermittently bacteremic, this test is also of limited utility in predicting cats that are potentially infectious for their owners. Serological testing appears to be of limited value for predicting bacteremia. However, the inability to detect *B. henselae* antibodies appears to be predictive of the absence of bacteremia, which may be useful information for immunocompromised individuals.

Despite some limitations of the cat population selected for our study, the large number of cats tested confirms the widespread prevalence of *B. henselae* infection in cats in northern California, especially in young, flea-infested, outdoor cats. Experimental studies are necessary to determine the kinetics and duration of bacteremia in cats. Similarly, studies need to be performed to better understand the modes of transmission of *B. henselae* from cat to cat and from cats to humans in order to develop strategies to prevent *B. henselae* infection.

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