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Bartonella Species as a Potential Cause of Epistaxis in Dogs

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Infection with a *Bartonella* species was implicated in three cases of epistaxis in dogs, based upon isolation, serology, or PCR amplification. These cases, in conjunction with previously published reports, support a potential role for *Bartonella* spp. as a cause of epistaxis in dogs and potentially in other animals, including humans.

CASE REPORTS

Case 1. A 6-year-old, mixed breed, spayed female dog from Rockingham, NC, was referred to the North Carolina State University Veterinary Teaching Hospital for evaluation of intermittent episodes of epistaxis that had occurred during the previous 2 years. Nasal bleeding had become nearly continuous during the 2-month period prior to referral. At the time of initial examination by the referring veterinarian, epistaxis was accompanied by thrombocytopenia and pyrexia. Following administration of tetracycline hydrochloride (dosage unknown) for 14 days, the epistaxis resolved. A year later, several episodes of epistaxis were again observed by the owner. Hematologic abnormalities then included a nonregenerative anemia (hematocrit, 11.0%; reference range, 37.0 to 55.0%), mature neutrophilic leukocytosis (granulocytes, 36.6; reference range, 6.0 to 16.9 $10^3/\mu l$ with 96% mature neutrophils), and thrombocytosis (platelet count, 562,000/μl; reference range, 175 to 500 $10^3/\mu l$). Biochemical abnormalities included hyperproteinemia (11.7 g/dl; reference range, 5.0 to 7.4 g/dl), hypoalbuminemia (1.9 g/dl; reference range, 2.7 to 4.4 g/dl), and hyperglobulinemia (9.8 g/dl; reference range, 1.6 to 3.6 g/dl). A coagulation profile was within normal limits. Tetracycline hydrochloride (10 mg/kg for 14 days) was reinstituted. Epistaxis returned shortly after antibiotic administration was completed. Several months later, the dog was referred to the North Carolina State University Veterinary Teaching Hospital for diagnostic evaluation of the epistaxis.

On physical examination, mucous membranes were pale. Fundic exam revealed an active chorioretinitis and tortuous retinal vessels, potentially associated with chronic hyperglobulinemia. There were focal areas of hemorrhage in the right eye. Blood pressure was normal. Hematological abnormalities included a mildly regenerative, microcytic, and hypochromic anemia, with normal numbers of white blood cells and platelets. Serum biochemical abnormalities included mild hypoglycemia, hyperproteinemia, hypoalbuminemia, hyperglobulinemia, hypocholesterolemia, decreased alkaline phosphatase activity, hyponatremia, and hyperkalemia. Urine was concentrated (specific gravity, 1.041) and contained a trace Bumin protein, with unremarkable sediment. A buccal mucosal bleeding time and a coagulation profile that included prothrombin time, partial thromboplastin time, fibrinogen, fibrinogen degradation products, and a manual platelet count were normal. Serum protein electrophoresis confirmed a polyclonal gammopathy.

Serologic test results included reciprocal antibody titers to *Ehrlichia canis*, *Ehrlichia chaffeensis*, and *Anaplasma phagocytophilum* antigens of >10,240, >10,240, and 2,560, respectively. Seroreactivity to *Bartonella vinsonii* subsp. *berkhoffii* and *Rickettsia rickettsii* antigens at reciprocal titers of 128 and 32, respectively, was also detected. Using a previously described approach, our attempts to perform PCRs on *Ehrlichia* DNA from EDTA-anticoagulated blood using *Ehrlichia* genus primers and *E. canis*, *E. chaffeensis*, *Ehrlichia ewingii*, and *A. phagocytophilum* species-specific primers were not successful (23). Using *Rickettsia* genus primers, rickettsial DNA was also not amplified from an EDTA blood sample (3).

In an attempt to isolate *Bartonella* species, rabbit blood agar plates were inoculated with EDTA blood, following lysis by freezing. After 1 week at 35°C with 5% CO_2, small white colonies were detected. The HaeIII restriction fragment length polymorphism (RFLP) pattern of PCR-amplified rRNA from the 16S to 23S intergenic spacer region of the agar-grown bacteria was consistent with previously described canine and coyote isolates of *B. vinsonii* subsp. *berkhoffii* type II (9, 21, 22). In an attempt to isolate an *Ehrlichia* species, white blood cells (buffy coat) obtained from 6 ml of EDTA-anticoagulated blood were inoculated into DH82 and HL60 cell lines. Morulae were not visualized in either DH82 or HL60 cell lines through the sixth week of culture; however, by Gimenez staining, intracellular, rod-shaped organisms compatible in morphology with *Bartonella* spp. were detected. The presence of *Bartonella vinsonii* subsp. *berkhoffii* in DH82 cocultured cells was confirmed by PCR using a previously described assay (18). Passage from the DH82 cell culture onto rabbit blood agar was not successful.

