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Isolation of *Bartonella vinsonii* subsp. *berkhoffii* Genotype II from a Boy with Epithelioid Hemangioendothelioma and a Dog with Hemangiopericytoma▽

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In this report, we describe isolation of *Bartonella vinsonii* subsp. *berkhoffii* genotype II from a boy with epithelioid hemangioendothelioma and a dog with hemangiopericytoma. These results suggest that *B. vinsonii* subsp. *berkhoffii* may cause vasoproliferative lesions in both humans and dogs.

CASE REPORTS

Case 1. A 13-year-old male presented with acute onset of severe right upper quadrant pain and hepatomegaly. The patient had a several month history of malaise and fatigue, which was attributed to mononucleosis (positive monospot test), but the boy was otherwise previously healthy. A computed tomography scan identified large heterogeneously enhancing tumors throughout the liver. The patient had a mild microcytic anemia (hemoglobin level, 12.5 g/dl; mean corpuscular volume, 71.1 fl) with very low serum iron (23 μg/dl), normal iron binding capacity (292 μg/dl), and low percent iron saturation (7.9%). The patient's level of C-reactive protein was elevated at 18 mg/liter. Liver function test results were normal except for a mildly elevated gamma-glutamyl transpeptidase level of 76 IU/liter (normal levels, 11 to 63 IU/liter). A biopsy specimen of the tumor was obtained laparoscopically. Histological analysis yielded a diagnosis of epithelioid hemangioendothelioma (EHE) with tumor cells staining strongly for endothelial markers CD31 and CD34. Subsequently and at different diagnostic time points, multiple venous blood samples, drawn following sterile skin preparation, were sent to the Intracellular Pathogens Research Laboratory of North Carolina State University (NCSU-IPRL) for culture in *Bartonella* alpha Proteobacteria growth medium (BAPGM) and 16S-23S intergenic spacer (internal transcribed spacer [ITS]) PCR as previously described (3, 4, 9). In addition, scrolls cut from the formalin-preserved, paraffin-embedded block of the EHE tumor were tested for *Bartonella* sp. DNA using 16S-23S ITS PCR. *Bartonella vinsonii* subsp. *berkhoffii* genotype II was initially amplified and sequenced directly from a venous blood sample (Table 1). Subsequently, *B. vinsonii* subsp. *berkhoffii* genotype II DNA was amplified and sequenced from the tissue block; this was done again for a third time from a second BAPGM enrichment blood culture. Four distinct *B. vinsonii* subsp. *berkhoffii* genotypes have been characterized based upon defined insertion and deletion sequences within the ITS region (5, 21). Only genotype II DNA was sequenced from the blood or tissue samples from this boy. After consultation with infectious disease physicians, antibiotic treatment was instituted. The antibiotic treatment consisted of triple-drug therapy for 12 weeks. Oral doxycycline and rifampin were given for 12 weeks. For the initial 2 weeks, intravenous gentamicin was given, which was replaced by oral azithromycin for the remaining 10 weeks. This regimen was chosen to achieve sufficient intracellular concentrations of rifampin and azithromycin and serum concentrations of doxycycline and to invoke the putative bactericidal properties of aminoglycosides for the treatment of *Bartonella* infection. Constitutional symptoms improved during the period of treatment, and improvement has continued during the subsequent year. The patient grew 5 cm and gained 7.7 kg. The patient reports rare, brief episodes of right upper quadrant pain but otherwise remains asymptomatic. Serial computed tomography scans during the year following treatment have shown no change in the size or number of tumors. The patient remains mildly anemic (hemoglobin level, 12.7 g/dl). However, the C-reactive protein concentrations (8 mg/liter) and gamma-glutamyl transpeptidase (58 IU/dl) dropped to near normal and normal values, respectively; other liver function test values have remained in the normal range. For over 1 year following antibiotic administration, *B. vinsonii* subsp. *berkhoffii* was not isolated and *Bartonella* sp. DNA was not amplified from five blood culture samples (direct extraction, BAPGM enrichment liquid culture, and agar plate subcultures all negative) (Table 1). There has also been a progressive decrease in seroreactivity to *Bartonella henselae*, *B. vinsonii* subsp. *berkhoffii* genotype I, and *B. vinsonii* subsp. *berkhoffii* genotype II antigens, eventually achieving undetectable levels (Table 1).

