


REVIEW

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Bartonella infections in cats and dogs including zoonotic aspects

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Abstract

Bartonellosis is a vector-borne zoonotic disease with worldwide distribution that can infect humans and a large number of mammals including small companion animals (cats and dogs). In recent years, an increasing number of studies from around the world have reported *Bartonella* infections, although publications have predominantly focused on the North American perspective. Currently, clinico-pathological data from Europe are more limited, suggesting that bartonellosis may be an infrequent or underdiagnosed infectious disease in cats and dogs. Research is needed to confirm or exclude *Bartonella* infection as a cause of a spectrum of feline and canine diseases. *Bartonella* spp. can cause acute or chronic infections in cats, dogs and humans. On a comparative medical basis, different clinical manifestations, such as periods of intermittent fever, granulomatous inflammation involving the heart, liver, lymph nodes and other tissues, endocarditis, bacillary angiomatosis, peliosis hepatis, uveitis and vasoproliferative tumors have been reported in cats, dogs and humans. The purpose of this review is to provide an update and European perspective on *Bartonella* infections in cats and dogs, including clinical, diagnostic, epidemiological, pathological, treatment and zoonotic aspects.

Keywords: *Bartonella*, Dog, Cat, Europe, Zoonosis

Background

Bartonella is a genus of Alphaproteobacteria within the family *Bartonellaceae*. *Bartonella* spp. are small, thin, short and slightly curved, gram-negative, hemotropic and rod-shaped bacteria [1]. They are catalase, oxidase, urease and nitrate reductase negative [1]. *Bartonella* spp. are fastidious, slow growing and facultative intracellular pathogens that are highly adapted to a broad spectrum of mammalian reservoir hosts and are mainly transmitted by arthropod vectors [2, 3]. Thirty-eight different *Bartonella* species have been isolated or detected from humans or from domestic and wild animals including bats, birds, canids, cattle, deer, felids, horses, marine mammals, rodents, sheep and reptiles [4–10]. *Bartonella* spp. are distributed throughout the world. In recent years, an increasing number of studies from around the world have reported canine and feline *Bartonella* infections. The purpose of this review is to provide an update while emphasizing European literature relative to *Bartonella* spp. infections in cats and dogs, including clinical,

diagnostic, epidemiological, pathological, treatment and zoonotic aspects.

Clinically relevant *Bartonella* species described in cats, dogs and humans

At least thirteen *Bartonella* species or subspecies have been recognized as agents of human disease, three species are reportedly responsible for the majority of clinical illness: *B. bacilliformis*, *B. quintana* and *B. henselae* [11]. Because serological testing for other *Bartonella* spp. is rarely performed in human medicine and due to difficulties associated with isolation or PCR amplification of these bacteria from patient specimens, it is possible that *B. koehlerae* [12, 13], *B. vinsonii berkhoffii*, as well as other species are under-recognized as a cause of human illness [14, 15].

Primary reservoirs, accidental hosts and the confirmed or suspected vectors for the main *Bartonella* species infecting cats and dogs with zoonotic potential are listed in Table 1. The most relevant species implicated in companion animal medicine are *B. clarridgeiae*, *B. elizabethae*, *B. henselae*, *B. koehlerae*, *B. quintana*, *B. rochalimae* and *B. vinsonii berkhoffii*. All of these species have been associated with severe illnesses in cats or dogs

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Table 1 *Bartonella* species that infect cats and dogs with zoonotic potential including primary reservoir, accidental host and vectors

<i>Bartonella</i> species	Primary reservoir	Vector	Accidental host
<i>B. bovis</i> (ex <i>weissii</i>)	Domestic cattle (<i>Bos taurus</i>)	Biting flies, ticks	Humans, cats, dogs
<i>B. volans</i> -like	Flying squirrel (Pteromyiinae)	Fleas	Humans, dogs, horses
<i>B. clarridgeiae</i>	Cats (<i>Felis catus</i>)	Cat flea (<i>Ctenocephalides felis</i>), ticks ^a	Humans, dogs
<i>B. elizabethae</i>	Rats (<i>Rattus norvegicus</i>)	Fleas	Humans, dogs
<i>B. grahamii</i>	Rodents	Rodent flea (<i>Ctenophthalmus nobilis</i>)	Humans, dogs
<i>B. henselae</i>	Cats (<i>Felis catus</i>), dogs (<i>Canis familiaris</i>)	Fleas, ticks ^a	Human, dogs
<i>B. koehlerae</i>	Cats (<i>Felis catus</i>), gerbils (<i>Meriones libicus</i>)	Fleas	Humans, dogs
<i>B. quintana</i>	Humans, gerbils (<i>Meriones libicus</i>)	Human body lice, fleas, bed bugs, pigeon mites ^a	Cats, dogs, monkeys
<i>B. rochalimae</i>	Canids	Fleas ^a (<i>Pulex irritans</i> , <i>Pulex simulans</i>), ticks ^a	Humans, dogs
<i>B. vinsonii arupensis</i>	Rodents	Deer tick (<i>Ixodes scapularis</i>)	Humans, dogs
<i>B. vinsonii berkhoffii</i>	Coyotes (<i>Canis latrans</i>), dogs (<i>Canis familiaris</i>), foxes (<i>Urocyon</i> spp.)	Ticks ^a , <i>Pulex</i> spp. ^a	Humans
<i>B. washoensis</i>	California ground squirrel (<i>Spermophilus beecheyi</i>), rabbits (<i>Oryctolagus cuniculus</i>)	Fleas, ticks ^a	Humans, dogs

^aNot confirmed

Details included in the table are provided in [16, 25, 40, 53, 57, 132, 175–183]

and all have zoonotic potential [16, 17]. Each *Bartonella* spp. appears to have co-evolved with a specific primary reservoir host which poses a source of infection for accidental hosts under natural exposure conditions [16].

The cat (*Felis catus*) is the primary but not sole reservoir for *B. henselae* [18], the causal agent of human cat scratch disease (CSD). Domestic cats are also principal reservoir hosts for *B. clarridgeiae* and *B. koehlerae*. Infected cats are thought to rarely develop clinical signs [19]. However, chronic, relapsing bacteremia can frequently be detected in infected cats and potential long-term consequences of relapsing bacteremia are unknown [20–22]. Cats can also be infected with *B. bovis* (ex *weissii*) and *B. quintana*, but the role of domestic cats in the epidemiology of these two *Bartonella* species has not been clearly established [21].

The dog (*Canis familiaris*) may also be a host for *B. henselae* and canines are considered the primary reservoirs for *B. vinsonii berkhoffii*, causing endocarditis in dogs and humans [23, 24]. Wild canids such as coyotes (*Canis latrans*) in California and potentially domestic dogs have been described as main reservoir hosts for *B. vinsonii berkhoffii*, as prolonged bacteremia also occurs in these animals [5, 25, 26]. *Bartonella henselae*, first isolated from a dog in Gabon in 2003 may be the *Bartonella* spp. that most often infects pet dogs [27]. Dogs can also be infected with *B. clarridgeiae*, *B. elizabethae*, *B. koehlerae*, *B. quintana*, *B. rochalimae* and *B. washoensis*, potentially causing similar disease manifestations as reported in humans, including bacillary angiomatosis, endocarditis, granulomatous hepatitis and granulomatous lymphadenitis, myocarditis, peliosis hepatis and others [20, 28–32]. Due to direct and frequent contact

with humans, pet and stray infected cats and dogs pose a potential risk for human infection [33].

Bartonella henselae also causes multiple other clinical entities in human patients, potentially related to the individual's immune status, variations in strain virulence, co-infection with other pathogens and co-morbidities [34]. Infection with *B. clarridgeiae* has been suspected in a few CSD cases and the organism has been isolated from one asymptomatic human blood donor [35]. *Bartonella koehlerae* has been associated with regional pain syndrome type I [13], hallucinations, sensory neuropathy, peripheral visual deficits [36], endocarditis [22] and other clinical conditions [12]. *Bartonella vinsonii berkhoffii* has been associated with human endocarditis and a spectrum of neurological symptoms [23, 24]. *Bartonella quintana*, the agent of trench fever, has been classically considered a human-specific species transmitted solely by human body lice [37]. However, *B. quintana* DNA has been detected in dogs with endocarditis [38] and healthy dogs [39, 40], cats [41, 42] and monkeys (*Macaca fascicularis* and *Macaca mulatta*) [43, 44].

Inter- and intra-species transmission

Intra-erythrocytic *Bartonella* organisms within the bloodstream are ingested by blood-sucking arthropod vectors, mainly fleas, lice, sand flies, biting flies and ticks, after which they are transmitted to a primary reservoir or to an accidental host [37] (Table 1). Vector transmission occurs in two primary ways: (i) inoculation of *Bartonella*-contaminated arthropod feces via animal scratches or bites or by self-inflicted contamination of wounds induced by the host scratching irritating arthropod bites. These are important modes of transmission

among primary reservoir and accidental hosts, including cats, dogs and humans [45–47]. (ii) The other primary mode of transmission is by vector bites, as confirmed for *Lutzomyia verrucarum* sand flies, the vector of *B. bacilliformis* among humans [48]. Experimentally, using an *in vitro* model, *Ixodes ricinus* ticks were able to infect mammalian blood with *B. henselae* [49]. Furthermore, the presence of *Bartonella* spp. DNA, particularly *B. henselae*, has been well documented in questing ticks from Europe and other continents [50–52]. Ticks have also been clinically implicated in the transmission of *Bartonella* infection to dogs or humans in the absence of other vectors or known modes of transmission [53–56]. Interestingly, regurgitation of *B. henselae* by cat fleas (*Ctenocephalides felis*) has been demonstrated experimentally [57], but additional studies are needed to confirm flea-bite transmission to animals or humans. It is important to note that non-vectorial modes of transmission are also possible such as transmission through needle stick injury to veterinarians [58] or by blood transfusion as documented experimentally in cats, dogs and humans [59–62].

Epidemiology, prevalence and distribution in Europe

Serology, PCR or culture-based clinico-epidemiological studies in cats and dogs in Europe are summarized in Tables 2 and 3 and Figs. 1 and 2. More than 50 feline and canine seroprevalence studies have been reported from different European countries (Tables 2, 3); however, culture or PCR confirmed cases of canine or feline bartonellosis have been infrequently reported. *Bartonella* spp. seroprevalence rates are high in cats in European Mediterranean countries, where temperature and humidity are favorable for flea and tick infestations [20] (Fig. 1). In Europe, *Bartonella* antibody prevalence in cats ranges from 0% in Norway [63] to 71.4% in Spain [64] (Table 2). Bacteremic prevalence rates for various combinations of *B. clarridgeiae*, *B. henselae* and *B. koehlerae* often approach 50–75% in feral cat populations worldwide [17]. Generally, the differences in serological or bacteremic prevalences are related to different climatic conditions, whether the cat population tested consisted of pet or stray cats and whether acaricide products were used routinely. Information regarding clinic-epidemiological studies performed in cats in other continents is summarized in Table 4.

Bartonella henselae infection is commonly encountered in cats and potentially dogs and humans worldwide [65] (Tables 2, 3, 4, 5). *Bartonella clarridgeiae*, *B. quintana*, *B. koehlerae* and *B. bovis* are less frequently isolated from domestic cats than *B. henselae*, potentially because these species are more difficult to isolate or are unevenly distributed worldwide (Tables 2, 4). In Europe,

B. clarridgeiae serological and molecular prevalence rates vary from 17 to 36%, while *B. quintana* seroprevalence rates range from 0 to 18%, among a few reported studies (Table 2). Interestingly, *B. koehlerae* and *B. bovis* have not yet been documented to infect cats in Europe although *B. koehlerae* DNA has been amplified from cat fleas in France [66].

Bartonella exposure or infection prevalence studies involving cats have been widely reported from around the world (Tables 2, 4), whereas fewer serological or isolation studies are available regarding *Bartonella* exposure or infection in dogs (Fig. 2). In the USA, one study found a 3.6 % *B. vinsonii berkhoffii* seroprevalence in 1920 clinically ill dogs. The *B. vinsonii berkhoffii* seroprevalence increased to 36 and 52% if the dogs were co-exposed to *Ehrlichia canis* or *Babesia canis*, respectively [67]. Another study found *B. henselae* IgG antibodies in 10.1% of healthy dogs and in 27.2% of sick dogs, whereas *B. vinsonii berkhoffii* IgG antibodies were detected in only 1% of healthy dogs and 4.7% of sick dogs [68]. A recent *Bartonella* seroepidemiology study from North America found overall low *B. henselae*, *B. koehlerae* and *B. vinsonii berkhoffii* seroprevalences in dogs in which a vector-borne disease was suspected [69]. In California, 102 out of 3417 (2.99%) sick dogs were seroreactive for at least one species of *Bartonella* antigen. Of these, 36 (35.3%) had antibodies against *B. henselae* only, 34 (33.3%) had antibodies against *B. clarridgeiae* only, 2 (2.0%) had antibodies against *B. vinsonii berkhoffii* only and 30 (29.4%) had antibodies against a combination of these antigens [70]. Although the sensitivity of *Bartonella* spp. indirect immunofluorescence assay (IFA) most likely under estimates overall seroprevalence, IFA specificity appears to approach 100% [71]. *Bartonella* seroprevalence data is more limited in Europe and other continents in dogs when compared to North America (Tables 3, 5). In Europe, 3% were *B. henselae*-seropositive in the UK [72] and 5.8% in Italy [73]. In Spain, *B. henselae* and *B. vinsonii berkhoffii* seroprevalences were 16.8 and 1.1%, respectively [74]. Moreover, it is important to remark that after a search in PubMed we found around seven times more reports of *Bartonella* infection in dogs in the USA than in Europe [5, 14, 28–31, 38, 75–100]. Information regarding clinic-epidemiological studies performed in dogs in other continents is summarized in Table 5.

The annual number of human cases of CSD in the USA is estimated to be 12,000 outpatients and 500 inpatients [101]. Comparative data have not been reported for European countries. By IFA testing, *B. henselae* seroprevalence rates reported for humans in Europe range between 3 and 30% [51, 102, 103]. A recent study that used six *Bartonella* spp. or genotype antigens to test 89 Spanish veterinarians documented a high *Bartonella* spp. seroprevalence

Table 2 *Bartonella* spp. clinico-epidemiological studies involving cats in Europe

Country (area, year)	Total no. of animals studied (lifestyle)	Percentage of positive animals			Confirmed <i>Bartonella</i> spp. and type using molecular methods	Reference
		Serology (method or antigen used) ^a	Blood PCR	Blood culture		
Albania (Tirana, 2014)	146 (client-owned)	nr	0.7	nr	<i>B. henselae</i>	[182]
Cyprus (2017)	174 (stray and client-owned)	nr	10.9	nr	<i>B. henselae</i>	[183]
Greece (Crete, Mykonos, Skopelos, Athens, 2017)	148 (stray)	58.8	4.7	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[184]
Greece (Thessaly, Macedonia, 2018)	100 (client-owned)	nr	8.5	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i> , <i>B. koehlerae</i>	[178]
Czech Republic (Prague, 2003)	61 (stray, client-owned and shelter)	nr	nr	8.0	<i>B. henselae</i> type II	[185]
Denmark (2002)	93 (stray and client-owned)	45.6	nr	22.6	<i>B. henselae</i> types I and II	[186]
France (Nancy, 1997)	94 (stray)	nr	nr	53	<i>B. henselae</i> types I and II, <i>B. clarridgeiae</i>	[187]
France (Paris, 2001)	436 (client-owned)	41.1	nr	16.5	<i>B. henselae</i> types I and II, <i>B. clarridgeiae</i>	[188]
France (Lyon, 2004)	99 (client-owned)	nr	nr	8.1	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[189]
Germany (Freiburg, 1997)	100 (client-owned)	nr	nr	13	<i>B. henselae</i>	[190]
Germany (southern and northern, 1999)	713 (stray and client-owned)	1	nr	nr	nr	[191]
Germany (Berlin, 2001)	193 (client-owned and stray)	nr	nr	20	<i>B. henselae</i> types I and II, <i>B. clarridgeiae</i>	[192]
Germany (Hannover and others, 2011)	507 (nr)	68.7 (ELISA)	nr	2.2	<i>B. henselae</i>	[193]
Germany (north-east, 2012)	256 (stray and client-owned)	37.1; 18.8 (<i>B. quintana</i>)	0	nr	na	[194]
Germany (southern, 2017)	479 (nr)	nr	2.5	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[195]
Italy (Tuscany, 2002)	427 (client-owned and shelter)	16.0	4.0	0	<i>B. henselae</i>	[196]
Italy (northern, 2002)	248 (nr)	nr	nr	9.7	<i>B. henselae</i>	[197]
Italy (northern, 2004)	1585 (stray)	39.0	nr	2.0	<i>B. henselae</i> types I and II, <i>B. clarridgeiae</i>	[198]
Italy (Sassari, 2007)	79 (stray and client-owned)	21.5	nr	nr	na	[199]
Italy (Sardinia, 2009)	55 (nr)	10.9	5.5	nr	<i>B. henselae</i>	[73]
Italy (southern, 2010)	85 (client-owned)	nr	83.5	nr	<i>B. henselae</i>	[148]
Italy (Sicily, 2012)	182 (stray and client-owned)	57.1	nr	nr	na	[200]
Italy (Pisa, 2012)	234 (client-owned)	33.3	11.1	nr	<i>B. henselae</i> types I and II	[201]
Italy (northern, 2013)	1340 (stray)	23.1	nr	17.0	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[202]
Italy (northern, 2016)	82 (stray)	30.4	nr	nr	na	[203]
Italy (southern, 2016)	42 (nr)	54.8	38.1	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[204]
Italy (Aeolian Islands, 2017)	330 (client-owned)	nr	3.9	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[205]
Ireland (Dublin area, 2010)	121 (client-owned)	26.5 (ELISA)	5.2	nr	<i>B. henselae</i> type II, <i>B. clarridgeiae</i>	[206]
Netherlands (1997)	163 (stray and client-owned)	51.8 (ELISA)	nr	22.0	<i>B. henselae</i>	[207]
Norway (2002)	100 (stray and client-owned)	0	nr	0	na	[63]
Poland (Varsaw, 2007)	137 (nr)	45.0	10.2	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[208]

