Vet. Res. 36 (2005) 383–410
© INRA, EDP Sciences, 2005
DOI: 10.1051/vetres:2005009

Review article

Factors associated with the rapid emergence of zoonotic *Bartonella* infections

Henri-Jean BOULOUIS[a], Chao-chin CHANG[b], Jennifer B. HENN[c], Rickie W. KASTEN[c], Bruno B. CHOMEL[c]*

[a] Microbiologie-Immunologie, École Nationale Vétérinaire d'Alfort, 7 avenue du Général de Gaulle, 94704 Maisons-Alfort, France
[b] Institute of Veterinary Public Health, School of Veterinary Medicine, National Chung Hsing University, 250 Kuo-Kuang Road, Taichung 402, Taiwan, Republic of China
[c] WHO/PAHO Collaborating Center on New and Emerging Zoonoses, Department of Population Health and Reproduction, School of Veterinary Medicine, University of California, Davis, CA 95616, USA

(Received 13 October 2004; accepted 17 December 2004)

Abstract – Within the last 15 years, several bacteria of the genus *Bartonella* were recognized as zoonotic agents in humans and isolated from various mammalian reservoirs. Based on either isolation of the bacterium or PCR testing, eight *Bartonella* species or subspecies have been recognized as zoonotic agents, including *B. henselae*, *B. elizabethae*, *B. grahamii*, *B. vinsonii* subsp. *arupensis*, *B. vinsonii* subsp. *berkhoffii*, *B. grahamii*, *B. washoensis* and more recently *B. koehlerae*. The present manuscript reviews the factors associated with the emergence of these zoonotic pathogens, including better diagnostic tools and methods to identify these fastidious bacteria, host immunosuppression (caused by infectious agents, cancer, aging or induced by immunosuppressive drugs), the interaction of co-infection by several infectious agents that may enhanced the pathogenecity of these bacteria, increased outdoor activity leading to exposure to wildlife reservoirs or vectors, poverty and low income associated with infestation by various ectoparasites, such as body lice and finally the dispersal of *Bartonellae* around the world. Furthermore, a description of the main epidemiological and clinical features of zoonotic *Bartonellae* is given. Finally, the main means for diagnosis, treatment and prevention of these diseases are presented.

***Bartonella* spp. / emerging zoonoses / cat / dog / rodents**

Table of contents

* Corresponding author: bbchomel@ucdavis.edu

1. INTRODUCTION

Within the last 15 years, several new bacteria of the genus *Bartonella* were recognized as emerging zoonotic agents in humans and isolated from several mammalian reservoirs. If cat scratch disease (CSD) was a well known zoonosis in search of an etiological agent, the recognition of *Bartonella henselae* as its main etiological agent lead to the recognition of several different clinical syndromes caused by this bacterium in humans and in carnivores. In fact, the recognition of *B. henselae* as the agent of CSD was indirectly the result of the identification of a new bacterium causing a new zoonosis called bacillary angiomatosis in immunocompromised individuals, mainly AIDS patients [191, 193]. Furthermore, several rodent-borne *Bartonella* emerged as zoonotic agents in both humans and dogs [52].

Bartonella spp. are fastidious hemotropic Gram-negative organisms that have been recently identified in a wide range of domestic and wild mammals [25]. Based on either isolation of the bacterium or PCR testing, eight *Bartonella* species or subspecies have been recognized as zoonotic agents, including *B. henselae*, *B. elizabethae*, *B. grahamii*, *B. vinsonii* subsp. *arupensis*, *B. vinsonii* subsp. *berkhoffii*, *B. grahamii*, *B. washoensis* [52] and more recently *B. koehlerae* [8]. At present, *B. clarridgeiae* is only considered as a possible zoonotic agent based on serological evidence in infected humans [136, 159, 205]. *Bartonella* species are usually vector-borne and the vector varies with the *Bartonella* species involved (i.e. sandflies for *B. bacilliformis* or human body lice for *B. quintana*) [52]. Although cat scratch disease (CSD) was described in France more than 50 years ago by Debré et al. [63], it is only in the last decade that *Bartonella henselae* was recognized as its etiological agent [69, 191, 235]. Cats represent the main reservoir of this bacterium, which is transmitted from cat to cat via the cat flea (*Ctenocephalides felis*) [46, 128]. Since the isolation of *B. henselae* from domestic cats in 1992, several new *Bartonella* species or subspecies have been identified in domestic and wild carnivores [52]. Similarly, new species of *Bartonella* have been identified in wild rodents and domestic and wild ruminants, with an increasing number of reports of human and canine infections caused by some of these rodent-borne *Bartonella* species.

2. FACTORS OF EMERGENCE OF ZOONOTIC *BARTONELLAE*

Several factors have lead to the emergence of *Bartonellae* as agents of zoonotic infections, which include:

2.1. Advanced diagnostic tools and methods

Among these, the development of molecular biology tools, especially the use of the polymerase chain reaction (PCR), improved the identification of these fastidious bacteria. Most human cases are now diagnosed based on PCR testing of tissue biopsies or serology using specific antigens, as isolation from the blood is quite uncommon from most cases [115]. Similarly, isolation of *Bartonella* from dogs is quite rare and most cases have been identified based on PCR of tissue samples, such as cardiac valves and liver biopsies [52].