Case 2. A 12-year-old female English sheepdog was referred to the North Carolina State University Oncology Service for evaluation of a recurrent right antebrachial mass. Three years earlier, a similar, large mass had been surgically resected by the referring veterinarian from the same anatomic site. One year later, a smaller, approximately 4.0- to 6.0-cm mass was removed after recurrence at the surgical excision site. Although

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TABLE 1. Serological, PCR, and culture results for a 13-year-old male with a hepatic epithelioid hemangioendothelioma and *Bartonella vinsonii* subsp. *berkhoffii* infection

Sampling date (mo/day/yr)	Sample	*Bartonella* IFA reciprocal titer[a]			PCR or BAPGM culture result[b]		
		B. henselae	*Bvb* I	*Bvb* II	Direct extraction	Enrichment culture	Blood agar plate isolate
1/2/2008	Blood	16	64	16	*Bvb* II	—	—
1/02/2008	Liver tissue	NA	NA	NA	*Bvb* II	NA	NA
1/9/2008	Blood	64	16	32	—	*Bvb* II	—
1/17/2008	Blood	128	32	64	—	—	—
2/14/2008	Blood	32	64	16	—	—	—
4/4/2008	Blood	128	16	64	—	—	—
6/17/2008	Blood	64	<16	32	—	—	—
1/19/2009	Blood	<16	<16	<16	—	—	—

[a] Abbreviations: IFA, indirect immunofluorescent-antibody assay; *Bvb* I, *Bartonella vinsonii* subsp. *berkhoffii* genotype I; *Bvb* II, *B. vinsonii* subsp. *berkhoffii* genotype II; NA, not applicable.
[b] *Bvb* II denotes 16S-23S ITS DNA sequence result that defines genotypes I to IV. NA, not applicable. —, negative PCR or BAPGM culture result.

no lameness was reported, the dog would frequently lick the masses, presumably due to pain or local irritation. Historically, the dog had otherwise been healthy.

At the time of referral, there were three distinct right foreleg masses measuring 0.5 by 0.3 by 1.5 cm on the medial surface of the right antebrachium, 3.0 by 3.0 by 1.5 cm on the cranial right antebrachium, and 4.0 by 4.5 by 2.0 cm on the lateral right antebrachium. The masses were discrete, nontender, fixed, and located between 2.0 and 5.0 cm distal to the olecranon. There was also a firm 2.0 by 2.0 by 1.0 cm mass on the medial aspect of the right rear leg. Complete blood count and serum biochemical profile values were normal. The dog was mildly proteinuric (urine specific gravity, 1.030; 2+ urine protein; negative urine sediment). Aspiration cytology of the right antebrachial and right medial thigh masses identified sheets or clusters of fusiform cells with a high nuclear to cytoplasmic ratio, basophilic cytoplasm, and prominent nucleoli, consistent with a mesenchymal neoplasm. On thoracic radiographs, there was no evidence of pulmonary metastases. Core biopsy specimens were obtained from the antebrachial and medial thigh masses. Histopathology of the masses identified densely packed and interweaving streams and fingerprint whorls of plump, elongated spindle-shaped cells separated by a scant fibrillar stroma, which contained numerous small blood vessels. Neoplastic cells occasionally whorled around small blood vessels. The cells contained scant to moderate amounts of amphophilic, weakly fibrillar cytoplasm, oval nuclei with finely stippled chromatin, one to two nucleoli per cell, and infrequent mitoses. There was mild anisokaryosis and anisocytosis and rare multinucleated cells. The location, morphology, and recurrent nature of these tumors were most consistent with hemangiopericytoma (HPC).