Table 2 *Bartonella* spp. clinico-epidemiological studies involving cats in Europe (Continued)

Country (area, year)	Total no. of animals studied (lifestyle)	Percentage of positive animals			Confirmed <i>Bartonella</i> spp. and type using molecular methods	Reference
		Serology (method or antigen used) ^a	Blood PCR	Blood culture		
Portugal (Lisbon, Evora, 2009)	51 (client-owned, shelter and stray)	64.9	67.7	nr	<i>B. henselae</i>	[209]
Portugal (1995)	14 (nr)	14.3 (<i>B. quintana</i>); 6.7	nr	nr	na	[210]
Portugal (2014)	649 (stray and client-owned)	nr	2.9	nr	<i>Bartonella</i> spp.	[211]
Spain (Barcelona, Tarragona, Mallorca, 2005)	115 (client-owned)	29.6	7.0	nr	<i>B. henselae</i>	[212]
Spain (Barcelona, Tarragona, Mallorca, 2006)	168 (client-owned)	71.4	17.0	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[64]
Spain (Barcelona, 2008)	100 (client-owned)	nr	1	nr	<i>B. clarridgeiae</i>	[213]
Spain (Madrid, 2012)	680 (client-owned and stray)	24.7	0.3	nr	<i>B. henselae</i>	[127]
Spain (Rioja, Catalonia, 2013)	147 (stray and client-owned)	nr	32	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[214]
Spain (multiple locations, 2015)	86 (client-owned)	50	nr	nr	<i>B. henselae</i>	[215]
Spain (Zaragoza, 2016)	47 (stray and shelter)	nr	38.29	nr	<i>B. henselae</i>	[216]
Spain (Catalonia, 2016)	116 (shelter)	35.3 (ELISA)	22.4	nr	<i>B. henselae</i> , <i>B. clarridgeiae</i>	[217]
Scotland (2011)	52 (client-owned and stray)	15.4 (ELISA)	5.8	nr	<i>B. henselae</i>	[218]
Sweden (different locations, 2002)	292 (nr)	0 (<i>B. quintana</i>); 25 (<i>B. elizabethae</i>); 1 (<i>B. henselae</i>)	nr	nr	na	[219]
Sweden (Stockholm, 2003)	91 (client-owned)	nr	nr	2.2	<i>B. henselae</i> type II	[220]
Switzerland (Tessin, northern, 1997)	728 (client-owned and shelter)	8.3	nr	nr	na	[150]
UK (Bristol, 2002)	360 (nr)	nr	nr	9.4	<i>B. henselae</i> types I and II	[221]
UK (2000)	148 (stray and client-owned)	41.2 (ELISA)	nr	nr	na	[72]

^aTested by IFA for *B. henselae* antigen unless another method or antigen is indicated

Abbreviations: ELISA enzyme-linked immunosorbent assay, IFA indirect immunofluorescence assay, na not applicable, nr not reported

(73.0%), as well as a high molecular prevalence (7.9%) using *Bartonella* alpha proteobacteria growth medium (BAPGM)/PCR [104]. Interestingly, the lowest IFA seroreactivity was found against *B. quintana* antigen (11.2%) and the highest, against *B. vinsonii berkhoffii* genotype III antigen (56%). Infection with *B. henselae*, *B. vinsonii berkhoffii* genotypes I and III, and *B. quintana* DNA was documented [104]. In a previous study carried out in Spain using a commercial enzyme-linked immunosorbent assay (ELISA) kit *B. henselae* seroprevalence in cat owners, and blood donors was 28.9 and 5.9%, respectively [103]. These lower percentages most likely reflect differences in the antigens used, and exposure risks among the study populations. It is relevant to remark that veterinary personnel have a major exposure risk compared to the general population [104].

Infection and pathogenesis

In animal models, mainly cat and mouse, after initial inoculation the infection cycle of *Bartonella* spp. is

initiated by colonization of the still enigmatic primary niche where the bacteria reside, persist and are periodically seeded into the bloodstream to cause the typical relapsing *Bartonella* spp. bacteremia [105]. Endothelial cells, lymph nodes, liver, spleen, kidney, dermis and the bone marrow are some of the proposed niches where *Bartonella* spp. have been isolated from mammals [106–112]. *Bartonella henselae* has been shown to infect erythrocytes, endothelial cells, macrophages, microglial cells and even human CD 34⁺ progenitor cells [113–116]. In a recent study, *Bartonella tribocorum* subcutaneous inoculated in rats led to bloodstream invasion through the lymphatic circulation [110], a finding that may have clinical implications for diseases such as chylothorax.

Bartonella tribocorum was able to resist macrophage phagocytosis and to inhibit pyroptosis at an early stage of infection [110]. Endothelial cells are an important target cell type in probably all mammals, including humans incidentally infected by zoonotic species [117]. The

Table 3 *Bartonella* spp. clinico-epidemiological studies performed in European dogs

Country (area, year)	Total no. of animals studied (lifestyle)	Percentage of positive animals ^a		Confirmed <i>Bartonella</i> spp. and type using molecular methods	Reference
		Serology (method or antigen used) ^b	Blood PCR		
Albania (Tirana, 2009)	30 (stray)	0 (ELISA)	0	na	[222]
Finland (southern, 2014)	390 (client-owned and hunting)	nr	0	na	[223]
Greece (Thessaloniki, 2009)	50 (client-owned sick)	nr	4	<i>B. rochalimae</i> , <i>Bartonella</i> strain HMD	[32]
Italy (Sassari, 2007)	58 (shelter, client-owned)	28.3	nr	na	[199]
Italy (Bologna, 2007)	381 (client-owned)	6	nr	na	[224]
Italy (Basilicata, Ginosa, 2009)	60 (shelter and client-owned)	6.6; 1.7 (<i>B. vinsonii berkhoffii</i>)	11.6	<i>B. henselae</i> , <i>B. vinsonii berkhoffii</i> types I and II, <i>Bartonella</i> strain HMD	[32]
Italy (Sardinia, 2009)	190 (nr)	9.5	0	na	[73]
Italy (Aeolian Islands, 2017)	263 (client-owned)	nr	0	na	[205]
Poland (Warsaw, 2007)	54 (nr)	5.0; 5.5 (<i>B. vinsonii berkhoffii</i>)	10.2	<i>B. henselae</i> , <i>B. vinsonii berkhoffii</i>	[208]
Poland (northwestern, 2011)	242 (client-owned and shelter)	nr	0.3	<i>Bartonella</i> spp.	[225]
Portugal (southern, 2014)	1010 (client-owned and stray)	nr	0	na	[211]
Spain (northern, 2006)	466 (client-owned)	16.8; 1.1 (<i>B. vinsonii berkhoffii</i>)	nr	na	[74]
Spain (Barcelona, 2009)	153 (nr)	nr	0	na	[226]
Spain (north-west, 2018)	61 (client-owned <i>Leishmania</i> infected sick dogs); 16 (client-owned healthy)	40 21	nr	na	[227]
Spain (north-west, north-east, south-east, 2018)	30 (client-owned dogs with culture negative endocarditis)	nr	26.6 ^c	<i>B. rochalimae</i> , <i>B. vinsonii berkhoffii</i> , <i>B. koehlerae</i>	[136]
Spain (north-east, 2018)	68 (client-owned dogs with pericardial effusion)	nr	0 ^d	na	[228]
UK (2000)	100 (client-owned)	3 (ELISA)	nr	na	[72]
UK (Bristol, 2002)	211 (nr)	nr	nr	na	[221]

^aBlood culture was not performed in any of the listed studies with the exception of one study performed in Bristol that did not isolate *Bartonella* in dogs studied [221]

^bTested by IFA for *B. henselae* antigen unless another method or antigen is indicated

^cSamples were from cardiac valve tissue and blood

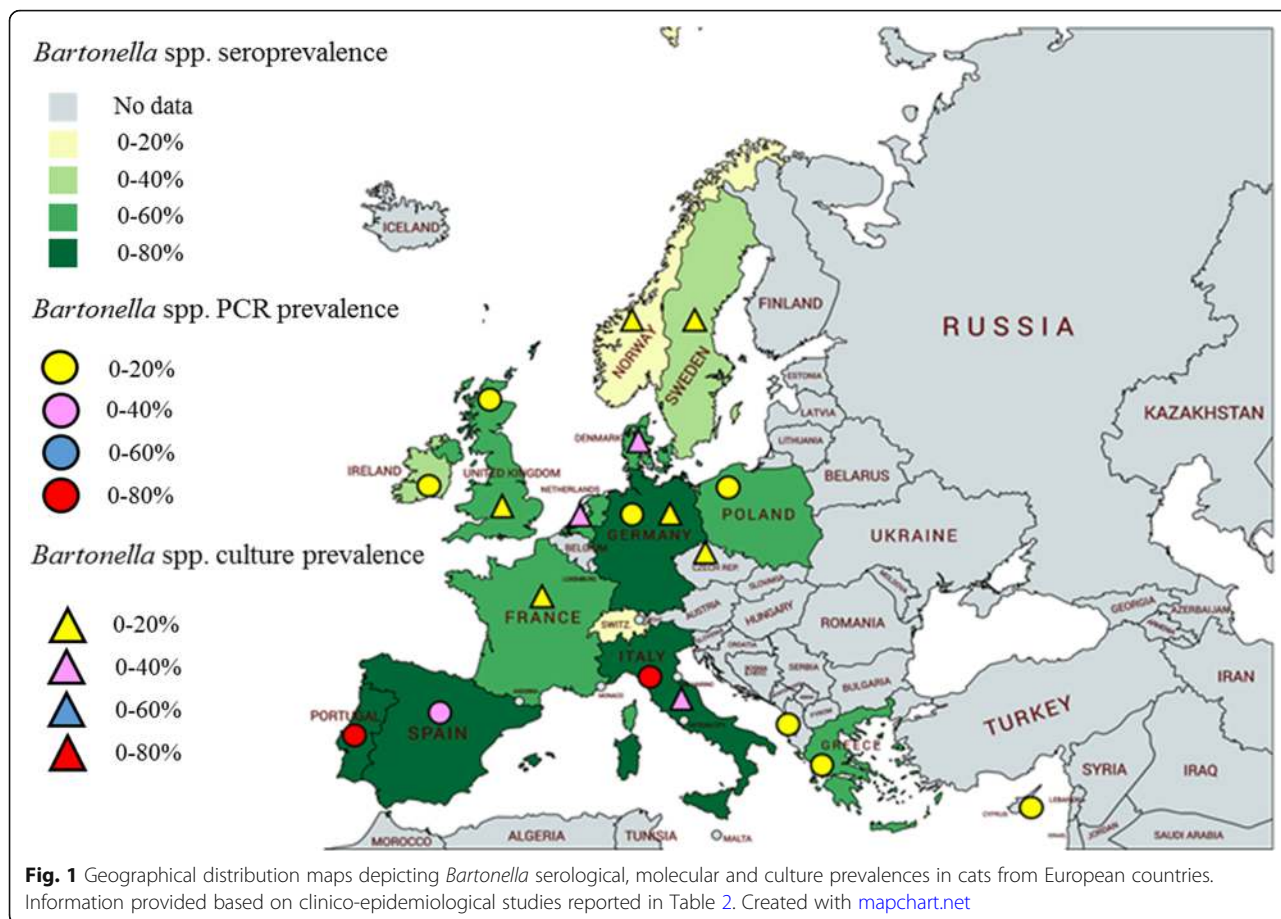
^dSamples were from pericardial effusion and blood

Abbreviations: ELISA enzyme-linked immunosorbent assay, IFA indirect immunofluorescence assay, na not applicable, nr not reported

tropism of *Bartonella* spp. for endothelial cells in conjunction with their proximity to the bloodstream suggest that endothelial cells are an important constituent of the primary niche [118]. In mammalian reservoir hosts, *Bartonella* spp. infection is characterized by chronic intraerythrocytic bacteremia whereas in accidental hosts the bacteria are less frequently documented in association with intraerythrocytic bacteremia, potentially due to a very low-level infection of erythrocytes [105, 119]. *Bartonella* spp. are able to colonize endothelial cells in both, accidental and reservoir hosts [120]. The endothelial or vascular niche provides the bacterium with a means of seeding the blood with organisms on a sporadic basis, potentially contributing to infection of CD34⁺ progenitor

cells in the bone marrow, as well as circulating erythrocytes and monocytes [16].

In dogs, *B. vinsonii berkhoffii* can induce vascular endothelial growth factor (VEGF) endothelial cell proliferations, as reported for *B. bacilliformis*, *B. henselae* and *B. quintana* in human patients [121] leading to vascular tumor formation [118] and vasoproliferation, particularly in patients with human immunodeficiency virus (HIV) or therapeutic suppression of the immune system [121]. There is *in vitro* evidence that *B. vinsonii berkhoffii* genotypes I, II and III are capable of inducing activation of hypoxia inducible factor-1 and production of VEGF, thereby providing mechanistic evidence as to how these bacteria could contribute to the development of



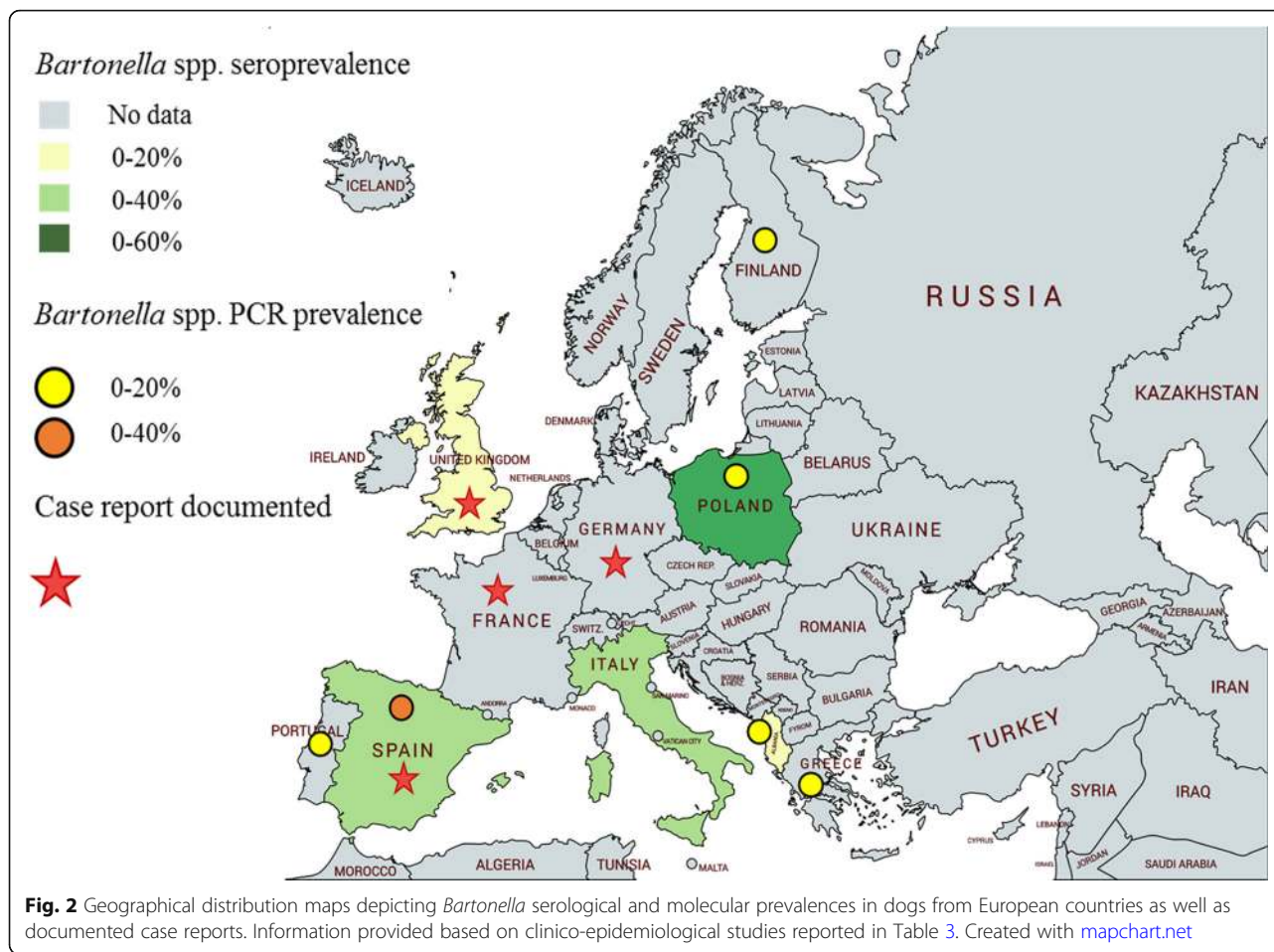
vasoproliferative lesions [121]. For this reason, infection with one or more *Bartonella* spp. may contribute to the pathogenesis of systemic reactive angioendotheliomatosis and hemangiopericytomas in animals [14, 122]. In human patients, activation of hypoxia inducible factor-1 and production of VEGF have been reported for *B. bacilliformis*, *B. henselae* and *B. quintana* [121] leading to vascular tumor formation [118] and vasoproliferation, particularly in patients with HIV or therapeutic suppression of the immune system [121]. Moreover, in humans, *Bartonella* spp. infections range from low to no morbidity (e.g. reactive, suppurative, or granulomatous lymphoid response in immunocompetent individuals), to occasional mortality (e.g. *B. quintana* infection), to substantial mortality in Peru due to the severe hemolytic anemia associated with *B. bacilliformis* [123].