2.2. Weakening of the host immune system associated with the emergence of immunocompromising diseases, organ transplant and cancer therapy

The first isolation of *B. henselae* was performed from the bloodstream of an AIDS patient presenting with very low CD4 counts [191], as severely immunocompromised people can be bacteremic for several weeks when suffering from bacillary angiomatosis [127]. Cases of bacillary angiomatosis were then associated with this bacterium when such patients had been exposed to a domestic cat (usually being scratched) [129]. Recently, a high rate of *Bartonella henselae* infection in HIV-positive outpatients in Johannesburg, South Africa was reported with almost 10% of the 188 patients being *Bartonella* bacteremic, as determined by nested polymerase chain reaction [87].

2.3. Co-infection by several infectious agents

Severe clinical forms of *B. henselae* infections have been reported in patients co-infected with other infectious organisms, such as *Borrelia* [78, 185], HIV [130] or Espstein-Barr virus [209]. In dogs, all *Bartonella* endocarditis cases reported in a study from northern California were seropositive for *A. phagocytophilum*, suggesting that co-infection by these two vector-borne agents could lead to this severe pathology [154]. Similarly, in the eastern USA and in Thailand, co-infection of dogs with several tick-borne pathogens, including *Bartonella* has been documented [27, 138, 181, 215, 220].

2.4. Increased outdoor activity, poverty and low income

Human exposure to some rodent-borne *Bartonellae*, especially *B. elizabethae* has been associated with exposure to rats among homeless people or intravenous drug users in urban areas of the USA [42, 56, 57, 77] or to outdoor activity in northern Europe, especially in orienteers in Sweden [155, 229]. Exposure to ticks has also been suggested for human infections [78, 152, 235]. Additionally, it was demonstrated that for dogs, living in a rural environment and being heavily exposed to ticks and fleas were risk factors associated with *Bartonella* infection [181]. In northern California, herding dogs were more likely to be *Bartonella* seropositive and toy dogs less likely to be seropositive than other breeds of dogs [107].

2.5. Dispersal of *Bartonellae* around the world

Ellis et al. [77] and Childs et al. [42] have both stated that: "accumulating data suggest an Old World origin for a group of bacteria that include *B. elizabethae*, a human pathogen first identified from the New World. The potential public health significance of these newly described organisms is undefined, but of international interest as their vertebrate reservoir has been introduced

throughout the world". Similarly, the distribution in various parts of the world of different genotypes/phenotypes of *B. henselae* by human's migrating with their pet cats may have occurred in the last few centuries. A recent report of the presence of *B. henselae* DNA in the teeth of cats buried in France between the XIIIth and XVIth Centuries indicated the presence of mainly genotype Houston I whereas in present times genotype Marseille is highly predominant in cats in that country [142]. It is also interesting to note that some reports [16, 68] have emphasized that *B. henselae* genotype Houston was more commonly identified in human cases of CSD whereas genotype Marseille was predominantly isolated within the respective cat populations.

3. BACTERIOLOGICAL FEATURES

Bartonellaceae are small gram-negative rods. Until recently, the genus *Bartonella* consisted of only one species, *B. bacilliformis*. The genus now combines all the species of the three genera *Bartonella, Rochalimaea*, and *Grahamella* into the family Bartonellaceae and the genus *Bartonella*; the family Bartonellaceae has also been removed from the order *Rickettsiales* [21, 30]. They are members of the alpha-2 subgroup of the alpha-proteobacteria. Most of these bacteria are erythrocyte-adherent bacilli. The present family consists of more than 20 species or subspecies, of which at least eight are human pathogens [52].

Bartonellaceae are fastidious, aerobic, short, pleomorphic gram-negative coccobacillary or bacillary rods (0.6 μm × 1.0 μm) that take from 5 to 15 days and up to 45 days on primary culture to form visible colonies on enriched blood-containing media, as they are highly hemin-dependent [44]. In infected tissues, Warthin-Starry silver impregnation stain reveals small bacilli, which tend to appear as clumps of tightly compacted organisms. Similarly, small organisms can be identified in red blood cells by May-Grünwald Giemsa coloration. *Bartonellae* have a close evolutionary homology with members of the genera *Brucella*, *Agrobacterium* and *Rhizobium*. Bartonellaceae have the ability to infect red blood cells and to cause prolonged intraerythrocytic bacteremia in their specific mammalian reservoir host [64]. Such an infection has been well described in an experimental model of infection of rats with *B. tribocorum* [207]. Furthermore, these bacteria are unique among all known bacterial pathogens in their ability to cause vasoproliferative lesions through their ability to invade endothelial cells and trigger proliferation and migration of these cells [64].