The dog was treated with doxycycline (10 mg/kg orally every 24 h for 8 weeks). Six weeks after doxycycline therapy, the referring veterinarian reported no additional episodes of epi-

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staxis, and there has been no reoccurrence of epistaxis during the subsequent 5 years.

Case 2. A 3-year-old female spayed Labrador retriever from Chester, South Carolina, developed epistaxis after an episode of reverse sneezing. Values obtained from a complete blood count and serum biochemical and coagulation profiles were within reference ranges. Therefore, no treatment was administered. One month later, epistaxis accompanied by lethargy and limping was observed by the owner, who was a veterinarian. Thrombocytopenia (platelet count, 24,000/μl) was the only hematological abnormality. Serum biochemical profile values were within reference ranges, and a *Dirofilaria immitus* antigen enzyme-linked immunosorbent assay result was negative. Antibodies to *E. canis* and *R. rickettsii* antigens were detected by a commercial laboratory at reciprocal titers of 640 and 128, respectively. Within 24 h of initiating treatment with doxycycline (5 mg/kg twice a day), the dog developed a cough, vomiting accompanied by hemoptysis, and dyspnea. Initial chest radiographs identified an increased interstitial lung pattern, which within several hours progressed to alveolar consolidation, presumptively associated with pulmonary hemorrhage or pulmonary edema secondary to *E. canis* pneumonitis. Doxycycline was continued for 3 weeks, and prednisone was administered in a tapered dose during the first 10 days to decrease pulmonary inflammation. Within 2 weeks the dog had returned to normal activities, at which time complete blood count and serum biochemical profile values were within reference ranges. The dog remained healthy for the next 3 months but again developed coughing, dyspnea, lethargy, thrombocytopenia (platelet count, 91,000/μl), interstitial pneumonitis, and bounding femoral pulses. A heart murmur was not initially auscultated but within days became evident over the mitral valve region. During an evaluation at an emergency clinic, a lung aspirate revealed pyogranulomatous inflammation with no cytological evidence of an infectious etiology. An echocardiogram identified aortic value endocarditis and mitral insufficiency. Antibodies to *B. vinsonii* subsp. *berkhoffii* antigens were detected at a reciprocal titer of 2,048. Attempts to amplify *Ehrlichia*, *Anaplasma*, or *Bartonella* species DNA from EDTA blood were not successful. Following a 6-week course of amoxicillin and enrofloxacin, the dog was maintained on furosemide and enalapril for 10 months, at which time intractable congestive heart failure necessitated euthanasia. No necropsy was performed.

Case 3. Approximately 4 years after the evaluation of dog 2, a 6-year-old, male, castrated American bulldog, residing in the same household in Chester, South Carolina, and owned by the same veterinarian as in case 2, developed unilateral epistaxis from the right nares and swelling of the muzzle. The dog was treated with diphenhydramine hydrochloride for a presumptive insect sting. There was no evidence of a bite or scratch wound. However, the owner had several cats, and the dog had access to a wooded area adjacent to the house. Hematological abnormalities included mild thrombocytopenia (platelet count, 158,000/μl) accompanied by platelet clumping, neutrophilia (13,515 neutrophils/μl), monocytosis (636 monocytes/μl), and lymphopenia (636 lymphocytes/μl). Hypercholesterolemia (339 mg/dl; reference range, 138 to 317) was the only biochemical serum abnormality. Antibodies to *B. vinsonii* subsp. *berkhoffii* and to *B. henselae* antigens were detected at reciprocal titers of 64. Antibodies to *Babesia canis*, *Bartonella burgdorferi*, *E. canis*, or *R. rickettsii* antigens were not detected. *Ehrlichia* species DNA was not detected by PCR. Due to the initial low *B. vinsonii* subsp. *berkhoffii* and *B. henselae* antibody titers, serum was obtained 10 days later, and again, a reciprocal immunofluorescent-antibody (IFA) titer of 64 was obtained for each organism. Real-time PCR results (see method below) were visualized and recorded as cycle threshold values for fluorescence over a negative-control reaction threshold (where DNA from blood of a healthy dog was used as a template). EDTA blood samples were obtained for real-time PCR prior to treatment and at 1 and 5 months following treatment. DNA extracted from the pretreatment blood sample showed a fluorescence signal during real-time PCR amplification of the 125-bp *Bartonella* 16S to 23S consensus rRNA internal transcribed spacer (ITS). Following conventional PCR, cloning, and sequencing of the pretreatment ITS amplicon, the DNA sequence was 98.9% (651 of 659 bases) similar to that of *Bartonella henselae* Houston I (GenBank accession number L35101). The next-closest ITS match in GenBank was *Bartonella koehlerae* (AF312490) at 85% similarity (560 of 659 bases).