The dog was referred to our teaching hospital in 1995, 2 years after the NCSU-IPRL had made the first isolate of *B. vinsonii* subsp. *berkhoffii* (ATCC type strain 93-CO-1) genotype I from a dog with endocarditis (1). Using *B. vinsonii* subsp. *berkhoffii* genotype I as the antigen source, indirect immunofluorescent-antibody titers ($n = 4$) were consistently 1:256 over the next 3 months, and a *Bartonella* sp. was isolated by lysis centrifugation blood culture. Retrospectively, the strain was determined to be *B. vinsonii* subsp. *berkhoffii* genotype II based on sequencing the 16S-23S intergenic spacer region in 2008, using a previously described approach (21).

Three months after the initial oncology consultation, the owners elected surgery. Mild basophilia (200 cells/μl; normal value, less than 100 basophils/μl) was the only hematological abnormality, and there were no serum biochemical abnormalities. The medial thigh mass was totally resected, and the three antebrachial masses were partially resected. The owner declined radiation therapy for the antebrachial mass. The dog was treated with enrofloxacin for 6 weeks at which time the *B. vinsonii* subsp. *berkhoffii* antibody titer was 1:128 and a lysis centrifugation blood culture was negative. Also in 2008, *B. vinsonii* subsp. *berkhoffii* genotype II DNA was amplified and sequenced from the paraffin-embedded biopsy specimen of the antebrachial HPC; the block had been stored for 13 years.

In this report, infection with *B. vinsonii* subsp. *berkhoffii* genotype II is described in a boy with EHE and a dog with HPC. Neoplastic recurrence at the same anatomic location over a 3-year period, in conjunction with the temporal association of *B. henselae* and *Bartonella quintana* with vasoproliferative lesions in human immunodeficiency virus-infected humans (25, 26), initiated our efforts to determine whether the dog was infected with a *Bartonella* sp. The boy was cultured after a literature search by an attending physician revealed a well-established association between *Bartonella* sp. infection, vascular endothelial growth factor (VEGF) induction and angioproliferative disease (6, 7, 13, 27). An association of increased tissue VEGF levels with the formation of hemangioendotheliomas lent credence to the hypothesis of a potential causal association between *Bartonella* infection and hemangioendothelioma (18, 30).

Dogs and humans infected with *Bartonella* spp. can develop similar disease manifestations and pathological lesions, including prototypical vasoproliferative lesions, such as bacillary angiomatosis and peliosis hepatis (2, 6). In humans, *Bartonella henselae* and *Bartonella quintana* cause cutaneous vasoproliferative lesions (bacillary angiomatosis) and parenchymal vasoproliferative lesions of the liver, spleen (bacillary peliosis), and less frequently other tissues, particularly in human immunodeficiency virus-infected patients (25, 26). The NCSU-IPRL recently cultured *B. vinsonii* subsp. *berkhoffii* genotype I from a dog with bacillary angiomatosis (J. Yager, E. B. Breitschwerdt, et al., unpublished data), and *B. henselae* DNA had previously

been amplified from the liver of a dog with peliosis hepatis (14). Long-lasting intravascular infection with *B. henselae* (for months to years) has been documented in naturally and experimentally infected cats (16, 17), and persistent intravascular bacteremia for 18 months with *B. vinsonii* subsp. *berkhoffii* genotype II was reported in a naturally infected healthy pet dog (15). More recently, persistent infection with *B. vinsonii* subsp. *berkhoffii* and *B. henselae*, as well as coinfection with both organisms, has been reported in immunocompetent people with substantial arthropod and animal contact (3, 4). The seemingly unique capability of bacteria of the genus *Bartonella* to invade and induce long-lasting intraerythrocytic and intraendothelial infections, in conjunction with the ability of at least three *Bartonella* spp. (*B. henselae*, *B. quintana*, and *Bartonella bacilliformis*) to induce VEGF-mediated vasoproliferative disease in immunocompromised or immunocompetent individuals suggests that these novel emerging bacterial pathogens might contribute to the development of other vascular tumors (7, 8, 12).