Clinical signs and laboratory abnormalities

The spectrum of disease manifestations associated with *Bartonella* spp. infections continues to expand, yet remains incompletely characterized in many domestic and wild animals [16]. Although most acute *Bartonella* infections are probably self-limiting, persistent infections appear to be associated with a wide variety of clinical signs

and pathological abnormalities in cats, dogs, and humans. *Bartonella* infections manifest from subclinical bacteremia (e.g. healthy animal and human blood donors) to encephalitis, fever of unknown origin, lymphadenomegaly, endocarditis and myocarditis, ocular disease (neuroretinitis, uveitis), skin inflammation and many other less common disease manifestations [124]. Some factors that could influence the appearance of disease manifestations include virulence differences among *Bartonella* spp. and strains, mode of transmission, differences in the host immune response, concurrent infectious or non-infectious diseases, immunosuppression and malnutrition [16, 125].

In the context of comparative medicine, One Health and pet ownership, *B. henselae*, *B. koehlerae* and *B. vinsonii berkhoffii* are the three *Bartonella* spp. most frequently associated with pathology in cats, dogs and humans. As reservoir host for *B. henselae* and *B. koehlerae*, cats can be sub clinically infected for months and even years [54]. However, more virulent strains of these species, as well as other *Bartonella* spp. for which cats are accidental hosts, appear to result in enhanced pathogenicity (Table 6). Furthermore, immunosuppressive viral infections like feline leukemia virus (FeLV) may predispose to *B. henselae* infection or



persistence in cats [126] (Table 6). Despite long-standing bloodstream infection in cats, complete blood count, serum biochemical profiles and urinalysis findings are frequently normal; however, laboratory abnormalities reported with some frequency in sick cats include anemia, eosinophilia, hyperproteinemia, hyperglobulinemia, neutropenia and thrombocytopenia [127]. In cats experimentally infected with *B. henselae* by blood transfusion, histopathological lesions revealed peripheral lymph node hyperplasia, splenic follicular hyperplasia, lymphocytic cholangitis/pericholangitis, lymphocytic hepatitis, lymphoplasmacytic myocarditis and interstitial lymphocytic nephritis [112]. These indicators of chronic inflammation support the need for long-term studies to determine if cats (or other animals) suffer biological consequences for long-standing infection with one or more *Bartonella* spp.

Currently, dogs appear to be an accidental rather than reservoir host for *B. henselae*, which is supported by the fact that this is the most frequently documented *Bartonella* spp. detected in sick dogs [128]. *Bartonella henselae* DNA was also the predominant *Bartonella* spp. amplified and

sequenced from dogs with splenic hemangiosarcomas [129]. To date, *B. henselae* is the only *Bartonella* spp. associated with peliosis hepatis in dogs and humans [130, 131]. *Bartonella henselae* has been associated with other disease manifestations in dogs (Table 6) such as pyogranulomatous lymphadenitis, hepatitis and pulmonary nodules, dermatitis, panniculitis and endocarditis [92, 93, 99, 132]. In humans, *B. henselae* causes cutaneous vasoproliferative lesions (bacillary angiomatosis) and parenchymal vasoproliferative lesions of the liver, spleen (bacillary peliosis), and less frequently other tissues, particularly in immunosuppressed individuals including transplant recipients, and HIV and cancer patients [14, 133] (Table 6).

Bartonella vinsonii berkhoffii was first isolated from a dog with endocarditis in 1993 [87]. In dogs, *B. vinsonii berkhoffii* infection has been associated with endocarditis, arrhythmias, myocarditis, granulomatous lymphadenitis and granulomatous rhinitis. Clinical cases of *B. vinsonii berkhoffii* infection in cats and humans have been rarely described in the literature and clinical findings are summarized in Table 6. Current studies indicate *Bartonella* spp. infections appear to be more

Table 4 Summary of main clinico-epidemiological studies carried out in cats in continents other than Europe

Continent	Area or country	<i>Bartonella</i> spp. seroprevalence (%)	PCR/Culture prevalence (%)	Confirmed <i>Bartonella</i> spp. and type	Reference
Africa	Eastern	11	nf	nf	[229]
	Northern	15.0–59.6	PCR: 0.9–23.5; Culture: 17.0	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[230–233]
	Southern	21.0–24.0	PCR: 7.8	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[234–236]
Asia	China	nf	PCR: 10.5–21.5; Culture: 5.8–18.6	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[237]
	Japan	8.8	PCR: 4.6; Culture: 2.0–20.0	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[238–240]
	Korea	nf	PCR: 41.8–44.1	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[241]
	Middle East	1.2–39.5	PCR: 9.4; Culture: 4.3–9.4	<i>B. clarridgeiae</i> , <i>B. henselae</i> type I, <i>B. koehlerae</i>	[242–246]
	Philippines	62.6–68.0	Culture: 61.0	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[247]
	Thailand	nf	Culture: 12.8–50.0	<i>B. clarridgeiae</i> , <i>B. henselae</i> types I and II	[248]
	Australia	Eastern	37	PCR: 26.2	<i>B. clarridgeiae</i> , <i>B. henselae</i>
	South New Wales (Sydney)	nf	Culture and PCR: 35.0	<i>B. henselae</i>	[250]
	Western and Dirk Hartog and Christmas islands	nf	PCR: 0–5.2	<i>B. henselae</i> , <i>B. koehlerae</i>	[250, 251]
North America	Centre	0–45.0	nf	nf	[252]
	East	10.0–85.2	PCR: 0–62.5	<i>B. clarridgeiae</i> , <i>B. henselae</i> types I and II, <i>B. koehlerae</i>	[243, 252–257]
	West	0–26.2	PCR: 27.0–27.7; Culture: 32.8	<i>B. clarridgeiae</i> , <i>B. henselae</i> types I and II, <i>B. koehlerae</i>	[252, 258, 259]
South America	Argentina	nf	PCR: 17.0	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[260]
	Brazil	15–68	PCR: 4.5–97.0; Culture: 45.5	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[261–264]
	Chile	5.6–8.0	PCR: 18.1; Culture: 41	<i>B. clarridgeiae</i> , <i>B. henselae</i> , <i>B. koehlerae</i>	[265, 266]
	Galapagos islands	75.0	PCR: 59.0	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[267]
	Guatemala	nf	PCR: 33.8; Culture 8.2	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[268]

Abbreviations: PCR polymerase chain reaction, *nf* not found

pathogenic in dogs and humans than in cats, potentially reflecting differences in host evolutionary adaptations to these vector-borne organisms.

To date, few cases of canine bartonellosis have been reported from Europe (Fig. 2) or other continents when compared with the USA, and the clinical findings match those described in dogs from the USA. *Bartonella*-associated inflammatory cardiomyopathy was described in a dog from Italy [95]. *Bartonella* infection in association with panniculitis, polyarthritits and meningitis was reported in a dog from England [75]. In France, *B. henselae* was amplified from blood of a dog with fever of unknown origin and granulomatous lymphadenitis [134] as well as from saliva in a subclinical German dog owned by a human patient suffering angioedema due to *B. henselae* [135]. In Spain, *B. koehlerae* DNA was amplified from blood and mitral valve tissue of a dog with

infective endocarditis [30] and *B. rochalimae*, *B. vinsonii berkhoffii* and *B. koehlerae* were detected by PCR in valve tissue or blood from eight out of 30 (26.6%) dogs with blood culture-negative endocarditis [136]. In another study seroreactivity to *B. henselae* was detected in a dog with a monoclonal gammopathy and *Bartonella* species DNA was amplified from splenic tissue [98].

Diagnosis and identification methods

Accurate diagnosis of *Bartonella* infections remains challenging. Currently there is no diagnostic technique for which a negative result assures the absence of infection. The most frequently used techniques for the detection of acute and chronic infections are specialized microbiological culture techniques, polymerase chain reaction (PCR), immunohistochemistry (IHC) and serology [137].

Table 5 Summary of main clinico-epidemiological studies carried out in dogs in continents other than Europe

Continent	Area or country	<i>Bartonella</i> spp. seroprevalence (%)	PCR / culture prevalence (%)	Confirmed <i>Bartonella</i> spp. and type	Reference
Africa	East	nf	PCR: 0	nf	[269]
	Central	nf	PCR: 2.3	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[27]
	North	19.5–47.4	PCR: 0.85–37.1	<i>B. clarridgeiae</i> , <i>B. elizabethae</i> , <i>B. henselae</i> , <i>B. rochalimae</i> , <i>B. vinsonii berkhoffii</i>	[230, 270–272]
	South	14	PCR: 0–9.0; Culture: 0	<i>B. henselae</i>	[233, 273, 274]
	West	nf	PCR: 0	nf	[275]
Asia	Middle East	6.6–47.4	Culture and PCR: 9.2–37.1	" <i>Candidatus Bartonella merieuxii</i> ", <i>B. vinsonii berkhoffii</i> (type III in one study)	[276–278]
	South Korea	nf	PCR: 0–29.6	<i>B. clarridgeiae</i> , <i>B. henselae</i>	[241, 279, 280]
	Sri Lanka	5.1	PCR: 3.38	<i>Bartonella</i> strain HMD	[281]
	Thailand	38	PCR: 1.8; Culture and PCR: 0.3–31.3	<i>B. clarridgeiae</i> , <i>B. elizabethae</i> , <i>B. grahamii</i> , <i>B. quintana</i> , <i>B. taylorii</i> , <i>B. vinsonii arupensis</i>	[40, 282–284]
	Vietnam	0	PCR: 0	nf	[281]
Australia	New South Wales and Northern Territory	0	Culture and PCR: 0	nf	[285]
North America	Centre	0–20	nf	nf	[69, 286]
	East	0–49	PCR: 9.2; Culture: 52.5	<i>B. bovis</i> , <i>B. henselae</i> , <i>B. koehlerae</i> , <i>B. vinsonii berkhoffii</i> , <i>B. volans</i> -like	[68, 69, 128, 286]
	West	0–29	PCR: 0–1.7; Culture: 2.2	<i>B. clarridgeiae</i> -like, <i>B. vinsonii berkhoffii</i>	[69, 286–288]
South America	Argentina	nf	PCR: 3	<i>B. clarridgeiae</i>	[260]
	Brazil	1.5–24.8	PCR and culture: 1	<i>B. henselae</i> , <i>B. vinsonii berkhoffii</i>	[262, 264, 281, 289]
	Chile	nf	PCR: 4.3	<i>B. henselae</i> , <i>B. vinsonii berkhoffii</i>	[290]
	Colombia	10.1	PCR: 0.77	<i>B. rochalimae</i> , <i>B. vinsonii berkhoffii</i>	[281]
	Galapagos Islands	nf	PCR: 13.6	<i>B. clarridgeiae</i> , <i>B. elizabethae</i> , <i>B. henselae</i>	[267]
	Peru	40–62	PCR: 10	<i>B. rochalimae</i> , <i>B. vinsonii berkhoffii</i> type III	[291]

Abbreviations: PCR polymerase chain reaction, nf not found

Specialized culture techniques including lysis centrifugation, cell culture isolation and growth enrichment in insect biochemical composition growth media are the “gold standard” for confirmation of *Bartonella* infection. Optimal samples for microbiological culture include blood, cerebrospinal fluid [138], joint fluid [81], pathological effusions [138] and tissue biopsies [139]. In reservoir-adapted hosts such as rodents and cats and infrequently in accidental hosts (sick dogs or humans), *Bartonella* spp. can be cultured successfully with agar plates containing 5% defibrinated rabbit or sheep blood, that are maintained at 35 °C in a high humidity chamber with 5% CO₂ concentration. Agar plate isolation requires prolonged incubation times: bacterial colonies may not be visible until 10–56 days after inoculation of the agar plate [140]. Because *Bartonella* spp. are fastidious,

slow-growing bacteria, a negative blood culture or biopsy culture after a long incubation period does not exclude suspected *Bartonella* infection [141]. Furthermore, the patient can be intermittently bacteremic as documented in feline *B. henselae* experimental infections [59, 112]. Similarly, testing serial blood specimens collected over a 7-day period enhanced microbiological documentation of *Bartonella* as reported in humans [142]. BAPGM, an optimized insect cell medium, has been used in an enrichment culture platform to enhance the growth of *Bartonella* spp. prior to attempted subculture bacterial isolation. The BAPGM, prior to PCR testing, has been used to increase sensitivity for documentation of infection, thereby facilitating a diagnosis of bartonellosis in cats, dogs and humans [16]. The BAPGM platform combines enrichment culture of a clinical

Table 6 Clinical sign, lesions and laboratory abnormalities reported in association with *Bartonella* infections in cats, dogs and humans

<i>Bartonella</i> spp.	Hosts ^a		
	Cats	Dogs ^b	Humans
<i>B. henselae</i>	Anemia (EI); diaphragmatic myositis (NI); endocarditis (NI); endomyocarditis - left ventricular; endocardial fibrosis complex (NI); eosinophilia (NI); fever (EI, NI); hyperglobulinemia (EI, NI); lethargy (EI, NI); lymphadenomegaly (EI); mild neurological signs (EI); pyogranulomatous myocarditis and uveitis, conjunctivitis, keratitis and corneal ulcers (NI); subclinical (EI, NI); thrombocytopenia (NI)	Endocarditis (NI); eosinophilia (NI); epistaxis (NI); fever (NI); granulomatous hepatitis (NI); hyperglobulinemia (NI); hyperinsulinemic hypoglycemia syndrome (NI); ineffective erythropoiesis (NI); lymphadenomegaly (NI); monoclonal gammopathy (NI); peliosis hepatis (NI); subclinical (EI, NI); thrombocytopenia (NI); vasoproliferative lesions (NI)	Arthralgia; arthritis; bacillary angiomatosis; CSD; endocarditis; erythema; granulomatous hepatitis; neuroretinitis; peliosis hepatis; pulmonary nodules; uveitis; vasoproliferative tumors
<i>B. vinsonii berkhoffii</i>	Endocardial fibrosis complex (NI); endomyocarditis - left ventricular; osteomyelitis (NI)	Anemia (NI); arrhythmias (NI); endocarditis (NI); epistaxis (NI); fever (NI); granulomatous lymphadenitis (NI); hemangiosarcoma (NI); myocarditis (NI); polyarthritis (NI); splenomegaly (NI); subclinical (EI, NI); thrombocytopenia (NI); uveitis (NI)	Endocarditis
<i>B. clarridgeiae</i>	NCR or subclinical	Endocarditis (NI); hepatic disease (NI)	CSD
<i>B. quintana</i>	NCR or subclinical	Endocarditis (NI); subclinical (NI)	Bacillary angiomatosis; endocarditis; fever; neuroretinitis; uveitis
<i>B. koehlerae</i>	Endomyocarditis - left ventricular; endocardial fibrosis complex	Endocarditis (NI); hyperinsulinemic hypoglycemia syndrome (NI); splenic disease (NI)	Endocarditis
<i>B. rochalimae</i>	NCR or subclinical (EI)	Endocarditis (NI); subclinical (EI)	Fever; splenomegaly
<i>B. washoensis</i>	NCR or subclinical	Endocarditis (NI)	Fever; myocarditis

^aDetails included in Table 6 are provided in [20–22, 29, 30, 39, 70, 91, 92, 96, 98, 99, 112, 127, 132, 136, 154, 160, 168–170, 289, 292–305]

^bPathology reported in dogs to date is mainly due to natural infection only

Abbreviations: CSD cat scratch disease, EI experimental infection, NI natural infection, NCR not clearly related (the reports did not completely prove the direct relation between the clinical findings and the *Bartonella* infection or the animals had subclinical infection)

specimen in the liquid growth medium for a minimum of 7 days, followed by a highly sensitive PCR assay designed to amplify all known *Bartonella* spp. [142]. When testing cat blood samples, *B. henselae* and *B. clarridgeiae* can often be isolated effectively using agar plates; however, isolation of the same *Bartonella* spp. from sick cats, dogs, horses or human blood samples using an identical isolation approach lacks sensitivity. Although additional optimization of *Bartonella* spp. isolation is needed, the introduction of BAPGM has facilitated the successful isolation of *B. henselae* and several other *Bartonella* spp. from dog, horse, human and wildlife blood samples [142–145].

The most employed tissue for *Bartonella* detection by PCR is peripheral blood. However, PCR for *Bartonella* spp. detection and characterization can be also performed after DNA extraction from cerebrospinal fluid, joint fluid, bacterial cultures, oral swabs, lymph node or other tissue samples or aspirates depending on each individual clinical case. To avoid DNA denaturation by formalin fixation, it is advisable to store tissues for future testing or submit fresh or fresh frozen specimens for PCR amplification of *Bartonella* DNA. Once the PCR is positive for the genus *Bartonella*, the species can

be determined using species-specific primers or optimally by DNA sequencing [146–149].

Seroconversion can be used to confirm acute *Bartonella* spp. infection by documenting a four-fold rise in antibody titer over a 2–3-week period [16]. To date, there has been minimal use of serology or other diagnostic modalities for testing cats or dogs with acute onset illness [56]. Serological tests used to detect antibodies include IFA, ELISA and western immunoblot [56]. Serological tests appear to have good specificity and can be used to confirm prior or ongoing infection, but due to poor sensitivity, serology is of more limited value for predicting bacteremia in dogs and potentially sick cats [69, 150]. In cats, high antibody titers often correlate with positive blood cultures or PCR amplification of *Bartonella* DNA directly from blood [140]. Alternatively, the inability to detect *B. henselae* antibodies appears to be predictive of the absence of bacteremia in healthy cats [151], but similar to dogs and humans, there are sick bacteremic cats that do not have detectable *Bartonella* spp. antibodies, for reasons that remain unclear [128]. It is important to note that only 50% of dogs infected with *B. vinsonii berkhoffii* and 25% of dogs infected with *B. henselae* have *Bartonella* specific IFA

antibody reactivity to the respective organism. PCR amplification of organism-specific gene fragments is often diagnostically useful for *Bartonella* cases in which culture and serology results are negative [128].