The dog was treated with azithromycin (10 mg/kg) once daily for 7 days and every other day for an additional 5 weeks. Reciprocal *B. vinsonii* subsp. *berkhoffii* and *B.* henselae titers at both 1 and 5 months following azithromycin administration were less than 16 and 64, respectively. Epistaxis was not observed during the 8-month follow-up period. Despite several extraction and PCR attempts, DNA for a *Bartonella* species was not detected in a blood sample obtained 1 month following treatment, but *Bartonella* genus DNA was again detected in a 5-month posttreatment sample. Whether this reflected reexposure or an incomplete treatment response was not determined.

PCR amplification of the ITS region. The presence of *Bartonella* species DNA from EDTA-anticoagulated blood samples from dog 3 was investigated by real-time PCR using a SmartCycler system II from Cepheid, Sunnyvale, CA. Sample DNA was prepared by using the QIAGEN DNA mini kit (QIAGEN Inc., Valencia, Calif.). After extraction, DNA concentration and purity were measured using an absorbance ratio between 260 and 280 nm. A PCR for *Bartonella* detection was designed to amplify a 125-bp consensus sequence within the 16S to 23S rRNA interspacer transcribed region. Amplification and detection of *Bartonella* DNA was performed using a 6-carboxyfluorescein-CCGCGTTTTTCAAAGCCCACGCGG-QUE-HEG-AGATGATGATCCCAAGCCTTCTGG (where QUE is a BlackHole Quencher 1 probe and HEG is hexaethylene glycol, a spacer that prevents polymerase readthrough) scorpion fluorescent uni-probe (Proligo, France) and a 5′ GGATRAA YYRGWAAACCTTYMYCGG 3′ (where R, W, Y, and M represent degenerate bases as follows: R, G or A; W, A or T; Y, C or T; and M, A or C) oligonucleotide as the antisense primer (Integrated DNA Technology, Inc., Coralville, IA). PCR amplifi cations were performed in a 25-μl final volume using Omnimix PCR beads (Cepheid), 2 μl of template DNA, 2 μl of 25 mM $MgCl_2$, and a scorpion probe and an antisense primer to final concentrations of 1.5 μM and 0.5 μM, respectively. PCR condit

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ions were as follows: one cycle of a hot start at 95°C for 2 min, followed by 45 cycles of denaturing at 94°C for 10 seconds, anne aling at 54°C for 10 seconds, and extension at 72°C for 10 seconds.

Discussion. In 1990, Relman and colleagues reported the use of PCR to identify the causative agent of bacillary angiomatosis, a cancer-like proliferative growth of blood vessels, found on cutaneous and visceral surfaces (33). This pivotal event, in conjunction with other temporally related clinical and pathological observations, began the discovery of what are classified today as *Bartonella* species and also initiated the subsequent description of many previously unrecognized or poorly characterized disease syndromes that are caused by these organisms. Members of the genus *Bartonella* are pleomorphic, gram-negative rods (1, 5, 7). As a result of evolutionary adaptation, *Bartonella* spp. induce persistent intracellular infection of erythrocytes and endothelial cells in a wide variety of animal species (5, 10, 11). Depending upon the immune competence of the infected individual and potentially other uncharacterized factors, there is tremendous clinical variability in disease expression in both dogs and people (1, 8).