Bartonella vinsonii subsp. *berkhoffii* genotype I was isolated for the first time from a dog with epistaxis, recent-onset seizures, and endocarditis in 1993 (1). Subsequently, three additional genotypes (designated II to IV), all of which have been implicated as a cause of endocarditis in dogs, were described based upon sequence differences in the *Bartonella* 16S-23S intergenic spacer region and the Pap31 gene (5, 21). Genotypes I, II, and III have also been implicated in humans with vascular infections (3, 4, 29). Although seemingly well-adapted on an evolutionary basis to induce persistent infection in canine reservoir hosts (dogs, foxes, and coyotes), *B. vinsonii* subsp. *berkhoffii* has only rarely been isolated from pet dogs (2, 6). In pet dogs, both seroprevalence studies and blood culture isolation studies indicate infrequent exposure to or active infection with any of the four *B. vinsonii* subsp. *berkhoffii* genotypes, whereas infection is more frequent in coyotes and feral dog populations (6, 21). Although a source of infection was not determined in either case, the dog in this case report was from a rural area and had experienced recurrent ectoparasite exposures. The boy had a tick bite roughly 1 year prior to the diagnosis of EHE, spent summers in heavily wooded areas, and lived in a suburb where coyote sightings are common. Coyotes are likely a reservoir host for *B. vinsonii* subsp. *berkhoffii* genotype II, and tick transmission of this subspecies has been proposed on the basis of epidemiological evidence (2, 6). In regard to human infections, there is one case of endocarditis and eight cases in which *B. vinsonii* subsp. *berkhoffii* was isolated or sequenced from blood cultures obtained from immunocompetent people with arthritis, fatigue, or neurological or neurocognitive abnormalities (3, 4, 29). Four of these eight individuals infected with *B. vinsonii* subsp. *berkhoffii* were coinfected with *B. henselae* and *B. vinsonii* subsp. *berkhoffii*, of which genotype II was sequenced from all but one person, who was infected with genotype I. We were unable to detect DNA evidence of *B. henselae* infection using species-specific primers in samples from the boy or the dog. Therefore, isolation of the same bacterial genotype from vascular tumors occurring in a dog and a human suggests that *B. vinsonii* subsp. *berkhoffii* may play a role in the development of some vasoproliferative tumors. Over a decade separated the efforts to isolate *B. vinsonii* subsp. *berkhoffii* from the dog and the human patient in this study. In the intervening period, there were important advances in the microbiological isolation and molecular detection of *Bartonella* spp. in blood and tissue samples from immunocompetent individuals, which continue to facilitate a redefinition of the pathogenic role of this genus in animals and humans (3, 4, 9).

In all mammals, including dogs and humans, endothelial cells appear to be an important target cell following direct or vector-borne transmission of a *Bartonella* sp. (6–8). Based upon in vitro infection of human endothelial cell lines, *B. henselae* has been shown to induce angiogenesis and endothelial cell proliferation (20). *Bartonella* spp. also subvert many functions of human endothelial cells, including the induction of mitogenic and proinflammatory genes, cytoskeletal rearrangements, and suppression of endothelial cell apoptosis (7, 8). Clinically, the resulting vascular proliferation induces tumor-like lesions (verruga peruana, bacillary angiomatosis, and peliosis hepatis), especially in immunocompromised individuals (2, 6, 7). VEGF is an important mediator of tumor angiogenesis, and its production has been specifically induced by *B. henselae* in vitro (13, 23). In addition, increased VEGF levels were found in tissues from patients with bacillary angiomatosis and peliosis hepatis (23). Recently, it has been shown that infection of human endothelial cells by *B. henselae* resulted in interleukin-8 (IL-8) production and upregulation of IL-8 receptors CXCR2 (23). IL-8 promotes angiogenesis through enhanced endothelial cell survival and enhanced vascular proliferation (13, 19, 23). The results of this study suggest that *B. vinsonii* subsp. *berkhoffii*, a *Bartonella* species that appears to have coevolved with canines (2, 6), may also contribute to vasoproliferative lesions in dogs and human beings, potentially by enhancing cell proliferation in conjunction with inhibition of apoptosis. Whether *Bartonella*-triggered vasoproliferation is a pathogenic strategy used by these bacteria to expand a specific host cell habitat (the endothelial cell) is currently unknown (12, 24).