Studies to date indicate that inflammatory lesions (e.g. pyogranulomatous inflammation) can be severe; however, few organisms are normally visualized [111]. Therefore, stains and techniques to better visualize bacteria in histological specimens are available such as Warthin-Starry staining or immunohistochemistry. *Bartonella* spp. as well as other bacteria such as *Helicobacter pylori* or *Legionella pneumophila* can be visualized in biopsied tissues using Warthin-Starry staining [152]. For this reason, other techniques like *Bartonella* immunohistochemistry, fluorescent *in situ* hybridization (FISH) and PCR can be used to confirm that the bacteria observed by Warthin-Starry staining of histopathological lesions are *Bartonella* spp. [153].

Immunohistochemistry, including confocal immunohistochemistry, has been used for the detection of *Bartonella* spp. in cat, dog and human tissues [38, 94, 153–157]. The principal advantage of immunohistochemistry over other antigen detection techniques is the ability to identify the organism directly in the tissue samples such as cardiac valves or lymphoid organs and thus more effectively establish correlations between antigen localization and histopathological lesions [158]. An immunoassay using two specific in-house *B. henselae* monoclonal antibodies (MAb) documented the intra-erythrocytic localization of this bacterium in three blood culture positive cats. That study concluded that direct fluorescence with a specific MAb is a sensitive, rapid and simple technique which could be useful for detecting *Bartonella* infections in healthy cats [159].

Clinical decision making in light of diagnostic results

The definitive diagnosis of bartonellosis in cats, dogs and, based upon more recent literature, humans [62, 104] remains a clinical, microbiological and pathological challenge. Based on the broad spectrum of historical and clinical abnormalities, bartonellosis is often among differential diagnostic considerations for various clinical problems. However, in many clinical situations, bartonellosis is either not considered diagnostically or becomes a diagnosis after exclusion of other compatible disease entities. However, it is important for clinicians to attempt to achieve diagnostic confirmation prior to embarking upon a long duration antibiotic therapy. A positive therapeutic response to antibiotics, in conjunction with seroreactivity or positive culture or PCR results, provides indirect support for a definitive diagnosis of bartonellosis. Prior or ongoing administration of antibiotics and potentially immunosuppressive drugs can adversely affect serological and molecular diagnostic test results [56, 160]. According to the experience of the authors and current literature, *Bartonella* infection should be investigated using both serology, culture and/or molecular methods (PCR) in healthy pets when: (i) screening cats and dogs as blood donors [60]; (ii) in pets owned by immunocompromised persons [161]; (iii) *Bartonella* infection has been diagnosed or is suspected in a pet owner [162]; and (iv) when there is a history of exposure to fleas, ticks, others arthropods or scratch or bite wound in sick pets [163]. Interpretation of various diagnostic results to guide clinical decision making are summarized in Table 7.

Table 7 Treatment decision based on culture, PCR and serology results in sick animals with suspected *Bartonella* infection [16, 59, 62, 104, 112, 128]

Diagnostic methods			<i>Bartonella</i> infection ^a	Treatment decisions options
Culture	PCR	Serology		
+	+	+	Confirmed	Treat
+	+	-	Confirmed	Treat
+	-	-	Confirmed	Treat
+	-	+	Confirmed	Treat
-	+	+	Confirmed	Treat
-	+	-	Confirmed	Treat
-	-	+	Bartonellosis not excluded; Repeat culture and PCR if the suspicion of clinical bartonellosis remains	Do not treat or treat empirically if disease progresses. Empirical treatment should not be routinely recommended
-	-	-	Bartonellosis not excluded; Repeat serology in 2–3 weeks or culture and PCR in a few days if the suspicion of clinical bartonellosis remains	Do not treat or treat empirically if disease progresses. Empirical treatment should not be routinely recommended

^aDespite diagnostic confirmation of bartonellosis in cats and dogs, as listed in the table, vector-borne disease co-infections, co-morbidities and other differential diagnoses should be evaluated in conjunction with or prior to administration of antimicrobial drugs
Key: +, positive; -, negative

Treatment

Antimicrobial therapy comprises the primary treatment modality and in most cases a combination of antibiotics is necessary to achieve disease resolution (Table 8). There is no standardized antibiotic protocol for treatment of bartonellosis in cats or dogs [164]. Data from controlled efficacy studies involving naturally-infected cats and dogs are lacking. While many antibiotics are effective *in vitro*, *in vivo* efficacy appears to vary among individual patients [25]. Treatments have varied depending upon the predominant tissue location of disease manifestations (e.g. endocard, brain, or blood stream infection).

Most laboratory-based antibiotic treatment studies indicate that complete clearance of *Bartonella* spp. from cats has not been achieved with antibiotics studied to date (doxycycline, amoxicillin, amoxicillin-clavulanic acid, enrofloxacin, erythromycin and rifampicin) [59, 164–166]. Results of these studies were variable with bacteremia apparently being eliminated in some cats [167, 168]. Serum antibody titers typically decrease rapidly (3–6 months) and remain below the limits of detection in animals that have a positive treatment response, and have presumably eliminated the infection [2]. Treatment in sick cats is recommended when *Bartonella* spp. are confirmed diagnostically and compatible disease entities (e.g. endocarditis, encephalitis, myocarditis, fever and uveitis) are suspected or confirmed (Table 8). Because widespread use of antibiotics contributes to antimicrobial resistance among non-targeted bacteria, antibiotic treatment is not routinely

recommended for healthy, *B. henselae* bacteremic cats, despite the risk of zoonotic transmission [167]. However, antibiotic treatment of bacteremic healthy cats living in a household with immunocompromised adults or young children is recommended. In these cases, treatment is aimed at decreasing bacterial load, minimizing the risk of additional vector exposure and thus decreasing the risk of transmission among pets or to humans.

An optimal protocol for treatment *Bartonella* spp. infection in dogs has also not been established. Use of an antibiotic capable of crossing lipid membranes and reaching high intracellular concentrations, such as amoxicillin, azithromycin, doxycycline and enrofloxacin is recommended [168–170]. Macrolides, like azithromycin, are effective but are not recommended as a first line antibiotic due to rapid development of resistance among *B. henselae* strains. Once genetically-mediated (mutation) resistance developed, *B. henselae* isolates were resistant to all macrolides [16]. For dogs with central nervous system involvement, a combination of doxycycline and rifampicin has been used successfully, but the use of rifampicin is not recommended in cats [167]. Aminoglycosides, used to treat human endocarditis, are recommended in conjunction with careful monitoring of renal function during the initial treatment of suspected *Bartonella* endocarditis or myocarditis in cats and dogs. A combination of doxycycline and amikacin represents a treatment option for *Bartonella* endocarditis in cats and dogs [16]. For dogs that are reasonably stable starting with one antibiotic (for example doxycycline at 5 mg/kg every 12 hours) and adding the

Table 8 Reported treatments in cats and dogs

Host	Clinical <i>Bartonella</i> spp. manifestations/species	Treatment	Dose/duration	Reference ^a
Cats	Bacteremia and uveitis/ <i>Bartonella</i> spp.	Doxycycline + Pradofloxacin	5 mg/kg PO q 12 h/4–6 weeks + 5 mg/kg PO q 12 h/4–6 weeks	[167]
		Doxycycline	10 mg/kg PO q 12–24 h/4–6 weeks	[170]
		Azithromycin	10 mg/kg PO q 24–48 h/ 7 days followed by every other day for 6–12 weeks	[169]
	Endocarditis/ <i>B. henselae</i>	Marbofloxacin + Azithromycin	5 mg/kg PO q 24 h/6 weeks + 10 mg/kg PO q 24 h for 7 days and then q 48 h/6 weeks	[294]
	Osteomyelitis and polyarthritis/ <i>B. vinsonii berkhoffii</i>	Amoxicillin-clavulanate + Azithromycin	62.5 mg PO q 12 h/2 months + 10 mg/kg PO q 48 h/3 months	[168]
Dogs	Splenic vasculitis, thrombosis and infarction/ <i>B. henselae</i>	Doxycycline + Trimethoprim-sulfamethoxazole	5–10 mg/kg PO q 12 h/4 weeks + 23 mg/kg, PO q 12 h/6 weeks	[28]
		Doxycycline + Enrofloxacin	5–15 mg/kg PO q 12 h + 5 mg/kg PO q 12 h /4–6 weeks	[169]
	Neurological and ocular disorders/ <i>Bartonella</i> spp.	Doxycycline + Rifampicin	5–10 mg/kg PO q 12 + 5 mg/kg PO q 24 h/ 4–6 weeks	
		Endocarditis/ <i>B. koehlerae</i>	Ampicillin + Enrofloxacin	22 mg/kg PO q 8 h + 5 mg/kg PO q 12–24 h /4–6 weeks
	Hemangiopericytoma/ <i>B. vinsonii berkhoffii</i>	Enrofloxacin	5 mg/kg PO q 12 h/4–6 weeks	[14]

^aDetails included in Table 8 are provided in references
Abbreviations: q every, PO oral administration

second antibiotic 5–7 days later may help to avoid a potential Jarisch-Herxheimer-like reaction that appears to be related to rapid bacterial injury/death. The Jarisch-Herxheimer-like reaction is typically associated with lethargy, fever, occasionally vomiting and commonly occurs in cats and dogs at 4–7 days after starting antibiotics. If a Jarisch-Herxheimer-like reaction occurs, it is not recommended to interrupt or change antibiotics; supportive therapy and anti-inflammatory steroids for a few days may help dogs through this period [167].

General treatment recommendations for feline and canine bartonellosis based upon the literature and the authors' experiences are summarized below:

- Diagnostic confirmation of clinical bartonellosis is recommended or a very high index of suspicion.
- Prolonged treatment periods (4–6 weeks) are recommended to avoid bacterial drug resistance and to achieve disease resolution.
- Antibiotics are currently the mainstay of treatment.
- It is not recommended to use macrolides as the first therapy option.
- Antibiotic combinations with various mechanisms of action, achieving therapeutic drug concentrations within cells and within plasma are needed to eradicate *Bartonella* infections.

Preventative measures

As vaccines are not available to prevent infection, flea and tick control are the only successful measures to prevent this vector-borne infection in healthy animals [166], to decrease the dispersion of these bacteria among canine and feline populations, and to decrease the risk of zoonotic pathogen transmission to humans [65]. Cats and dogs should be protected from flea and tick infestations year-round by the regular use of acaricides in the form of collars, spot-on or spray-on or oral formulations [171]. Furthermore, both people and pets should avoid contact with stray dogs and cats. In the context of One Health, the authors support the future development of vaccines to protect pets against infection with *B. henselae* and *B. vinsonii berkhoffii* and thereby decrease reservoir potential and zoonotic risks.

In households with immunosuppressed persons or young children, if their pets are determined as bacteremic, antibiotic treatment and routine acaricide use are recommended for these pets. When acquiring a new cat or dog, into a household with immunocompromised individuals and children, choosing an adult animal will lower the possibility of acquiring a *Bartonella* spp. bacteremic pet [25, 65].

Blood transfusion has also been identified as a risk factor for the transmission of *Bartonella* infections. Screening of blood donors for *Bartonella* infections, should be considered [37, 60].

Conclusions

Based upon the recent and ongoing discovery of novel *Bartonella* spp. in hosts such as bats [172, 173] and rodents [174], it is likely that additional *Bartonella* spp., in conjunction with their respective reservoir host and vector, will be described. Furthermore, as *Bartonella* spp. transmission routes are not fully understood, research efforts should focus on modes of transmission so that appropriate control measures can be implemented to prevent the pathogen transmission between animals and from animals to humans. *Bartonella* spp. seroprevalence rates in cats and dogs in Europe and other parts of the world do not correspond with the low number of reported clinical cases, especially in dogs, potentially because *Bartonella* infections are underdiagnosed. The limited number of reported cases of *Bartonella* spp. infection compromises our collective ability to establish a complete list of clinical conditions or specific pathologies related to this infection. In conclusion, more efforts are needed in both research and clinical settings to characterize the medical importance of *Bartonella* spp. infections in cats and dogs. Additionally, randomized case control studies are needed to assess treatment efficacy and to establish an optimal protocol for the treatment of chronic bartonellosis in cats, dogs and humans. Efforts to develop safe and effective vaccines are needed to protect pets and their families.

Abbreviations

BAPGM: *Bartonella* alpha proteobacteria growth medium; CO₂: Carbon dioxide; CSD: Cat scratch disease; EI: Experimental infection; ELISA: Enzyme-linked immunosorbent assay; FeLV: Feline leukemia virus; FISH: Fluorescent in situ hybridization; HIV: Human immunodeficiency virus; IFA: Indirect immunofluorescence assay; IgG: Immunoglobulin G; IHC: Immunohistochemistry; MAb: Monoclonal antibody; NA: Not applicable; NCR: Not clearly related; NI: Natural infection; NF: not found; nr: Not reported; PCR: Polymerase chain reaction; PO: Oral administration; q: Every; VEGF: Vascular endothelial growth factor

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LSG conceived the manuscript. AAF wrote, and EB and LSG edited the first draft. All authors read and approved the final manuscript.

Ethics approval and consent to participate

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Not applicable.

Competing interests

LSG and AAF declare that they have no competing interests. In conjunction with Dr Sushama Sontakke and North Carolina State University, EBB holds

U.S. patent no. 7,115,385; Media and Methods for cultivation of microorganisms, which was issued on 3rd October 2006. He is a co-founder, shareholder and Chief Scientific Officer for Galaxy Diagnostics, a company that provides advanced diagnostic testing for the detection of *Bartonella* species infections.