Of comparative medical importance, *Bartonella* spp. can be detected in both dogs and people with lymphadenitis, endocarditis, peliosis hepatis, and granulomatous hepatitis (1, 10, 13, 20, 25, 32). As dogs and people develop very similar pathological lesions when infected with *Bartonella* spp., the dog may be a good natural model for human bartonellosis, and clearly, observations related to human disease manifestations have facilitated advancements in our understanding of canine bartonellosis. As examples, *B. vinsonii* subsp. *berkhoffii* can cause endocarditis and *B. henselae* can cause peliosis hepatis in both dogs and humans (2, 19, 33, 34). As discussed below, granulomatous disease has been reported to occur in both dogs and humans infected with *Bartonella* spp. This study provides preliminary evidence to support a role for *Bartonella vinsonii* subsp. *berkhoffii* as a potential cause or cofactor in the development of epistaxis in dogs. Based upon previously documented similarities in disease expression, the potential association of *Bartonella* species infection with epistaxis in dogs may also prove to be of comparative medical importance in the future.

Historically, epistaxis was considered a hallmark of ehrlichiosis in working military dogs stationed in Southeast Asia during the Vietnam War (28). However, to our knowledge, epistaxis has never been reported in conjunction with experimental *E. canis* infections. Recently, we obtained serological evidence indicating that over half (17 of 33 [52%]) of a population of *E. canis* seroreactive dogs from Thailand also had antibodies to *B. vinsonii* subsp. *berkhoffii* (37). Therefore, it is possible that dogs stationed in Vietnam were unknowingly coinfected with *E. canis* and *B. vinsonii* subsp. *berkhoffii*. Honadel and colleagues found a much lower *B. vinsonii* subsp. *berkhoffii* seroprevalence in 162 out of 1,872 (8.7%) healthy working military dogs owned by the federal government and stationed throughout the United States (16). However, of the 30 dogs in the Honadel study that were seroreactive to *E. canis* antigens, 13 (43%) were also seroreactive to *B. vinsonii* subsp. *berkhoffii*, providing additional support for the possibility of coinfection with these two organisms among working military dogs. Two other reports from our laboratory identified lower levels of *B. vinsonii* subsp. *berkhoffii* seroreactivity (69 out of 1,920 [3.6%]) in sick dogs from North Carolina and Virginia and in healthy or sick dogs examined at animal shelters or veterinary hospitals in Rhode Island (6 out of 277 [2.2%]) (15, 29). Importantly, in the study by Pappalardo and colleagues, 36% of sera obtained from *E. canis* seroreactors was also seroreactive to *B. vinsonii* subsp. *berkhoffii* antigens, emphasizing a frequent environmental association between these two organisms (29). Currently, there is limited information regarding the pathogenic role or the prevalence of *B. henselae* antibodies in dogs. In contrast to *B. vinsonii* subsp. *berkhoffii*, antibodies to *B. henselae* antigens among dogs from the southeastern United States are much more prevalent in both healthy (10.1%) and sick (27.2%) dog populations (36). The diagnostic relevance of low-level antibodies to both *B. vinsonii* subsp. *berkhoffi* and *B. henselae* in dog 3, from which the DNA of a potentially novel species or subspecies most closely related to *B. henselae* was amplified, is unknown. By IFA testing, canine cross-reactivity to these two organisms is not predictable, which may be due to infection with a closely related species or subspecies (36). It is possible that dog 3 was infected with two organisms, but only *B. henselae*-like DNA was detected by ITS PCR, cloning, and sequencing.

All three dogs in this study had antibodies to *B. vinsonii* subsp. *berkhoffii*. Fortunately, *B. vinsonii* subsp. *berkhoffii* seroreactivity is infrequently found among healthy or sick dogs, suggesting that the detection of antibodies to this organism might correlate with active infection and potentially with clinical disease (15, 29). This factor is of particular importance when considering the microbiological data generated from case 2 of this report, where epistaxis predated the development of endocarditis. Although *Bartonella* DNA was not amplified from the blood, dog 2 had a very high reciprocal *B. vinsonii* subsp. *berkhoffii* titer (2,048), in conjunction with endocarditis, a well-recognized entity induced by this *Bartonella* sp. in dogs (2, 4, 6, 25). Confirming an association between *Bartonella* antibody detection and active infection in dogs and people has been hampered by the lack of diagnostic sensitivity associated with current culture and PCR methods. Efforts in our laboratory to overcome these limitations indicate that the current lack of sensitivity for culture and for PCR in dogs infected with *Bartonella* spp. is related to the small number of organisms circulating in the blood at the time of sample collection (R. Maggi and E. B. Breitschwerdt, unpublished data). Failure to amplify *Bartonella* DNA from EDTA-anticoagulated blood from chronically infected dogs might reflect bacterial localization within the vascular endothelium or other tissues, accompanied by few circulating intraerythrocytic organisms. Based upon serological evidence, it appears that dogs exposed to *E. canis*, from both the United States and Thailand, are frequently exposed to and are potentially coinfected with *B. vinsonii* subsp. *berkhoffii*. Therefore, it is now appropriate to reconsider the extent to which *E. canis*, *B. vinsonii* subsp. *berkhoffii*, coinfection with these two organisms, or infection with other *Bartonella* spp. contributes to the development of epistaxis in dogs. Prospective studies will be necessary to examine the respective role of each organism as a cause of epistaxis because currently veterinarians are more likely to test