HPC is a vascular neoplasm thought to originate from pericytes, capillary subendothelial lining cells predominantly found in distal extremity vessels (11, 22). As described in this report, these tumors in dogs are generally subcutaneous and tend to involve the limbs (11, 22). HPCs are most often found in adult dogs, they do not occur more often in male or female dogs, local recurrence is common, and metastasis is rare (11, 22). EHE is a rare vascular neoplasm having a malignant potential between benign hemangioma and angiosarcoma. First described by Weiss and Enzinger in 1982 (30), EHE is characterized by positive immunostains for endothelial antigens CD34 and factor VIII. EHE typically presents with various combinations of hepatic, pulmonary, cutaneous, or bony disease. The natural history is extremely unpredictable, and there is substantial interpatient variability in disease progression. Intervals of rapid growth are frequently interrupted by long periods of quiescence. EHE is generally unresponsive to standard cytotoxic chemotherapy and radiation therapy. Despite anecdotal reports of success with antiangiogenics, there have been no clinical trials of this approach. Surgery is considered the treatment of choice in hepatic disease, where options include resection for localized disease or transplant for the more common presentation of multilobar, multicentric liver involvement, as would be the case for the boy in this report. In two large

studies, there was a high percentage of long-term survivors following liver transplant, even in the presence of metastases (18, 28). If the proposed association of *Bartonella* spp. with EHE were confirmed, it is plausible that eradicating the bacterial infection or interrupting *Bartonella*-induced angiogenic, and proliferative cell signals could slow tumor progression and improve patient outcomes.

On a comparative medical basis, dogs and humans infected with *Bartonella* spp. can develop similar disease manifestations, including endocarditis, granulomatous lymphadenitis, granulomatous hepatitis, bacillary angiomatosis, peliosis hepatis, seizures, and arthritis (2, 6). Therefore, medical information generated in one species (dogs or human beings) can prove beneficial while attempting to characterize the role of *Bartonella* species as a pathogen in the comparable species. As is true of many other infectious diseases, a "one medicine" approach to the current clinical and research understanding of canine and human bartonellosis has proven beneficial for the health care of animals and human patients (10, 31). During the past decade, researchers have provided substantial evidence to support a role of infectious agents, including bacteria, viruses, mycoplasmas, and protozoa, as cofactors in the development of cancer in humans. Substantial epidemiologic and microbiological research is needed to test the potential causal relationship of *Bartonella* sp. infection with EHE and HPC and to determine whether members of the genus *Bartonella* will be added to the list of oncogenic infectious agents in the future.

The dog *B. vinsonii* subsp. *berkhoffii* genotype II isolate reported in this study was obtained by Brandee Pappalardo while a Ph.D. student in the Intracellular Pathogens Research Laboratory at North Carolina State University. We thank Julie Bradley for providing *Bartonella* serological test results, Tonya Lee for editorial assistance, and the many clinicians who facilitated the care of these patients.