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References

- Deng H, Le Rhun D, Buffet J-PR, Cotté V, Read A, Birtles RJ, et al. Strategies of exploitation of mammalian reservoirs by *Bartonella* species. *Vet Res.* 2012;43:15.
- Breitschwerdt EB, Maggi RG, Chomel BB, Lappin MR. Bartonellosis: an emerging infectious disease of zoonotic importance to animals and human beings. *J Vet Emerg Crit Care.* 2010;20:8–30.
- Chomel BB, Kasten RW, Sykes JE, Boulouis H-J, Breitschwerdt EB. Clinical impact of persistent *Bartonella* bacteremia in humans and animals. *Ann N Y Acad Sci.* 2003;990:267–78.
- Lappin MR, Kordick DL, Breitschwerdt EB. *Bartonella* spp. antibodies and DNA in aqueous humour of cats. *J Feline Med Surg.* 2000;2:61–8.
- Kordick DL, Breitschwerdt EB. Persistent infection of pets within a household with three *Bartonella* species. *Emerg Infect Dis.* 1998;4:325–8.
- Valentine KH, Harms C, Cadenas MB, Birkenheuer AJ, Marr HS, Braun-McNeill J, et al. *Bartonella* DNA in loggerhead sea turtles. *Emerg Infect Dis.* 2007;13:949–50.
- Chang CC, Chomel BB, Kasten RW, Heller RM, Kocan KM, Ueno H, et al. *Bartonella* spp. isolated from wild and domestic ruminants in North America. *Emerg Infect Dis.* 2000;6:306–11.
- Dehio C, Sauder U, Hiestand R. Isolation of *Bartonella schoenbuchensis* from *Lipoptena cervi*, a blood-sucking arthropod causing deer ked dermatitis. *J Clin Microbiol.* 2004;42:5320–3.
- Jones SL, Maggi R, Shuler J, Alward A, Breitschwerdt EB. Detection of *Bartonella henselae* in the blood of 2 adult horses. *J Vet Intern Med.* 2008;22:495–8.
- Alsarraaf M, Mohallah EME, Mierzejewska EJ, Behnke-Borowczyk J, Welc-Fałęciak R, Bednarska M, et al. Description of *Candidatus Bartonella fadhilae* n. sp. and *Candidatus Bartonella sanaae* n. sp. (*Bartonellaceae*) from *Dipodillus dasyurus* and *Sekeetamys calurus* (*Gerbillinae*) from the Sinai Massif (Egypt). *Vector Borne Zoonotic Dis.* 2017;17:483–94.
- Lamas C, Curi A, Bóia M, Lemos E. Human bartonellosis: seroepidemiological and clinical features with an emphasis on data from Brazil - a review. *Mem Inst Oswaldo Cruz.* 2008;103:221–35.
- Breitschwerdt EB, Maggi RG, Robert Mozayeni B, Hegarty BC, Bradley JM, Mascarelli PE. PCR amplification of *Bartonella koehlerae* from human blood and enrichment blood cultures. *Parasit Vectors.* 2010;3:76.
- Vera CP, Maggi RG, Woods CW, Mascarelli PE, Breitschwerdt EB. Spontaneous onset of complex regional pain syndrome Type I in a woman infected with *Bartonella koehlerae*. *Med Microbiol Immunol.* 2014;203:101–7.
- Breitschwerdt EB, Maggi RG, Varanat M, Linder KE, Weinberg G. Isolation of *Bartonella vinsonii* subsp. *berkhoffii* genotype II from a boy with epithelioid hemangioendothelioma and a dog with hemangiopericytoma. *J Clin Microbiol.* 2009;47:1957–60.
- Breitschwerdt EB, Maggi RG, Farmer P, Mascarelli PE. Molecular evidence of perinatal transmission of *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella henselae* to a child. *J Clin Microbiol.* 2010;48:2289–93.
- Breitschwerdt EB. Bartonellosis, One Health and all creatures great and small. *Vet Dermatol.* 2017;28:96–21.
- Chomel BB, Kasten RW. Bartonellosis, an increasingly recognized zoonosis. *J Appl Microbiol.* 2010;109:743–50.
- Jaffe DA, Chomel BB, Kasten RW, Breitschwerdt EB, Maggi RG, McLeish A, et al. *Bartonella henselae* in small Indian mongooses (*Herpestes auro-punctatus*) from Grenada, West Indies. *Vet Microbiol.* 2018;216:119–22.
- Chomel BB, Kasten RW, Floyd-Hawkins K, Chi B, Yamamoto K, Roberts-Wilson J, et al. Experimental transmission of *Bartonella henselae* by the cat flea. *J Clin Microbiol.* 1996;34:1952–6.
- Chomel BB, Boulouis H-J, Maruyama S, Breitschwerdt EB. *Bartonella* spp. in pets and effect on human health. *Emerg Infect Dis.* 2006;12:389–94.
- Chomel BB, Boulouis HJ, Breitschwerdt EB. Cat scratch disease and other zoonotic *Bartonella* infections. *J Am Vet Med Assoc.* 2004;224:1270–9.
- Avidor B, Graidly M, Efrat G, Leibowitz C, Shapira G, Schattner A, et al. *Bartonella koehlerae*, a new cat-associated agent of culture-negative human endocarditis. *J Clin Microbiol.* 2004;42:3462–8.
- Roux V, Ekykn SJ, Wyllie S, Raoult D. *Bartonella vinsonii* subsp. *berkhoffii* as an agent of afebrile blood culture-negative endocarditis in a human. *J Clin Microbiol.* 2000;38:1698–700.
- Clarte L, Ampof K, Thorell EA, Sanderson S, Doby E, Pavia AT, et al. *Bartonella vinsonii* endocarditis in an adolescent with congenital heart disease. *Pediatr Infect Dis J.* 2012;31:531–4.
- Breitschwerdt EB, Kordick DL. *Bartonella* infection in animals: carriership, reservoir potential, pathogenicity, and zoonotic potential for human infection. *Clin Microbiol Rev.* 2000;13:428–38.
- Chang CC, Kasten RW, Chomel BB, Simpson DC, Hew CM, Kordick DL, et al. Coyotes (*Canis latrans*) as the reservoir for a human pathogenic *Bartonella* sp.: molecular epidemiology of *Bartonella vinsonii* subsp. *berkhoffii* infection in coyotes from central coastal California. *J Clin Microbiol.* 2000;38:4193–200.
- Gundi VAKB, Bourry O, Davoust B, Raoult D, La Scola B. *Bartonella claridgeiae* and *B. henselae* in dogs, Gabon. *Emerg Infect Dis.* 2004;10:2261–2.
- Friedenberg SG, Balakrishnan N, Guillaumin J, Cooper ES, Lewis K, Russell DS, et al. Splenic vasculitis, thrombosis, and infarction in a febrile dog infected with *Bartonella henselae*. *J Vet Emerg Crit Care.* 2015;25:789–94.
- Kitchell BE, Fan TM, Kordick D, Breitschwerdt EB, Wollenberg G, Lichtensteiger CA. Peliosis hepatis in a dog infected with *Bartonella henselae*. *J Am Vet Med Assoc.* 2000;216:519–23.
- Tabar M-D, Altet L, Maggi RG, Altimira J, Roura X. First description of *Bartonella koehlerae* infection in a Spanish dog with infective endocarditis. *Parasit Vectors.* 2017;10:247.
- Chomel BB, Wey AC, Kasten RW. Isolation of *Bartonella washoensis* from a dog with mitral valve endocarditis. *J Clin Microbiol.* 2003;41:5327–32.
- Diniz PPVP, Billeter SA, Otranto D, De Capraris D, Petanides T, Mylonakis ME, et al. Molecular documentation of *Bartonella* infection in dogs in Greece and Italy. *J Clin Microbiol.* 2009;47:1565–7.
- Ihler GM. *Bartonella bacilliformis*: dangerous pathogen slowly emerging from deep background. *FEMS Microbiol Lett.* 1996;144:1–11.
- Keret D, Giladi M, Kletter Y, Wientroub S. Cat-scratch disease osteomyelitis from a dog scratch. *J Bone Joint Surg Br.* 1998;80:766–7.
- Vieira-Damiani G, Diniz PPV de P, Pitassi LHU, Sowry S, Scorpio DG, Lania BG, et al. *Bartonella claridgeiae* bacteremia detected in an asymptomatic blood donor. *J Clin Microbiol.* 2015;53:352–6.
- Breitschwerdt EB, Mascarelli PE, Schweickert LA, Maggi RG, Hegarty BC, Bradley JM, et al. Hallucinations, sensory neuropathy, and peripheral visual deficits in a young woman infected with *Bartonella koehlerae*. *J Clin Microbiol.* 2011;49:3415–7.
- Regier Y, O'Rourke F, Kempf VAJ. *Bartonella* spp. - a chance to establish One Health concepts in veterinary and human medicine. *Parasit Vectors.* 2016;9:261.
- Kelly P, Rolain JM, Maggi R, Sontakke S, Keene B, Hunter S, et al. *Bartonella quintana* endocarditis in dogs. *Emerg Infect Dis.* 2006;12:1869–72.
- Duncan AW, Marr HS, Birkenheuer AJ, Maggi RG, Williams LE, Correa MT, et al. *Bartonella* DNA in the blood and lymph nodes of golden retrievers with lymphoma and in healthy controls. *J Vet Intern Med.* 2008;22:89–95.
- Bai Y, Kosoy MY, Boonmar S, Sawatwong P, Sangmaneeet S, Peruski LF. Enrichment culture and molecular identification of diverse *Bartonella* species in stray dogs. *Vet Microbiol.* 2010;146:314–9.
- Breitschwerdt EB, Maggi RG, Sigmon B, Nicholson WL. Isolation of *Bartonella quintana* from a woman and a cat following putative bite transmission. *J Clin Microbiol.* 2007;45:270–2.
- La VD, Tran-Hung L, Aboudharam G, Raoult D, Drancourt M. *Bartonella quintana* in domestic cat. *Emerg Infect Dis.* 2005;11:1287–9.
- O'Rourke LG, Pitulle C, Hegarty BC, Kraycirik S, Killary KA, Grosenstein P, et al. *Bartonella quintana* in cynomolgus monkey (*Macaca fascicularis*). *Emerg Infect Dis.* 2005;11:1931–4.

44. Huang R, Liu Q, Li G, Li D, Song X, Birtles RJ, et al. *Bartonella quintana* infections in captive monkeys, China. *Emerg Infect Dis*. 2011;17:1707–9.
45. Mosbacher ME, Klotz S, Klotz J, Pinnas JL. *Bartonella henselae* and the potential for arthropod vector-borne transmission. *Vector Borne Zoonotic Dis*. 2011;11:471–7.
46. Guptill L. Bartonellosis. *Vet Clin North Am Small Anim Pract*. 2003;33:809–25.
47. Foil L, Andress E, Freeland RL, Roy AF, Rutledge R, Triche PC, et al. Experimental infection of domestic cats with *Bartonella henselae* by inoculation of *Ctenocephalides felis* (Siphonaptera: Pulicidae) feces. *J Med Entomol*. 1998;35:625–8.
48. Battisti JM, Lawyer PG, Minnick MF. Colonization of *Lutzomyia verrucarum* and *Lutzomyia longipalpis* sand flies (Diptera: Psychodidae) by *Bartonella bacilliformis*, the etiologic agent of Carrion's disease. *PLoS Negl Trop Dis*. 2015;9:0004128.
49. Cotté V, Bonnet S, Le Rhun D, Le Naour E, Chauvin A, Boulouis HJ, et al. Transmission of *Bartonella henselae* by *Ixodes ricinus*. *Emerg Infect Dis*. 2008;14:1074–80.
50. Edyta, Chmielewski T, Sochon E, Tylewska-Wierzbiana S. *Bartonella henselae* in *Ixodes ricinus* ticks removed from dogs. *Vector Borne Zoonotic Dis*. 2007;7:189–92.
51. Müller A, Reiter M, Schötta AM, Stockinger H, Stanek G. Detection of *Bartonella* spp. in *Ixodes ricinus* ticks and *Bartonella* seroprevalence in human populations. *Ticks Tick Borne Dis*. 2016;7:763–7.
52. Pennisi M-G, Persichetti M-F, Serrano L, Altet L, Reale S, Gulotta L, et al. Ticks and associated pathogens collected from cats in Sicily and Calabria (Italy). *Parasit Vectors*. 2015;8:512.
53. Lucey D, Dolan MJ, Moss CW, Garcia M, Hollis DG, Wegner S, et al. Relapsing illness due to *Rochalimaea henselae* in immunocompetent hosts: implication for therapy and new epidemiological associations. *Clin Infect Dis*. 1992;14:683–8.
54. Breitschwerdt EB, Maggi RG, Nicholson WL, Cherry NA, Woods CW. *Bartonella* sp. bacteremia in patients with neurological and neurocognitive dysfunction. *J Clin Microbiol*. 2008;46:2856–61.
55. Maggi RG, Ericson M, Mascarelli PE, Bradley JM, Breitschwerdt EB. *Bartonella henselae* bacteremia in a mother and son potentially associated with tick exposure. *Parasit Vectors*. 2013;6:101.
56. Golly E, Breitschwerdt EB, Balakrishnan N, Moore D, Bizikova P. *Bartonella henselae*, *Bartonella koehlerae* and *Rickettsia rickettsii* seroconversion and seroreversion in a dog with acute-onset fever, lameness, and lymphadenopathy followed by a protracted disease course. *Vet Parasitol Reg*. 2017;7:19–24.
57. Bouhsira E, Ferrandez Y, Liu M, Franc M, Boulouis HJ, Biville F. *Ctenocephalides felis* an in vitro potential vector for five *Bartonella* species. *Comp Immunol Microbiol Infect Dis*. 2013;36:105–11.
58. Oliveira AM, Maggi RG, Woods CW, Breitschwerdt EB. Suspected needle stick transmission of *Bartonella vinsonii* subspecies *berkhoffii* to a veterinarian. *J Vet Intern Med*. 2010;24:1229–32.
59. Kordick DL, Breitschwerdt EB. Relapsing bacteremia after blood transmission of *Bartonella henselae* to cats. *Am J Vet Res*. 1997;58:492–7.
60. Wardrop KJ, Birkenheuer A, Blais MC, Callan MB, Kohn B, Lappin MR, et al. Update on canine and feline blood donor screening for blood-borne pathogens. *J Vet Intern Med*. 2016;30:15–35.
61. Núñez MA, Contreras K, Depix MS, Geoffroy E, Villagra N, Mellado S, et al. Prevalencia de *Bartonella henselae* en donantes de sangre y riesgo de transmisión sanguínea en Chile. *Rev Chil Infectología*. 2017;34:539–43.
62. Pitassi LHU, de Paiva Diniz PPV, Scorpio DG, Drummond MR, Lania BG, Barjas-Castro ML, et al. *Bartonella* spp. bacteremia in blood donors from Campinas, Brazil. *PLoS Negl Trop Dis*. 2015;9:0003467.
63. Bergh K, Bevanger L, Hanssen I, Loseth K. Low prevalence of *Bartonella henselae* infections in Norwegian domestic and feral cats. *Apimis*. 2002;110:309–14.
64. Solano-Gallego L, Hegarty B, Espada Y, Llull J, Breitschwerdt E. Serological and molecular evidence of exposure to arthropod-borne organisms in cats from northeastern Spain. *Vet Microbiol*. 2006;118:274–7.
65. Pennisi MG, Marsilio F, Hartmann K, Lloret A, Addie D, Belák S, et al. *Bartonella* species infection in cats: ABCD guidelines on prevention and management. *J Feline Med Surg*. 2013;15:563–9.
66. Rolain J-M, Franc M, Davoust B, Raoult D. Molecular detection of *Bartonella quintana*, *B. koehlerae*, *B. henselae*, *B. clarridgeiae*, *Rickettsia felis*, and *Wolbachia pipientis* in cat fleas, France. *Emerg Infect Dis*. 2003;9:338–42.
67. Pappalardo BL, Correa MT, York CC, Peat CY, Breitschwerdt EB. Epidemiologic evaluation of the risk factors associated with exposure and seroreactivity to *Bartonella vinsonii* in dogs. *Am J Vet Res*. 1997;58:467–71.
68. Solano-Gallego L, Bradley J, Hegarty B, Sigmon B, Breitschwerdt E. *Bartonella henselae* IgG antibodies are prevalent in dogs from southeastern USA. *Vet Res*. 2004;35:585–95.
69. Lashnits E, Correa M, Hegarty BC, Birkenheuer A, Breitschwerdt EB. *Bartonella* seroepidemiology in dogs from North America, 2008–2014. *J Vet Intern Med*. 2018;32:222–31.
70. Henn JB, Liu C-H, Kasten RW, VanHorn BA, Beckett LA, Kass PH, et al. Seroprevalence of antibodies against *Bartonella* species and evaluation of risk factors and clinical signs associated with seropositivity in dogs. *Am J Vet Res*. 2005;66:688–94.
71. Hegarty BC, Bradley JM, Lappin MR, Balakrishnan N, Mascarelli PE, Breitschwerdt EB. Analysis of seroreactivity against cell culture-derived *Bartonella* spp. antigens in dogs. *J Vet Intern Med*. 2014;28:38–41.
72. Barnes A, Bell SC, Isherwood DR, Bennett M, Carter SD. Evidence of *Bartonella henselae* infection in cats and dogs in the United Kingdom. *Vet Rec*. 2000;147:673–7.
73. Zobba R, Chessa G, Mastrandrea S, Parpaglia MLP, Patta C, Masala G. Serological and molecular detection of *Bartonella* spp. in humans, cats and dogs from northern Sardinia, Italy. *Clin Microbiol Infect*. 2009;15:134–5.
74. Solano-Gallego L, Llull J, Osso M, Hegarty B, Breitschwerdt E. A serological study of exposure to arthropod-borne pathogens in dogs from northeastern Spain. *Vet Res*. 2006;37:231–44.
75. Mellor PJ, Fetz K, Maggi RG, Haugland S, Dunning M, Villiers EJ, et al. Alpha1-proteinase inhibitor deficiency and *Bartonella* infection in association with panniculitis, polyarthritis, and meningitis in a dog. *J Vet Intern Med*. 2006;20:1023–8.
76. Michau TM, Breitschwerdt EB, Gilger BC, Davidson MG. *Bartonella vinsonii* subspecies *berkhoffii* as a possible cause of anterior uveitis and choroiditis in a dog. *Vet Ophthalmol*. 2003;6:299–304.
77. Pappalardo BL, Brown T, Gookin JL, Morrill CL, Breitschwerdt EB. Granulomatous disease associated with *Bartonella* infection in 2 dogs. *J Vet Intern Med*. 2000;14:37–42.
78. Tuttle AD, Birkenheuer AJ, Juopperi T, Levy MG, Breitschwerdt EB. Concurrent bartonellosis and babesiosis in a dog with persistent thrombocytopenia. *J Am Vet Med Assoc*. 2003;223:1306–10.
79. Shelnutt LM, Balakrishnan N, DeVanna J, Batey KL, Breitschwerdt EB. Death of military working dogs due to *Bartonella vinsonii* subspecies *berkhoffii* genotype III endocarditis and myocarditis. *Mil Med*. 2017;182:e1864–9.
80. Balakrishnan N, Pritchard J, Ericson M, Grindem C, Phillips K, Jennings S, et al. Prostatitis, steatitis, and diarrhea in a dog following presumptive flea-borne transmission of *Bartonella henselae*. *J Clin Microbiol*. 2014;52:3447–52.
81. Diniz PPV de P, Wood M, Maggi RG, Sontakke S, Stepink M, Breitschwerdt EB. Co-isolation of *Bartonella henselae* and *Bartonella vinsonii* subsp. *berkhoffii* from blood, joint and subcutaneous seroma fluids from two naturally infected dogs. *Vet Microbiol*. 2009;138:368–72.
82. Henn JB, Gabriel MW, Kasten RW, Brown RN, Koehler JE, MacDonald KA, et al. Infective endocarditis in a dog and the phylogenetic relationship of the associated "*Bartonella rochalimae*" strain with isolates from dogs, gray foxes, and a human. *J Clin Microbiol*. 2009;47:787–90.
83. Cadenas MB, Bradley J, Maggi RG, Takara M, Hegarty BC, Breitschwerdt EB. Molecular characterization of *Bartonella vinsonii* subsp. *berkhoffii* genotype III. *J Clin Microbiol*. 2008;46:1858–60.
84. Saunders GK, Monroe WE. Systemic granulomatous disease and sialometaplasia in a dog with *Bartonella* infection. *Vet Pathol*. 2006;43:391–2.
85. Chomel BB, Mac Donald KA, Kasten RW, Chang CC, Wey AC, Foley JE, et al. Aortic valve endocarditis in a dog due to *Bartonella clarridgeiae*. *J Clin Microbiol*. 2001;39:3548–54.
86. Breitschwerdt EB, Hegarty BC, Maggi R, Hawkins E, Dyer P. *Bartonella* species as a potential cause of epistaxis in dogs. *J Clin Microbiol*. 2005;43:2529–33.
87. Kordick DL, Swaminathan B, Greene CE, Wilson KH, Whitney AM, O'Connor S, et al. *Bartonella vinsonii* subsp. *berkhoffii* subsp. nov., isolated from dogs; *Bartonella vinsonii* subsp. *vinsonii*; and emended description of *Bartonella vinsonii*. *Int J Syst Bacteriol*. 1996;46:704–9.
88. Breitschwerdt EB, Kordick DL, Malarky DE, Keene B, Hadfield TL, Wilson K. Endocarditis in a dog due to infection with a novel *Bartonella* subspecies. *J Clin Microbiol*. 1995;33:154–60.
89. Yager JA, Best SJ, Maggi RG, Varanat M, Znajda N, Breitschwerdt EB. Bacillary angiomatosis in an immunosuppressed dog. *Vet Dermatol*. 2010;21:420–8.