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for exposure to *E. canis* and not test for exposure to *B. vinsonii* subsp. *berkhoffii* or *B. henselae* antibodies in dogs with epistaxis.

In searching the literature for other cases of *Bartonella* species infection in dogs, progressively severe epistaxis was reported in the 3-year-old female Labrador retriever from which the American Type Culture Collection type strain of *B. vinsonii* subsp. *berkhoffii* type I was isolated in 1993 (2). Similar to case 2 in this report, that dog was concurrently seroreactive to *E. canis* and *B. vinsonii* subsp. *berkhoffii* antigens by IFA testing and subsequently developed endocarditis. In a recent report of two dogs with fulminant pulmonary edema and aortic valvular endocarditis attributed to *B. vinsonii* subsp. *berkhoffii*, epistaxis was reported in one of the dogs 6 weeks prior to the referral examination, which was necessitated by acute onset of respiratory distress (35). *Ehrlichia canis* antibodies were not detected in that dog, but *Anaplasma phagocytophilum* antibodies (reciprocal titer of 800) were reported (35). Similar to dog 3 in this report, dog 6 in a previous study with aortic valve endocarditis and a *B. vinsonii* subsp. *berkhoffii* reciprocal IFA titer of 8,192 had epistaxis but no serological evidence of *E. canis* exposure (4). An assessment of case-based evidence derived from this study and from previous studies suggests that infection with *B. vinsonii* subsp. *berkhoffii* alone, or in conjunction with *E. canis*, may cause epistaxis in dogs. This conclusion is supported by the following observations. (i) Epistaxis persisted in dogs 1 and 2 of this report despite prior treatment with tetracycline hydrochloride and doxycycline, respectively, for canine ehrlichiosis. Following the isolation of *Bartonella vinsonii* subsp. *berkhoffii*, dog 1 was treated with doxycycline for a much longer duration (8 weeks versus 2 weeks with tetracycline hydrochloride), which resulted in the resolution of epistaxis during the 5-year follow-up period. In dog 1, *E. canis*-induced hyperglobulinemia may have resulted in a hyperviscosity syndrome, which could also contribute to a tendency to develop epistaxis. (ii) Although dogs 1 and 2 were seroreactive to *E. canis* antigens, we were unable to document active infection by PCR amplification of *E. canis* DNA from peripheral blood samples. We were also unable to isolate *E. canis* or *A. phagocytophilum* from the blood of dog 1 with DH82 and HL60 cell cultures, respectively. At the time of initial evaluation for epistaxis, dog 3 was *B. vinsonii* subsp. *berkhoffii* and *B. henselae* seroreactive on two occasions, 10 days apart, but lacked *E. canis* antibodies, and PCR did not detect *E. canis* DNA. (iii) While continuing to experience episodes of epistaxis, following antibiotic administration for ehrlichiosis, *Bartonella vinsonii* subsp. *berkhoffii* was isolated on a blood agar plate and in DH82 cell culture from the blood of dog 1 in this report, and *B. henselae*-like DNA was amplified and sequenced from the blood of dog 3. (iv) On a comparative medical basis, epistaxis has been reported in children infected with *B. henselae* and in alcoholic adults infected with *Bartonella quintana* (12, 14). Although the respective contributions of *E. canis*, *B. vinsonii* subsp. *berkhoffii*, or other *Bartonella* spp. to the development of epistaxis in dogs clearly requires additional clarification, clinicians should pursue a diagnosis of bartonellosis in dogs and perhaps other animal species with unexplained epistaxis. Despite the diagnostic and therapeutic complexities associated with polymicrobial vector-borne infections, such as ehrlichiosis and bartonellosis, it has become increasingly important to document potential pathogen interactions in coinfected individuals.