REFERENCES

1. **Breitschwerdt, E. B., D. L. Kordick, D. E. Malarkey, B. Keene, T. L. Hadfield, and K. Wilson.** 1995. Endocarditis in a dog due to infection with a novel *Bartonella* subspecies. J. Clin. Microbiol. **33:**154–160.
2. **Breitschwerdt, E. B., and R. G. Maggi.** Comparative medical features of canine and human bartonellosis. Clin. Microbiol. Infect., in press.
3. **Breitschwerdt, E. B., R. G. Maggi, A. W. Duncan, W. L. Nicholson, B. C. Hegarty, and C. W. Woods.** 2007. *Bartonella* species in blood of immunocompetent persons with animal and arthropod contact. Emerg. Infect. Dis. **13:**938–941.
4. **Breitschwerdt, E. B., R. G. Maggi, W. L. Nicholson, N. A. Cherry, and C. W. Woods.** 2008. *Bartonella* sp. bacteremia in patients with neurological and neurocognitive dysfunction. J. Clin. Microbiol. **46:**2856–2861.
5. **Cadenas, M. B., J. Bradley, R. G. Maggi, M. Takara, B. C. Hegarty, and E. B. Breitschwerdt.** 2008. Molecular characterization of *Bartonella vinsonii* subsp. *berkhoffii* genotype III. J. Clin. Microbiol. **46:**1858–1860.
6. **Chomel, B. B., H. J. Boulouis, S. Maruyama, and E. B. Breitschwerdt.** 2006. *Bartonella* spp. in pets and effect on human health. Emerg. Infect. Dis. **12:**389–394.
7. **Dehio, C.** 2004. Molecular and cellular basis of *Bartonella* pathogenesis. Annu. Rev. Microbiol. **58:**365–390.
8. **Dehio, C.** 2008. Infection-associated type IV secretion systems of *Bartonella* and their diverse roles in host cell interaction. Cell. Microbiol. **10:**1591–1598.
9. **Duncan, A. W., R. G. Maggi, and E. B. Breitschwerdt.** 2007. A combined approach for the enhanced detection and isolation of *Bartonella* species in dog blood samples: pre-enrichment liquid culture followed by PCR and subculture onto agar plates. J. Microbiol. Methods **69:**273–281.
10. **Gibbs, E. P. J.** 2005. Emerging zoonotic epidemics in the interconnected global community. Vet. Rec. **157:**673–679.
11. **Handharyani, E., K. Ochiai, T. Kadosawa, and T. J. Umemura.** 1999. Canine hemangiopericytoma: an evaluation of metastatic potential. Vet. Diagn. Investig. **11:**474–478.
12. **Kempf, V. A., N. Hitziger, T. Riess, and I. B. Autenrieth.** 2002. Do plant and human pathogens have a common pathogenicity strategy? Trends Microbiol. **10:**269–275.
13. **Kempf, V. A. J., B. Volkmann, M. Schaller, C. A. Sander, K. Alitalo, T. Rieß, and I. B. Autenrieth.** 2001. Evidence of a leading role for VEGF in *Bartonella henselae*-induced endothelial cell proliferations. Cell. Microbiol. **3:**623–632.
14. **Kitchell, B. E., T. M. Fan, D. Kordick, E. B. Breitschwerdt, G. Wollenberg, and C. A. Lichtensteiger.** 2000. Peliosis hepatis in a dog infected with *Bartonella henselae*. J. Am. Vet. Med. Assoc. **216:**517, 519–523.
15. **Kordick, D. L., and E. B. Breitschwerdt.** 1998. Persistent infection of pets within a household with three *Bartonella* species. Emerg. Infect. Dis. **4:**325–328.
16. **Kordick, D. L., T. T. Brown, K. O. Shin, and E. B. Breitschwerdt.** 1999. Clinical and pathological evaluation of chronic *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats. J. Clin. Microbiol. **37:**1536–1547.
17. **Kordick, D. L., K. H. Wilson, D. J. Sexton, T. L. Hadfield, H. A. Berkhoff, and E. B. Breitschwerdt.** 1995. Prolonged *Bartonella* bacteremia in cats associated with cat-scratch disease patients. J. Clin. Microbiol. **33:**3245–3251.