90. Breitschwerdt EB, Maggi RG. A confusing case of canine vector-borne disease: clinical signs and progression in a dog co-infected with *Ehrlichia canis* and *Bartonella vinsonii* ssp. *berkhoffii*. *Parasit Vectors*. 2009;2(Suppl. 1):S3.
91. Gillespie TN, Washabau RJ, Goldschmidt MH, Cullen JM, Rogala AR, Breitschwerdt EB. Detection of *Bartonella henselae* and *Bartonella clarridgeiae* DNA in hepatic specimens from two dogs with hepatic disease. *J Am Vet Med Assoc*. 2003;222:47–51.
92. Tucker MD, Sellon RK, Tucker RL, Wills TB, Simonsen A, Maggi RG, et al. Bilateral mandibular pyogranulomatous lymphadenitis and pulmonary nodules in a dog with *Bartonella henselae* bacteremia. *Can Vet J La Rev Vet Can*. 2014;55:970–4.
93. Cross JR, Rossmeisl JH, Maggi RG, Breitschwerdt EB, Duncan RB. *Bartonella*-associated meningoradiculoneuritis and dermatitis or panniculitis in 3 dogs. *J Vet Intern Med*. 2008;22:674–8.
94. Rossi MA, Balakrishnan N, Linder KE, Messa JB, Breitschwerdt EB. Concurrent *Bartonella henselae* infection in a dog with panniculitis and owner with ulcerated nodular skin lesions. *Vet Dermatol*. 2015;26:60–3.
95. Santilli RA, Battaia S, Perego M, Tursi M, Grego E, Marzufero C, et al. *Bartonella*-associated inflammatory cardiomyopathy in a dog. *J Vet Cardiol*. 2016;19:74–81.
96. Breitschwerdt EB, Goldkamp C, Castleman WL, Cullen JM, Mascarelli PE, Thalhem L, et al. Hyperinsulinemic hypoglycemia syndrome in 2 dogs with bartonellosis. *J Vet Intern Med*. 2014;28:1331–5.
97. Bradley JM, Mascarelli PE, Trull CL, Maggi RG, Breitschwerdt EB. *Bartonella henselae* infections in an owner and two papillon dogs exposed to tropical rat mites (*Ornithonyssus bacoti*). *Vector Borne Zoonotic Dis*. 2014;14:703–9.
98. Tabar MD, Maggi RG, Altet L, Vilafranca M, Francino O, Roura X. Gammopathy in a Spanish dog infected with *Bartonella henselae*. *J Small Anim Pract*. 2011;52:209–12.
99. Morales SC, Breitschwerdt EB, Washabau RJ, Matisse I, Maggi RG, Duncan AW. Detection of *Bartonella henselae* DNA in two dogs with pyogranulomatous lymphadenitis. *J Am Vet Med Assoc*. 2007;230:681–5.
100. Berkowitz ST, Gannon KM, Carberry CA, Cortes Y. Resolution of spontaneous hemoabdomen secondary to peliosis hepatis following surgery and azithromycin treatment in a *Bartonella* species infected dog. *J Vet Emerg Crit Care*. 2016;26:851–7.
101. Nelson CA, Saha S, Mead PS. Cat-scratch disease in the United States, 2005–2013. *Emerg Infect Dis*. 2016;22:1741–6.
102. Tea A, Alexiou-Daniel S, Arvanitidou M, Diza E, Antoniadis A. Occurrence of *Bartonella henselae* and *Bartonella quintana* in a healthy Greek population. *Am J Trop Med Hyg*. 2003;68:554–6.
103. Blanco Ramos JR, Oteo Revuelta JA, Martínez de Artoia V, Ramalle Gomara E, García Pineda A, Ibarra Cucalon V, et al. Seroepidemiology of *Bartonella henselae* infection in a risk group. *Rev Clin Esp*. 1998;198:805–9.
104. Oteo JA, Maggi R, Portillo A, Bradley J, García-Álvarez L, San-Martín M, et al. Prevalence of *Bartonella* spp. by culture, PCR and serology, in veterinary personnel from Spain. *Parasit Vectors*. 2017;10:553.
105. Schülein R, Seubert A, Gille C, Lanz C, Hansmann Y, Piémont Y, et al. Invasion and persistent intracellular colonization of erythrocytes. A unique parasitic strategy of the emerging pathogen *Bartonella*. *J Exp Med*. 2001; 193:1077–86.
106. da Silva MN, Vieira-Damiani G, Ericson ME, Gupta K, de Almeida AR, Drummond MR, et al. Acute and late *Bartonella henselae* murine model infection. *Vector Borne Zoonotic Dis*. 2017;17:206–8.
107. Silva MN, Vieira-Damiani G, Ericson ME, Gupta K, Gilioli R, de Almeida AR, et al. *Bartonella henselae* transmission by blood transfusion in mice. *Transfusion*. 2016;56:1556–9.
108. Karem KL, Dubois KA, McGill SL, Regnery RL. Characterization of *Bartonella henselae*-specific immunity in BALB/c mice. *Immunology*. 1999;97:352–8.
109. Dehio C. *Bartonella* interactions with endothelial cells and erythrocytes. *Trends Microbiol*. 2001;9:279–85.
110. Hong J, Li Y, Hua X, Bai Y, Wang C, Zhu C, et al. Inhibition of phagocytosis and pyroptosis of macrophages promotes *Bartonella* invasion into the bloodstream through lymphatic circulation. *J Infect Dis*. 2016;4:526.
111. Balakrishnan N, Cherry NA, Linder KE, Pierce E, Sontakke N, Hegarty BC, et al. Experimental infection of dogs with *Bartonella henselae* and *Bartonella vinsonii* subsp. *berkhoffii*. *Vet Immunol Immunopathol*. 2013;156:153–8.
112. Kordick DL, Brown TT, Shin K, Breitschwerdt EB. Clinical and pathologic evaluation of chronic *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats. *J Clin Microbiol*. 1999;37:1536–47.
113. Mändle T, Einsele H, Schaller M, Neumann D, Vogel W, Autenrieth IB, et al. Infection of human CD34+ progenitor cells with *Bartonella henselae* results in intraerythrocytic presence of *B. henselae*. *Blood*. 2005;106:1215–22.
114. Kempf VA, Volkmann B, Schaller M, Sander CA, Alitalo K, Riess T, et al. Evidence of a leading role for VEGF in *Bartonella henselae*-induced endothelial cell proliferations. *Cell Microbiol*. 2001;3:623–32.
115. Maeno N, Oda H, Yoshiie K, Wahid MR, Fujimura T, Matayoshi S. Live *Bartonella henselae* enhances endothelial cell proliferation without direct contact. *Microb Pathog*. 1999;27:419–27.
116. Muñana KR, Vitek SM, Hegarty BC, Kordick DL, Breitschwerdt EB. Infection of fetal feline brain cells in culture with *Bartonella henselae*. *Infect Immun*. 2001;69:564–9.
117. Dehio C. Molecular and cellular basis of *Bartonella* pathogenesis. *Annu Rev Microbiol*. 2004;58:365–90.
118. Dehio C. *Bartonella*-host-cell interactions and vascular tumour formation. *Nat Rev Microbiol*. 2005;3:621–31.
119. Abbott RC, Chomel BB, Kasten RW, Floyd-Hawkins KA, Kikuchi Y, Koehler JE, et al. Experimental and natural infection with *Bartonella henselae* in domestic cats. *Comp Immunol Microbiol Infect Dis*. 1997;20:41–51.
120. Pulliainen AT, Dehio C. Persistence of *Bartonella* spp. stealth pathogens: from subclinical infections to vasoproliferative tumor formation. *FEMS Microbiol Rev*. 2012;36:563–99.
121. Beerlage C, Varanat M, Linder K, Maggi RG, Cooley J, Kempf VAJ, et al. *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella henselae* as potential causes of proliferative vascular diseases in animals. *Med Microbiol Immunol*. 2012;201:319–26.
122. Fuji RN, Patton KM, Steinbach TJ, Schulman FY, Bradley GA, Brown TT, et al. Feline systemic reactive angioendotheliomatosis: eight cases and literature review. *Vet Pathol*. 2005;42:608–17.
123. Maguñá C, Guerra H, Ventosilla P. Bartonellosis. *Clin Dermatol*. 2009;27:271–80.
124. Mazur-Melewska K, Mania A, Kemnitz P, Figliorowicz M, Służewski W. Cat-scratch disease: a wide spectrum of clinical pictures. *Postepy Dermatol Alergol*. 2015;32:216–20.
125. Stützer B, Hartmann K. Chronic Bartonellosis in Cats. *J Feline Med Surg*. 2012;14:612–21.
126. Buchmann AU, Kershaw O, Kempf VAJ, Gruber AD. Does a feline leukemia virus infection pave the way for *Bartonella henselae* infection in cats? *J Clin Microbiol*. 2010;48:3295–300.
127. Aylló T, Paulo P, Diniz VP, Breitschwerdt EB, Villaescusa A, Rodríguez-Franco F, et al. Vector-borne diseases in client-owned and stray cats from Madrid, Spain. *Vector Borne Zoonotic Dis*. 2012;12:143–50.
128. Pérez C, Maggi RG, Diniz PPV, Breitschwerdt EB. Molecular and serological diagnosis of *Bartonella* infection in 61 dogs from the United States. *J Vet Intern Med*. 2011;25:805–10.
129. Varanat M, Maggi RG, Linder KE, Breitschwerdt EB. Molecular prevalence of *Bartonella*, *Babesia*, and hemotropic *Mycoplasma* sp. in dogs with splenic disease. *J Vet Intern Med*. 2011;25:1284–91.
130. Ahsan N, Holman MJ, Riley TR, Abendroth CS, Langhoff EG, Yang HC. Peliosis hepatis due to *Bartonella henselae* in transplantation: a hemato-hepato-renal syndrome. *Transplantation*. 1998;65:1000–3.
131. Koehler JE, Sanchez MA, Garrido CS, Whitfield MJ, Chen FM, Berger TG, et al. Molecular epidemiology of *Bartonella* infections in patients with bacillary angiomatosis-peliosis. *N Engl J Med*. 1997;337:1876–83.
132. Pérez Vera C, Paulo P, Diniz VP, Pultorak EL, Maggi RG, Breitschwerdt EB. An unmatched case controlled study of clinicopathologic abnormalities in dogs with *Bartonella* infection. *Comp Immunol Microbiol Infect Dis*. 2013;36:481–7.
133. Breitschwerdt EB. Bartonellosis: One Health perspectives for an emerging infectious disease. *ILAR J*. 2014;55:46–58.
134. Drut A, Bublot I, Breitschwerdt EB, Chabanne L, Vayssier-Taussat M, Cadore J-L. Comparative microbiological features of *Bartonella henselae* infection in a dog with fever of unknown origin and granulomatous lymphadenitis. *Med Microbiol Immunol*. 2014;203:85–91.
135. Lösch B, Wank R. Life-threatening angioedema of the tongue: the detection of the RNA of *B. henselae* in the saliva of a male patient and his dog as well as of the DNA of three *Bartonella* species in the blood of the patient. *BMJ Case Rep*. 2014;bcrc2013203107.
136. Roura X, Santamarina G, Tabar M-D, Francino O, Altet L. Polymerase chain reaction detection of *Bartonella* spp. in dogs from Spain with blood culture-negative infectious endocarditis. *J Vet Cardiol*. 2018;20:267–75.
137. Clarridge JE, Raich TJ, Pirwani D, Simon B, Tsai L, Rodríguez-Barradas MC, et al. Strategy to detect and identify *Bartonella* species in routine clinical

- laboratory yields *Bartonella henselae* from human immunodeficiency virus-positive patient and unique *Bartonella* strain from his cat. *J Clin Microbiol*. 1995;33:2107–13.
138. Weeden AL, Cherry NA, Breitschwerdt EB, Cheves AG, Wamsley HL. *Bartonella henselae* in canine cavity effusions: prevalence, identification, and clinical associations. *Vet Clin Pathol*. 2017;46:326–30.
 139. Lee SA, Plett SK, Luetkemeyer AF, Borgo GM, Ohliger MA, Conrad MB, et al. *Bartonella quintana* aortitis in a man with AIDS, diagnosed by needle biopsy and 16S rRNA gene amplification. *J Clin Microbiol*. 2015;53:2773–6.
 140. Breitschwerdt EB. Feline bartonellosis and cat scratch disease. *Vet Immunol Immunopathol*. 2008;123:167–71.
 141. Burzo ML, Antonelli M, Pecorini G, Favuzzi AMR, Landolfi R, Flex A. Fever of unknown origin and splenomegaly: a case report of blood culture negative endocarditis. *Medicine*. 2017;96:e9197.
 142. Pultorak EL, Maggi RG, Mascarelli PE, Breitschwerdt EB. Serial testing from a 3-day collection period by use of the *Bartonella* Alphaproteobacteria growth medium platform may enhance the sensitivity of *Bartonella* species detection in bacteremic human patients. *J Clin Microbiol*. 2013;51:1673–7.
 143. Duncan AW, Maggi RG, Breitschwerdt EB. 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*. 2007;69:273–81.
 144. Davenport AC, Mascarelli PE, Maggi RG, Breitschwerdt EB. Phylogenetic diversity of bacteria isolated from sick dogs using the BAPGM enrichment culture platform. *J Vet Intern Med*. 2013;27:854–61.
 145. Dümmler JS, Scorpio DG. *Bartonella*. In: *Manual of clinical microbiology*. 11th ed. Washington: ASM Press; 2015. p. 873–86.
 146. Diddi K, Chaudhry R, Sharma N, Dhawan B. Strategy for identification & characterization of *Bartonella henselae* with conventional molecular methods. *Indian J Med Res*. 2013;137:380–7.
 147. Namekata DY, Kasten RW, Boman DA, Straub MH, Siperstein-Cook L, Couvelaire K, et al. Oral shedding of *Bartonella* in cats: correlation with bacteremia and seropositivity. *Vet Microbiol*. 2010;46:371–5.
 148. Pennisi MG, La Camera E, Giacobbe L, Orlandella BM, Lentini V, Zummo S, et al. Molecular detection of *Bartonella henselae* and *Bartonella clarridgeiae* in clinical samples of pet cats from southern Italy. *Res Vet Sci*. 2010;88:379–84.
 149. Duncan AW, Maggi RG, Breitschwerdt EB. *Bartonella* DNA in dog saliva. *Emerg Infect Dis*. 2007;13:1948–50.
 150. Glaus T, Hofmann-Lehmann R, Greene C, Glaus B, Wolfensberger C, Lutz AH. Seroprevalence of *Bartonella henselae* infection and correlation with disease status in cats in Switzerland. *J Clin Microbiol*. 1997;35:2883–5.
 151. Chomel BB, Abbott RC, Kasten RW, Floyd-Hawkins KA, Kass PH, Glaser CA, et al. *Bartonella henselae* prevalence in domestic cats in California: risk factors and association between bacteremia and antibody titers. *J Clin Microbiol*. 1995;33:2445–50.
 152. Reller LB, Weinstein MP, Procop GW, Wilson M. Infectious disease pathology. *Clin Infect Dis*. 2001;32:1589–601.
 153. Varanat M, Broadhurst J, Linder KE, Maggi RG, Breitschwerdt EB. Identification of *Bartonella henselae* in 2 cats with pyogranulomatous myocarditis and diaphragmatic myositis. *Vet Pathol*. 2012;49:608–11.
 154. Varanat M, Broadhurst J, Linder KE, Maggi RG, Breitschwerdt EB. Clinical and diagnostic aspects of feline cutaneous leishmaniasis in Venezuela. *Vet Pathol*. 2012;49:608–11.
 155. Pachirat O, Kosoy M, Bai Y, Prathani S, Puapairoj A, Zeidner N, et al. The first reported case of *Bartonella* endocarditis in Thailand. *Infect Dis Rep*. 2011;3:e9.
 156. Caponetti GC, Pantanowitz L, Marconi S, Havens JM, Lamps LW, Otis CN. Evaluation of immunohistochemistry in identifying *Bartonella henselae* in cat-scratch disease. *Am J Clin Pathol*. 2009;131:250–6.
 157. Buchmann AU, Kempf VAJ, Kershaw O, Gruber AD. Peliosis hepatis in cats is not associated with *Bartonella henselae* infections. *Vet Pathol*. 2010;47:163–6.
 158. Webster JD, Miller MA, DuSold D, Ramos-Vara J. Effects of prolonged formalin fixation on the immunohistochemical detection of infectious agents in formalin-fixed, paraffin-embedded tissues. *Vet Pathol*. 2010;47:529–35.
 159. Rolain JM, La SB, Liang Z, Davoust B, Raoult AD. Immunofluorescent detection of intraerythrocytic *Bartonella henselae* in naturally infected cats. *J Clin Microbiol*. 2001;39:2978–80.
 160. Randell MG, Balakrishnan N, Gunn-Christie R, Mackin A, Breitschwerdt EB. *Bartonella henselae* infection in a dog with recalcitrant ineffective erythropoiesis. *Vet Clin Pathol*. 2018;47:45–50.
 161. Balakrishnan N, Musulin S, Varanat M, Bradley JM, Breitschwerdt EB. Serological and molecular prevalence of selected canine vector borne pathogens in blood donor candidates, clinically healthy volunteers, and stray dogs in North Carolina. *Parasit Vectors*. 2014;7:116.
 162. Breitschwerdt EB, Maggi RG, Lantos PM, Woods CW, Hegarty BC, Bradley JM. *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella henselae* bacteremia in a father and daughter with neurological disease. *Parasit Vectors*. 2010;3:29.
 163. Stull JW, Stevenson KB. Zoonotic disease risks for immunocompromised and other high-risk clients and staff: promoting safe pet ownership and contact. *Vet Clin North Am Small Anim Pract*. 2015;45:377–92.
 164. Brunt J, Guptill L, Kordick DL, Kudrak S, Lappin MR. American Association of Feline Practitioners 2006 Panel report on diagnosis, treatment, and prevention of *Bartonella* spp. infections. *J Feline Med Surg*. 2006;8:213–26.
 165. Guptill L. Feline bartonellosis. *Vet Clin North Am Small Anim Pract*. 2010;40:1073–90.
 166. Greene CE, McDermott M, Jameson PH, Atkins CL, Marks AM. *Bartonella henselae* infection in cats: evaluation during primary infection, treatment, and rechallenge infection. *J Clin Microbiol*. 1996;34:1682–5.
 167. Breitschwerdt EB. Treatment of canine and feline bartonellosis. https://cvm.ncsu.edu/documents/vector-borne-treatment_bartonellosis/. Accessed May 2014.
 168. Varanat M, Travis A, Lee W, Maggi RG, Bissett SA, Linder KE, et al. Recurrent osteomyelitis in a cat due to infection with *Bartonella vinsonii* subsp. *berkhoffii* genotype II. *J Vet Intern Med*. 2009;23:1273–7.
 169. Breitschwerdt EB, Chomel BB. Canine bartonellosis. In: Greene CE, editor. *Infectious Diseases of the Dog and Cat*. 4th ed. St. Louis: Elsevier; 2011. p. 552–62.
 170. Lappin MR, Black JC. *Bartonella* spp infection as a possible cause of uveitis in a cat. *J Am Vet Med Assoc*. 1999;214:1205–7.
 171. Lappin MR, Davis WL, Hawley JR, Brewer M, Morris A, Stanneck D. A flea and tick collar containing 10% imidacloprid and 4.5% flumethrin prevents flea transmission of *Bartonella henselae* in cats. *Parasit Vectors*. 2013;6:26.
 172. Urushadze L, Bai Y, Osikowicz L, McKee C, Sidamonidze K, Putkaradze D, et al. Prevalence, diversity, and host associations of *Bartonella* strains in bats from Georgia (Caucasus). *Trop Dis*. 2017;12:e0005428.
 173. Stuckey MJ, Boulouis H-J, Cliquet F, Picard-Meyer E, Servat A, Aréchiga-Ceballos N, et al. Potentially zoonotic *Bartonella* in bats from France and Spain. *Emerg Infect Dis*. 2017;23:539–41.
 174. Rozental T, Ferreira MS, Guterres A, Mares-Guia MA, Teixeira BR, Gonçalves J, et al. Zoonotic pathogens in Atlantic Forest wild rodents in Brazil: *Bartonella* and *Coxiella* infections. *Acta Trop*. 2017;168.
 175. Telford SR, Wormseer GP. *Bartonella* spp. transmission by ticks not established. *Emerg Infect Dis*. 2010;16:379–84.
 176. Billeter SA, Levy MG, Chomel BB, Breitschwerdt EB. Vector transmission of *Bartonella* species with emphasis on the potential for tick transmission. *Med Vet Entomol*. 2008;22:1–15.
 177. Melter O, Arvand M, Votýpka J, Hulínská D. *Bartonella quintana* transmission from mite to family with high socioeconomic status. *Emerg Infect Dis*. 2012;18:163–5.
 178. Mylonakis ME, Schreeg M, Chatzis MK, Pearce J, Marr HS, Saridomichelakis MN, et al. Molecular detection of vector-borne pathogens in Greek cats. *Ticks Tick Borne Dis*. 2018;9:171–5.
 179. Lantos PM, Maggi RG, Ferguson B, Varkey J, Park LP, Breitschwerdt EB, et al. Detection of *Bartonella* species in the blood of veterinarians and veterinary technicians: a newly recognized occupational hazard? *Vector Borne Zoonotic Dis*. 2014;14:563–70.
 180. Cherry NA, Jones SL, Maggi RG, Davis JL, Breitschwerdt EB. *Bartonella* spp. infection in healthy and sick horses and foals from the southeastern United States. *J Vet Intern Med*. 2012;26:1408–12.
 181. Oksi J, Rantala S, Kilpinen S, Silvennoinen R, Vornanen M, Veikkolainen V, et al. Cat scratch disease caused by *Bartonella grahamii* in an immunocompromised patient. *J Clin Microbiol*. 2013;51:2781–4.
 182. Silaghi C, Knaus M, Rapti D, Kusi I, Shukullari E, Hamel D, et al. Survey of *Toxoplasma gondii* and *Neospora caninum*, haemotropic mycoplasmas and other arthropod-borne pathogens in cats from Albania. *Parasit Vectors*. 2014;7:62.
 183. Attipa C, Pappasoulitios K, Solano-Gallego L, Baneth G, Nachum-Biala Y, Sarvani E, et al. Prevalence study and risk factor analysis of selected bacterial, protozoal and viral, including vector-borne, pathogens in cats from Cyprus. *Parasit Vectors*. 2017;10:130.
 184. Diakou A, Di Cesare A, Accettura PM, Barros L, Iorio R, Paoletti B, et al. Intestinal parasites and vector-borne pathogens in stray and free-roaming