The pathophysiology of epistaxis in dogs infected with *B. vinsonii* subsp. *berkhoffii* is unknown. As *Bartonella* species can directly invade and colonize endothelial cells or indirectly induce vascular proliferative lesions in a variety of tissues, epistaxis may be related to vascular inflammation or alternatively might be caused by blood vessel weakness associated with uncontrolled vascular proliferation (11, 24, 27). Experimental evidence indicates that *B. henselae* causes endothelial proliferation by inducing macrophage production of vascular endothelial growth factor (19). *Bartonella vinsonii* subsp. *berkhoffii* can also induce immune suppression characterized by defects in monocytic phagocytosis, $CD8^+$ T lymphocytopenia, and impaired antigen presentation within lymph nodes (31). Alterations in immune regulation might logically contribute to colonization of the nasal epithelium by opportunistic bacteria and subsequently epistaxis. Previously, *B. vinsonii* subsp. *berkhoffii* DNA was found in a surgical biopsy specimen obtained from an 11-year-old mixed-breed dog, examined because of a 6-week history of serous nasal discharge (30). That dog was also concurrently seroreactive to both *E. canis* and *B. vinsonii* subsp. *berkhoffii* antigens, and multifocal granulomatous inflammation with fibrosis was the histological diagnosis. Although not the focus of this report, current evidence indicates that *Bartonella* spp. can induce granulomatous inflammation, including involvement of lymph nodes, lung, spleen, liver, and other tissues, in both dogs and people (13, 17, 30). Granulomatous pneumonitis, due to *B. henselae* infection, occurred in a renal transplant recipient who had extensive exposure to cats (8). Potentially consistent with *Bartonella* infection, a cytological diagnosis of pulmonary granulomatous inflammation was reported for dog 2 of this study, in conjunction with radiographic evidence of interstitial pneumonitis. *Bartonella vinsonii* subsp. *berkhoffii* has recently been implicated as a cause of acute respiratory distress, severe radiographic pulmonary infiltrates, and cardiogenic edema secondary to aortic valvular endocarditis in two dogs, of which one dog experienced epistaxis prior to referral evaluation (35). Collectively, these cases suggest that bartonellosis should be considered in the differential diagnosis of granulomatous inflammatory disease, infiltrative pulmonary disease, or nasal disease in dogs.

From a diagnostic perspective, thrombocytopenia and neutrophilic leukocytosis have been reported to occur in approximately half the dogs with *B. vinsonii* subsp. *berkhoffii* seroreactivity, with monocytosis and eosinophilia found in approximately one-third of these cases (4, 6). Thrombocytopenia was found at some time point during the evaluation of all three dogs in this study, but the decrease in platelet numbers was not severe enough in any of the dogs to be the sole cause of hemorrhage. It should be noted that immediately prior to referral and the isolation of *B. vinsonii* subsp. *berkhoffii*, dog 1 had a thrombocytosis rather than a thrombocytopenia. Thrombocytosis has been previously described for both dogs and people infected with *B. henselae* (26).

The means by which *B. vinsonii* subsp. *berkhoffii* is transmitted to dogs remains unclear; however, epidemiological evidence supports transmission by an arthropod vector, potentially *Rhipicephalus sanguineous* (23, 29). *Rhipicephalus sanguineous* is a known vector of *E. canis* and *Babesia canis*. Concurrent detection of seroreactivity to *B. vinsonii* subsp. *berkhoffii* in dogs with *E. canis*

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and *B. canis* antibodies supports potential transmission by *R. sanguineous* (4, 23, 29, 30, 37). As *Bartonella* species can be transmitted by a variety of insect vectors, routine use of acaracides and structured ectoparasite prevention programs are of critical importance for disease prevention in dogs. Currently, the spectrum of disease associated with *Bartonella* infection in dogs and people continues to be defined. Based upon evolving clinical evidence, *B. vinsonii* subsp. *berkhoffii* and *B. henselae* or a closely related species appear to cause epistaxis in dogs, independently of the dogs' *E. canis* infection status. Given the pathophysiologic similarities of *Bartonella* infection in dogs and human patients, studies aimed at identifying the role of *Bartonella* spp. as a cause of unexplained epistaxis, particularly in children, may be justified.

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