18. **Lerut, J. P., G. Orlando, R. Adam, M. Schiavo, J. Klempnauer, D. Mirza, E. Boleslawski, A. Burroughs, C. F. Sellés, D. Jaeck, R. Pfitzmann, M. Salizzoni, G. Söderdahl, R. Steininger, A. Wettergren, V. Mazzaferro, Y. P. Le Treut, and V. Karam.** 2007. The place of liver transplantation in the treatment of hepatic epitheloid hemangioendothelioma: report of the European liver transplant registry. Ann. Surg. **24:**949–957.
19. **Li, A., S. Dubey, M. L. Varney, B. J. Dave, and R. K. Singh.** 2003. IL-8 directly enhanced endothelial cell survival, proliferation, and matrix metalloproteinases production and regulated angiogenesis. J. Immunol. **170:**3369–3376.
20. **Maeno, N., H. Oda, K. Yoshiie, R. Wahid, T. Fujmura, and S. Matayoshi.** 1999. Live *Bartonella henselae* enhances endothelial cell proliferation without direct contact. Microb. Pathog. **27:**419–427.
21. **Maggi, R. G., B. Chomel, B. C. Hegarty, J. Henn, and E. B. Breitschwerdt.** 2006. A *Bartonella vinsonii berkhoffii* typing scheme based upon 16S-23S ITS and Pap31 sequences from dog, coyote, gray fox, and human isolates. Mol. Cell. Probes **20:**128–134.
22. **Mazzei, M., F. Millanta, S. Citi, D. Lorenzi, and A. Poli.** 2002. Hemangiopericytoma: histological spectrum, immunohistochemical characterization and prognosis. Vet. Dermatol. **13:**15–21.
23. **McCord, A. M., S. I. Resto-Ruiz, and E. A. Anderson.** 2006. Autocrine role for interleukin-8 in *Bartonella henselae*-induced angiogenesis. Infect. Immun. **74:**5185–5190.
24. **Merrell, D. S., and S. Falkow.** 2004. Frontal and stealth attack strategies in microbial pathogenesis. Nature **430:**250–256.
25. **Perkocha, L. A., S. M. Geaghan, T. S. B. Yen, S. L. Nishimura, S. P. Chan, R. Garcia-Kennedy, G. Honda, A. C. Stoloff, H. Z. Klein, R. L. Goldman, S. Van Meter, L. D. Ferrell, and P. E. LeBoit.** 1990. Clinical and pathological features of bacillary peliosis hepatis in association with human immunodeficiency virus infection. N. Engl. J. Med. **323:**1581–1586.
26. **Relman, D. A., J. S. Loutit, T. M. Schmidt, S. Falkow, and L. S. Tompkins.** 1990. The agent of bacillary angiomatosis: an approach to the identification of uncultured pathogens. N. Engl. J. Med. **323:**1573–1580.
27. **Resto-Ruiz, S. I., M. Schmiederer, D. Sweger, C. Newton, T. W. Klein, H. Friedman, and B. E. Anderson.** 2002. Induction of a potential paracrine angiogenic loop between human THP-1 macrophages and human microvascular endothelial cells during *Bartonella henselae* infection. Infect. Immun. **70:**4564–4570.
28. **Rodriguez, J. A., N. S. Becker, C. A. O'Mahony, J. A. Goss, and T. A. Aloia.** 2008. Long-term outcomes following liver transplantation for hepatic hemangioendothelioma: the UNOS experience from 1987 to 2005. J. Gastrointest. Surg. **12:**110–116.
29. **Roux, V., S. J. Eykyn, S. Wyllie, and D. Raoult.** 2000. *Bartonella vinsonii* subsp. *berkhoffii* as an agent of afebrile blood culture-negative endocarditis in a human. J. Clin. Microbiol. **38:**1698–1700.
30. **Weiss, S. W., and F. M. Enzinger.** 1982. Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. Cancer **50:**970–981.
31. **Zinsstag, J., E. Schelling, F. Roth, B. Bonfoh, D. de Savigny, and M. Tanner.** 2005. Human benefits of animal interventions for zoonosis control. Lancet **366:**2142–2145.