- cats living in continental and insular Greece. *PLoS Negl Trop Dis*. 2017;11:e0005335.
185. Melter O. Detection and characterization of feline *Bartonella henselae* in the Czech Republic. *Vet Microbiol*. 2003;93:261–73.
 186. Chomel BB, Boulouis H-J, Petersen H, Kasten RW, Yamamoto K, Chang C-C, et al. Prevalence of *Bartonella* infection in domestic cats in Denmark. *Vet Res*. 2002;33:205–13.
 187. Heller R, Artois M, Xemar V, De Briel D, Gehin H, Jaulhac B, et al. Prevalence of *Bartonella henselae* and *Bartonella clarridgeiae* in stray cats. *J Clin Microbiol*. 1997;35:1327–31.
 188. Gurfield AN, Boulouis H-J, Chomel BB, Kasten RW, Heller R, Bouillin C, et al. Epidemiology of *Bartonella* infection in domestic cats in France. *Vet Microbiol*. 2001;80:185–98.
 189. Rolain J-M, Locatelli C, Chabanne L, Davoust B, Raoult D. Prevalence of *Bartonella clarridgeiae* and *Bartonella henselae* in domestic cats from France and detection of the organisms in erythrocytes by immunofluorescence. *Clin Diagn Lab Immunol*. 2004;11:423–5.
 190. Sander A, Hler CB, Pelz K, Von Cramm E, Bredt W. Detection and identification of two *Bartonella henselae* variants in domestic cats in Germany. *J Clin Microbiol*. 1997;35:584–7.
 191. Haimerl M, Tenter AM, Simon K, Rommel M, Hilger J, Autenrieth IB. Seroprevalence of *Bartonella henselae* in cats in Germany. *J Med Microbiol*. 1999;48:849–56.
 192. Arvand M, Klose AJ, Schwartz-Porsche D, Hahn H, Wendt C. Genetic variability and prevalence of *Bartonella henselae* in cats in Berlin, Germany, and analysis of its genetic relatedness to a strain from Berlin that is pathogenic for humans. *J Clin Microbiol*. 2001;39:743–6.
 193. Mietze A, Morick D, Köhler H, Harrus S, Dehio C, Nolte I, et al. Combined MLST and AFLP typing of *Bartonella henselae* isolated from cats reveals new sequence types and suggests clonal evolution. *Vet Microbiol*. 2011;148:238–45.
 194. Morgenthal D, Hamel D, Arndt G, Silaghi C, Pfister K, Kempf VAJ, et al. Prevalence of *haemotropic Mycoplasma* spp., *Bartonella* spp. and *Anaplasma phagocytophilum* in cats in Berlin/Brandenburg (Northeast Germany). *Berl Munch Tierarztl Wochenschr*. 2012;125:418–27.
 195. Bergmann M, Englert T, Stuetzer B, Hawley JR, Lappin MR, Hartmann K. Prevalence of *Bartonella* species infections in cats in southern Germany. *Vet Rec*. 2017;180:325.
 196. Ebani VV, Cerri D, Andreani E. Cat scratch disease. Survey on the presence of *Bartonella henselae* among cats of Tuscany. *New Microbiol*. 2002;25:307–13.
 197. Cabassi CS, Farnetti E, Casali B, Taddei S, Donofrio G, Galvani G, et al. Isolation of *Bartonella henselae* from domestic cats in an Italian urban area. *New Microbiol*. 2002;25:253–7.
 198. Fabbri M, Vicari N, Tranquillo M, Pozzi C, Prati P, De Meneghi D, et al. Prevalence of *Bartonella henselae* in stray and domestic cats in different Italian areas: evaluation of the potential risk of transmission of *Bartonella* to humans. *Parassitologia*. 2004;46:127–9.
 199. Pinna Parpaglia ML, Masu G, Masala G, Porcu R, Zobia R, Pintori G, et al. Seroprevalence of *Bartonella henselae* in dogs and cats in Sassari. *Vet Res Commun*. 2007;31:317–20.
 200. Mansueto P, Pepe I, Cillari E, Arcoleo F, Micalizzi A, Bonura F, et al. Prevalence of antibodies anti- *Bartonella henselae* in western sicily: children, blood donors, and cats. *J Immunoass Immunochem*. 2012;33:18–25.
 201. Ebani VV, Bertelloni F, Fratini F. Occurrence of *Bartonella henselae* types I and II in central Italian domestic cats. *Res Vet Sci*. 2012;93:63–6.
 202. Brunetti E, Fabbri M, Ferraioli G, Prati P, Filice C, Sasseria D, et al. Cat-scratch disease in northern Italy: atypical clinical manifestations in humans and prevalence of *Bartonella* infection in cats. *Eur J Clin Microbiol Infect Dis*. 2013;32:531–4.
 203. Spada E, Canzi I, Baggiani L, Perego R, Vitale F, Miglizzo A, et al. Prevalence of *Leishmania infantum* and co-infections in stray cats in northern Italy. *Comp Immunol Microbiol Infect Dis*. 2016;45:53–8.
 204. Persichetti M-F, Solano-Gallego L, Serrano L, Altet L, Reale S, Masucci M, et al. Detection of vector-borne pathogens in cats and their ectoparasites in southern Italy. *Parasit Vectors*. 2016;9:247.
 205. Otranto D, Napoli E, Latrofa MS, Annoscia G, Tarallo VD, Greco G, et al. Feline and canine leishmaniosis and other vector-borne diseases in the Aeolian Islands: pathogen and vector circulation in a confined environment. *Vet Parasitol*. 2017;236:144–51.
 206. Juvet F, Lappin MR, Brennan S, Mooney CT. Prevalence of selected infectious agents in cats in Ireland. *J Feline Med Surg*. 2010;12:476–82.
 207. Bergmans AMC, De Jong CMA, Van Amerongen G, Schot CS, Schouls ALM. Prevalence of *Bartonella* species in domestic cats in the Netherlands. *J Clin Microbiol*. 1997;35:2256–61.
 208. Podsiadly E, Chmielewski T, Marczak R, Sochon E, Tylewska-Wierzbanowska S. *Bartonella henselae* in the human environment in Poland. *Scand J Infect Dis*. 2007;39:956–62.
 209. Alves AS, Milhano N, Santos-Silva M, Santos AS, Vilhena M, de Sousa R. Evidence of *Bartonella* spp., *Rickettsia* spp. and *Anaplasma phagocytophilum* in domestic, shelter and stray cat blood and fleas, Portugal. *Clin Microbiol Infect*. 2009;15(Suppl. 2):1–3.
 210. Childs JE, Olson JG, Wolf A, Cohen N, Fakile Y, Rooney JA, et al. Prevalence of antibodies to *Rochalimaea* species (cat-scratch disease agent) in cats. *Vet Rec*. 1995;136:519–20.
 211. Maia C, Ramos C, Coimbra M, Bastos F, Martins A, Pinto P, et al. Bacterial and protozoal agents of feline vector-borne diseases in domestic and stray cats from southern Portugal. *Parasit Vectors*. 2014;7:115.
 212. Pons I, Sanfeliu I, Quesada M, Anton E, Sampere M, Font B, et al. Prevalence of *Bartonella henselae* in cats in Catalonia, Spain. *Am J Trop Med Hyg*. 2005;72:453–7.
 213. Tabar MD, Altet L, Francino O, Sánchez A, Ferrer L, Roura X. Vector-borne infections in cats: molecular study in Barcelona area (Spain). *Vet Parasitol*. 2008;151:332–6.
 214. Gil H, Escudero R, Pons I, Rodríguez-Vargas M, García-Esteban C, Rodríguez-Moreno I, et al. Distribution of *Bartonella henselae* variants in patients, reservoir hosts and vectors in Spain. *PLoS One*. 2013;8:e68248.
 215. Gracia MJ, Marcén JM, Pinal R, Calvete C, Rodes D. Prevalence of *Rickettsia* and *Bartonella* species in Spanish cats and their fleas. *J Vector Ecol*. 2015;40:233–9.
 216. Alamá Valtierra M, Simón Valencia C, Fuertes Negro H, Unzueta Galarza A, Flores Somarriva B, Halaihel KN. Molecular epidemiology of *Bartonella henselae* in stray and sheltered cats of Zaragoza, Spain. *Rev Esp Salud Publica*. 2016;90:E5.
 217. Ravicini S, Pastor J, Hawley J, Brewer M, Castro-López J, Beall M, et al. Prevalence of selected infectious disease agents in stray cats in Catalonia, Spain. *JFMS Open Rep*. 2016;2:2055116916634109.
 218. Bennett AD, Gunn-Moore DA, Brewer M, Lappin MR. Prevalence of *Bartonella* species, haemoplasmas and *Toxoplasma gondii* in cats in Scotland. *J Fel Med Surg*. 2011;13:553–7.
 219. Hjelm E, McGill S, Blomqvist G. Prevalence of antibodies to *Bartonella henselae*, *B. elizabethae* and *B. quintana* in Swedish domestic cats. *Scand J Infect Dis*. 2002;34:192–6.
 220. Olsson Engvall E, Fasth C, Brandstrom B, Fermer C, Blomqvist G, Englund L. Prevalence of *Bartonella henselae* in young, healthy cats in Sweden. *Vet Rec*. 2003;152:366–9.
 221. Birtles RJ, Laycock G, Day MJ, Kenny MJ, Shaw SE. Prevalence of *Bartonella* species causing bacteraemia in domesticated and companion animals in the United Kingdom. *Vet Rec*. 2002;151:225–9.
 222. Hamel D, Silaghi C, Knaus M, Visser M, Kusi I, Rapti D, et al. Detection of *Babesia canis* subspecies and other arthropod-borne diseases in dogs from Tirana, Albania. *Wien Klin*. 2009;121:42.
 223. Pérez Vera C, Kapiainen S, Junnikkala S, Aaltonen K, Spillmann T, Vapalahti O. Survey of selected tick-borne diseases in dogs in Finland. *Parasit Vectors*. 2014;7:285.
 224. Di Francesco A, Sanguinetti V, Gallina L, Gavioli R, Piva S, Baldelli R. Prevalence of antibodies to *Bartonella henselae* in dogs in Italy. *Vet Rec*. 2007;161:489–90.
 225. Rymaszewska A, Adamska M. Molecular evidence of vector-borne pathogens coinfecting dogs from Poland. *Acta Vet Hung*. 2011;59:215–23.
 226. Tabar M-D, Francino O, Altet L, Sanchez A, Ferrer L, Roura X. PCR survey of vectorborne pathogens in dogs living in and around Barcelona, an area endemic for leishmaniosis. *Vet Rec*. 2009;164:112–6.
 227. Baxarias M, Álvarez-Fernández A, Martínez-Orellana P, Montserrat-Sangrà S, Ordeix L, Rojas A, et al. Does co-infection with vector-borne pathogens play a role in clinical canine leishmaniosis? *Parasit Vectors*. 2018;11:135.
 228. Tabar M-D, Movilla R, Serrano L, Altet L, Francino O, Roura X. PCR evaluation of selected vector-borne pathogens in dogs with pericardial effusion. *J Small Anim Pract*. 2018;59:248–52.
 229. Tiao N, Darrington C, Molla B, Saville WJA, Tilahun GKOC. An investigation into the seroprevalence of *Toxoplasma gondii*, *Bartonella* spp., feline immunodeficiency virus (FIV), and feline leukaemia virus (FeLV) in cats in Addis Ababa, Ethiopia. *Epidemiol Infect*. 2013;141:1029–33.

230. Bessas A, Leulmi H, Bitam I, Zaidi S, Ait-Oudhia K, Raoult D, et al. Molecular evidence of vector-borne pathogens in dogs and cats and their ectoparasites in Algiers, Algeria. *Comp Immunol Microbiol Infect Dis*. 2016;45:23–8.
231. Azzag N, Haddad N, Durand B, Petit E, Ammouche A, Chomel B, et al. Population structure of *Bartonella henselae* in Algerian urban stray cats. *PLoS One*. 2012;7:43621.
232. Al-Kappany YM, Lappin MR, Kwok OCH, Abu-Elwafa SA, Hilali M, Dubey JP. Seroprevalence of *Toxoplasma gondii* and concurrent *Bartonella* spp., feline immunodeficiency virus, feline leukemia virus, and *Dirofilaria immitis* infections in Egyptian cats. *J Parasitol*. 2011;97:256–8.
233. Trataris AN, Rossouw J, Arntzen L, Karstaedt A, Freaun J. *Bartonella* spp. in human and animal populations in Gauteng, South Africa, from 2007 to 2009. *Onderstepoort J Vet Res*. 2012;79:452.
234. Lobetti R, Lappin MR. Prevalence of *Toxoplasma gondii*, *Bartonella* species and haemoplasma infection in cats in South Africa. *J Feline Med Surg*. 2012;14:857–62.
235. Kelly PJ, Rooney JJ, Marston EL, Jones DC, Regnery RL. *Bartonella henselae* isolated from cats in Zimbabwe. *Lancet*. 1998;351:1706.
236. Kelly PJ, Matthewman LA, Hayter D, Downey S, Wray K, Bryson NR, et al. *Bartonella (Rochalimaea) henselae* in southern Africa: evidence for infections in domestic cats and implications for veterinarians. *J S Afr Vet Assoc*. 1996;67:182–7.
237. Yuan C, Zhu C, Wu Y, Pan X, Hua X. Bacteriological and molecular identification of *Bartonella* species in cats from different regions of China. *PLoS Negl Trop Dis*. 2011;5:e1301.
238. Maruyama S, Nakamura Y, Kabeya H, Tanaka S, Sakai TKY. Prevalence of *Bartonella henselae*, *Bartonella clarridgeiae* and the 16S rRNA gene types of *Bartonella henselae* among pet cats in Japan. *J Vet Med Sci*. 2000;62:273–9.
239. Sato S, Kabeya H, Negishi A, Tsujimoto H, Nishigaki KEY. Molecular survey of *Bartonella henselae* and *Bartonella clarridgeiae* in pet cats across Japan by species-specific nested-PCR. *Epidemiol Infect*. 2017;145:2694–700.
240. Maruyama S, Kabeya H, Nakao R, Tanaka S, Sakai T, Xuan X, et al. Seroprevalence of *Bartonella henselae*, *Toxoplasma gondii*, FIV and FeLV infections in domestic cats in Japan. *Microbiol Immunol*. 2003;47:147–53.
241. Kim Y, Seo K, Lee J, Choi E, Lee H, Hwang C, et al. Prevalence of *Bartonella henselae* and *Bartonella clarridgeiae* in cats and dogs in Korea. *J Vet Sci*. 2009;10:85–7.
242. Switzer AD, McMillan-Cole AC, Kasten RW, Stuckey MJ, Kass PH, Chomel BB. *Bartonella* and *Toxoplasma* infections in stray cats from Iraq. *Am J Trop Med Hyg*. 2013;89:1219–24.
243. Baneth G, Kordick DL, Hegarty BC, Breitschwerdt EB. Comparative seroreactivity to *Bartonella henselae* and *Bartonella quintana* among cats from Israel and North Carolina. *Vet Microbiol*. 1996;50:95–103.
244. Guzel M, Celebi B, Yalcin E, Koenhemi L, Mamak N, Pasa S, et al. A serological investigation of *Bartonella henselae* infection in cats in Turkey. *J Vet Med Sci*. 2011;73:1513–6.
245. Celebi B, Kilic S, Aydin N, Tarhan G, Carhan A, Babur C. Investigation of *Bartonella henselae* in cats in Ankara, Turkey. *Zoonoses Public Health*. 2009;56:169–75.
246. Gutiérrez R, Morick D, Gross I, Winkler R, Abdeen Z, Harrus S. *Bartonella* in domestic and stray cats from Israel: comparison of bacterial cultures and high-resolution melt real-time PCR as diagnostic methods. *Vector Borne Zoonotic Dis*. 2013;13:857–64.
247. Chomel BB, Carlos ET, Kasten RW, Yamamoto K, Chang C-C, Carlos RS, et al. *Bartonella henselae* and *Bartonella clarridgeiae* infection in domestic cats from the Philippines. *Am J Trop Med Hyg*. 1999;60:593–7.
248. Maruyama S, Sakai T, Morita Y, Tanaka S, Kabeya H, Boonmar S, et al. Prevalence of *Bartonella* species and 16S rRNA gene types of *Bartonella henselae* from domestic cats in Thailand. *Am J Trop Med Hyg*. 2001;65:783–7.
249. Barrs V, Beatty J, Wilson B, Evans N, Gowan R, Baral R, et al. Prevalence of *Bartonella* species, *Rickettsia felis*, haemoplasmas and the *Ehrlichia* group in the blood of cats and fleas in eastern Australia. *Aust Vet J*. 2010;88:160–5.
250. Branley J, Wolfson C, Waters P, Gottlieb T, Bradbury R. Prevalence of *Bartonella henselae* bacteremia, the causative agent of cat scratch disease, in an Australian cat population. *Pathology*. 1996;28:262–5.
251. Dybing NA, Jacobson C, Irwin P, Algar D, Adams PJ. *Bartonella* species identified in rodent and feline hosts from island and mainland western Australia. *Vector Borne Zoonotic Dis*. 2016;16:238–44.
252. Jameson P, Greene C, Regnery R, Dryden M, Marks A, Brown J, et al. Prevalence of *Bartonella henselae* antibodies in pet cats throughout regions of North America. *J Infect Dis*. 1995;172:1145–9.
253. Dubey JP, Bhatia CR, Lappin MR, Ferreira LR, Thorn A, Kwok OCH. Seroprevalence of *Toxoplasma gondii* and *Bartonella* spp. antibodies in cats from Pennsylvania. *J Parasitol*. 2009;95:578–80.
254. Jinks MR, English RV, Gilger BC. Causes of endogenous uveitis in cats presented to referral clinics in North Carolina. *Vet Ophthalmol*. 2016;19:30–7.
255. Tomas A, Pultorak EL, Gruen ME, Breitschwerdt EB, Lascelles BDX. Relationship between degenerative joint disease, pain, and *Bartonella* spp. seroreactivity in domesticated cats. *J Vet Intern Med*. 2015;29:21–7.
256. Lappin MR, Hawley J. Presence of *Bartonella* species and *Rickettsia* species DNA in the blood, oral cavity, skin and claw beds of cats in the United States. *Vet Dermatol*. 2009;20:509–14.
257. Luria BJ, Levy JK, Lappin MR, Breitschwerdt EB, Legendre AM, Hernandez JA, et al. Prevalence of infectious diseases in feral cats in northern Florida. *J Feline Med Surg*. 2004;6:287–96.
258. Fleischman DA, Chomel BB, Kasten RW, Stuckey MJ, Scarlet J, Liu H, et al. *Bartonella* infection among cats adopted from a San Francisco shelter, revisited. *Appl Environ Microbiol*. 2015;81:6446–50.
259. Eberhardt JM, Neal K, Shackelford T, Lappin MR. Prevalence of selected infectious disease agents in cats from Arizona. *J Feline Med Surg*. 2006;8:164–8.
260. Cicuttin GL, Brambati DF, De Gennaro MF, Carmona F, Isturiz ML, Pujol LE, et al. *Bartonella* spp. in cats from Buenos Aires, Argentina. *Vet Microbiol*. 2014;168:225–8.
261. Drummond MR, Lania BG, de Paiva Diniz PP, Gilioli R, Demolin DMR, Scorpio DG, et al. Improvement of *Bartonella henselae* DNA detection in cat blood samples by combining molecular and culture methods. *J Clin Microbiol*. 2018;56:e01732–17.
262. Vissotto De Paiva Diniz PP, Maggi RG, Schwartz DS, Cadenas MB, Bradley JM, Hegarty B, et al. Canine bartonellosis: serological and molecular prevalence in Brazil and evidence of co-infection with *Bartonella henselae* and *Bartonella vinsonii* subsp. *berkhoffii*. *Vet. Res*. 2007;38:697–710.
263. Braga MD, Diniz PP, André MR, de Bortoli CP, Machado RZ. Molecular characterisation of *Bartonella* species in cats from São Luís, state of Maranhão, north-eastern Brazil. *Mem Inst Oswaldo Cruz*. 2012;107:772–7.
264. Fontalvo MC, Favacho ARM, Araujo AC, Santos NMD, Oliveira GMB, Aguiar DM, et al. *Bartonella* species pathogenic for humans infect pets, free-ranging wild mammals and their ectoparasites in the Caatinga biome, northeastern Brazil: a serological and molecular study. *Brazilian J Infect Dis*. 2017;21:290–6.
265. Müller A, Walker R, Bittencourt P, Machado RZ, Benevenuto JL, DO Amaral RB, et al. Prevalence, hematological findings and genetic diversity of *Bartonella* spp. in domestic cats from Valdivia, southern Chile. *Parasitology*. 2017;144:773–82.
266. Ferrés M, Abarca K, Godoy P, García P, Palavecino E, Méndez G, et al. Presence of *Bartonella henselae* in cats: natural reservoir quantification and human exposition risk of this zoonoses in Chile. *Rev Med Chil*. 2005;133:1465–71.
267. Levy JK, Crawford PC, Lappin MR, Dubovi EJ, Levy MG, Alleman R, et al. Infectious diseases of dogs and cats on Isabela Island, Galapagos. *J Vet Intern Med*. 2008;22:60–5.
268. Bai Y, Rizzo MF, Alvarez D, Moran D, Peruski LF, Kosoy M. Coexistence of *Bartonella henselae* and *B. clarridgeiae* in populations of cats and their fleas in Guatemala. *J Vector Ecol*. 2015;40:327–32.
269. Proboste T, Kalema-Zikusoka G, Altet L, Solano-Gallego L, Fernández de Mera IG, Chirife AD, et al. Infection and exposure to vector-borne pathogens in rural dogs and their ticks, Uganda. *Parasit Vectors*. 2015;8:306.
270. Azzag N, Petit E, Gandoin C, Bouillin C, Ghalmi F, Haddad N, et al. Prevalence of select vector-borne pathogens in stray and client-owned dogs from Algiers. *Comp Immunol Microbiol Infect Dis*. 2015;38:1–7.
271. Kernif T, Aissi M, Doumandji S-E, Chomel BB, Raoult D, Bitam I. Molecular evidence of *Bartonella* infection in domestic dogs from Algeria, North Africa, by polymerase chain reaction (PCR). *Am J Trop Med Hyg*. 2010;83:298–300.
272. Henn JB, Vanhorn BA, Kasten RW, Kachani M, Chomel BB. Antibodies to *Bartonella vinsonii* subsp. *berkhoffii* in Moroccan dogs. *Am J Trop Med Hyg*. 2006;74:222–3.
273. Williams BM, Berentsen A, Shock BC, Teixeira M, Dunbar MR, Becker MS, et al. Prevalence and diversity of *Babesia*, *Hepatozoon*, *Ehrlichia*, and *Bartonella* in wild and domestic carnivores from Zambia, Africa. *Parasitol Res*. 2014;113:911–8.
274. Kelly PJ, Eoghain GN, Raoult D. Antibodies reactive with *Bartonella henselae* and *Ehrlichia canis* in dogs from the communal lands of Zimbabwe. *J S Afr Vet Assoc*. 2004;75:116–20.

275. Clarke LL, Ballweber LR, Allen K, Little SE, Lappin MR. Prevalence of select vector-borne disease agents in owned dogs of Ghana. *J S Afr Vet Assoc.* 2014;85:996.
276. Chomel BB, McMillan-Cole AC, Kasten RW, Stuckey MJ, Sato S, Maruyama S, et al. *Candidatus Bartonella merieuxii*, a potential new zoonotic *Bartonella* species in canids from Iraq. *PLoS Negl Trop Dis.* 2012;6:1843.
277. Baneth G, Breitschwerdt EB, Hegarty BC, Pappalardo B, Ryan J. A survey of tick-borne bacteria and protozoa in naturally exposed dogs from Israel. *Vet Parasitol.* 1998;74:133–42.
278. Celebi B, Carhan A, Kilic S, Babur C. Detection and genetic diversity of *Bartonella vinsonii* subsp. *berkhoffii* strains isolated from dogs in Ankara, Turkey. *J Vet Med Sci.* 2010;72:969–73.
279. Suh G-H, Ahn K-S, Ahn H-H, Kim H-J, Leutenegger C, Shin S. Serological and molecular prevalence of canine vector-borne diseases (CVBDs) in Korea. *Parasit Vectors.* 2017;10:146.
280. Han Ji, Chang DW, Na KJ. A multiplex quantitative real-time polymerase chain reaction panel for detecting neurologic pathogens in dogs with meningoencephalitis. *J Vet Sci.* 2015;16:341–7.
281. Brenner EC, Chomel BB, Singhasivanon OU, Namekata DY, Kasten RW, Kass PH, et al. *Bartonella* infection in urban and rural dogs from the tropics: Brazil, Colombia, Sri Lanka and Vietnam. *Epidemiol Infect.* 2013;141:54–61.
282. Suksawat J, Xuejie Y, Hancock SI, Hegarty BC, Nilkumhang P, Breitschwerdt EB. Serologic and molecular evidence of coinfection with multiple vector-borne pathogens in dogs from Thailand. *J Vet Intern Med.* 2001;15:453–62.
283. Billeter SA, Sangmaneedet S, Kosakewich RC, Kosoy MY. *Bartonella* species in dogs and their ectoparasites from Khon Kaen Province, Thailand. *Southeast Asian J Trop Med Public Health.* 2012;43:1186–92.
284. Inoue K, Maruyama S, Kabeya H, Kawanami K, Yanai K, Jitchum S, et al. Prevalence of *Bartonella* infection in cats and dogs in a metropolitan area, Thailand. *Epidemiol Infect.* 2009;137:1568.
285. Shapiro AJ, Brown G, Norris JM, Bosward KL, Marriot DJ, Balakrishnan N, et al. Vector-borne and zoonotic diseases of dogs in north-west New South Wales and the Northern Territory, Australia. *BMC Vet Res.* 2017;13:238.
286. Honadel TE, Chomel BB, Yamamoto K, Chang C, Farver TB. Seroepidemiology of *Bartonella vinsonii* subsp. *berkhoffii* exposure among healthy dogs. *J Am Vet Med Assoc.* 2001;219:480–4.
287. Diniz PPVP, Beall MJ, Omark K, Chandrashekar R, Daniluk DA, Cyr KE, et al. High prevalence of tick-borne pathogens in dogs from an Indian reservation in northeastern Arizona. *Vector Borne Zoonotic Dis.* 2010;10:117–23.
288. Henn JB, Gabriel MW, Kasten RW, Brown RN, Theis JH, Foley JE, et al. Gray foxes (*Urocyon cinereoargenteus*) as a potential reservoir of a *Bartonella clarridgeiae*-like bacterium and domestic dogs as part of a sentinel system for surveillance of zoonotic arthropod-borne pathogens in northern California. *J Clin Microbiol.* 2007;45:2411–8.
289. de Paiva Diniz PPV, Schwartz DS, de Moraes HSA, Breitschwerdt EB. Surveillance for zoonotic vector-borne infections using sick dogs from southeastern Brazil. *Vector Borne Zoonotic Dis.* 2007;7:689–97.
290. Müller A, Soto F, Sepúlveda M, Bittencourt P, Benevenuto JL, Ikeda P, et al. *Bartonella vinsonii* subsp. *berkhoffii* and *B. henselae* in dogs. *Epidemiol Infect.* 2018;146:1202–4.
291. Diniz PPVP, Morton BA, Tngrian M, Kachani M, Barrón EA, Gavidia CM, et al. Infection of domestic dogs in Peru by zoonotic *Bartonella* species: a cross-sectional prevalence study of 219 asymptomatic dogs. *PLoS Negl Trop Dis.* 2013;7:e2393.
292. Guptill L, Slater L, Wu CC, Lin TL, Glickman LT, Welch DF, et al. Experimental infection of young specific pathogen-free cats with *Bartonella henselae*. *J Infect Dis.* 1997;176:206–16.
293. Chomel BB, Wey AC, Kasten RW, Stacy BA, Labelle P. Fatal case of endocarditis associated with *Bartonella henselae* type I infection in a domestic cat. *J Clin Microbiol.* 2003;41:5337–9.
294. Perez C, Hummel JB, Keene BW, Maggi RG, Diniz PPVP, Breitschwerdt EB. Successful treatment of *Bartonella henselae* endocarditis in a cat. *J Feline Med Surg.* 2010;12:483–6.
295. Ketring KL, Zuckerman EE, Hardy WDJ. *Bartonella*: a new etiological agent of feline ocular disease. *J Am Anim.* 2004;40:6.
296. Whittemore JC, Hawley JR, Radecki SV, Steinberg JD, Lappin MR. *Bartonella* species antibodies and hyperglobulinemia in privately owned cats. *J Vet Intern Med.* 2012;26:639–44.
297. Breitschwerdt EB, Hegarty BC, Hawkins E, Dyer P, Maggi R. *Bartonella* species as a potential cause of epistaxis in dogs. *J Clin Microbiol.* 2005;43:2529–33.
298. Goodman RA, Breitschwerdt EB. Clinicopathologic findings in dogs seroreactive to *Bartonella henselae* antigens. *Am J Vet Res.* 2005;66:2060–4.
299. Vuković-Arar Z, Janjetović Z, Sekelj S, Sapina L, Pajić-Penavić I. Neuroretinitis caused by *Bartonella quintana*. *Med Glas.* 2012;9:435–7.
300. Kalogeropoulos C, Koumpoulis I, Mentis A, Pappa C, Zafeiropoulos P, Aspiotis M. *Bartonella* and intraocular inflammation: a series of cases and review of literature. *Clin Ophthalmol.* 2011;5:817–29.
301. Caniza MA, Granger DL, Wilson KH, Washington MK, Kordick DL, Frush DP, et al. *Bartonella henselae*: etiology of pulmonary nodules in a patient with depressed cell-mediated immunity. *Clin Infect Dis.* 1995;20:1505–11.
302. Chomel BB, Ermel RW, Kasten RW, Henn JB, Fleischman DA, Chang CC. Experimental infection of dogs with various *Bartonella* species or subspecies isolated from their natural reservoir. *Vet Microbiol.* 2014;168:169–76.
303. Chomel BB, Henn JB, Kasten RW, Nieto NC, Foley J, Papageorgiou S, et al. Dogs are more permissive than cats or guinea pigs to experimental infection with a human isolate of *Bartonella rochalimae*. *Vet Res.* 2009;40:27.
304. Chomel BB, Kasten RW, Stuckey MJ, Breitschwerdt EB, Maggi RG, Henn JB, et al. Experimental infection of cats with *Afpia felis* and various *Bartonella* species or subspecies. *Vet Microbiol.* 2014;172:505–10.
305. Donovan T, Balakrishnan N, Carvalho Barbosa I, McCoy T, Breitschwerdt E, Fox P. *Bartonella* spp. as a possible cause or cofactor of feline endomyocarditis-left ventricular endocardial fibrosis complex. *J Comp Pathol.* 2018;162:29–42.

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