Traditionally, *Bartonella* are cultivated in semisolid nutrient agar containing fresh rabbit blood (or sheep or horse blood) at 35 °C (except for *B. bacilliformis*, which grows best at 28 °C) in 5% CO_2. On primary isolation, some *Bartonella*, such as *B. henselae, B. clarridgeiae, B. vinsonii*, or *B. elizabethae* have colonies with a white, rough, dry, raised appearance and pit the medium. They are hard to break up or transfer. Because of the slow growth of these bacteria, standard biochemical methods for identification may not be applicable. The *Bartonella* are catalase, oxidase, urease and nitrate reductase negative [25]. Measurement of preformed enzymes and standard testing has revealed differences between *Bartonella* species. Most species are biochemically inert except for the production of peptidases [25].

Molecular genetic methods such as restriction fragment length polymorphism (RFLP) of genes encoding citrate synthase, 16S rRNA or 16S–23S rRNA spacer region, and more recently analysis based on polymerase chain reaction (PCR) of random, repetitive extragenic palindromic sequences have been used to distinguish strains and species of *Bartonella.* RFLP or sequence analysis of 16S rRNA, citrate synthase genes after PCR amplification both directly from specimens or pure cultures have been largely used for detecting and characterizing *Bartonella*. More recently, identification has also been performed with the amplification of the 16S-23S rRNA intergenic

spacer region (ITS) [201] or protein-coding genes. The genes the more widely used are those coding for the citrate synthase (*gltA*), the heat shock protein (*groEL*), the riboflavine (*ribC*), the RNA polymerase beta subunit (*rpoB*), a cell division protein (*ftsZ*) and a 17 kDa antigen [145].

4. EPIDEMIOLOGICAL FEATURES

4.1. Zoonotic *Bartonellae* with a feline or canine reservoir

Cat scratch disease is certainly the most common *Bartonella* zoonosis worldwide. Human cases have been reported from several continents, including North America, Europe, Australia, and from most countries where investigators looked for such an infection [25, 52]. It has been estimated that more than 22 000 human cases occurred in the USA in 1992, with an estimated incidence of disease in ambulatory patients of 9.3 per 100 000 persons per year [113]. In the Netherlands, the estimated number of CSD was 2 000 cases per year or 12.5 cases/100 000 persons [17]. Therefore, such observations suggest that worldwide several thousand cases of CSD may occur every year in many countries. Overall, CSD is more likely to occur in children and young adults [35]. Transmission from cat to human mainly occurs directly by a cat scratch and possibly via a cat bite [35] or possibly by a flea or a tick bite [152, 197, 235]. However, it is now suggested that flea bites are an unlikely mode of infection and that flea feces may be the only infecting material that could be inoculated by a cat scratch [83, 84]. *B. henselae* DNA was recently detected in a biting fly, raising concern about the role of these biting insects as *Bartonella* vector [54]. In immunocompromised individuals, bacillary angiomatosis and bacillary peliosis caused by *B. henselae* are usually associated with exposure to cats and cat fleas [127, 129]. However, bacillary peliosis was a clinical feature seen only in patients infected with *B. henselae* [129]. Different *Bartonella* species, but more frequently *B. henselae* and *B. quintana*, can cause human endocarditis [31]. An estimated 3% of all cases of human endocarditis have been attributed to *Bartonella* infection [189]. However, only *B. henselae* is considered to be zoonotic among these two *Bartonella* species. In Sweden, the emergence of orienteering (countryside running based on navigational acuity using map and compass-reading skills) was marked between 1979 and 1992 by an elevated rate of sudden unexpected cardiac deaths in top-ranked competitors [229]. Four of these deaths were likely caused by *B. henselae* and *B. quintana*, as DNA was detected in the cardiac tissue of 4 of the 5 cases tested and in the lung of the fifth case, whereas no *Bartonella* DNA was detected in six control hearts.

In humans, *B. clarridgeiae* antibodies have been reported in a suspect case of CSD and in a patient with a chest-wall abscess [136, 159]. Furthermore, anti-flagella (FlaA) specific antibodies against *B. clarridgeiae* were detected in 3.9% of 724 patients with lymphadenopathy [205]. However, significant cross-reactivity between *B. henselae* and *B. clarridgeiae* was noted in a recent study from Japan [219]. These serological investigations suggest that *B. clarridgeiae* may be a minor causative agent of CSD.

More recently, the first human case of endocarditis associated with *B. koehlerae*, was reported from Israel [8]. Furthermore, these authors were able to isolate *B. koehlerae* from a bacteremic stray cat from that country.

Domestic cats are the main reservoir for *B. henselae*, *B. clarridgeiae* and *B. koehlerae* [45, 128, 192]. Sero-epidemiological and bacteriological studies have demonstrated the worldwide distribution of *B. henselae* infection in domestic cats. *B. henselae* antibody prevalence varies from 5% to 80%, and bacteremia prevalence ranges from a few percent to more than half of the population tested, according to the geographical location and the cat status (pet or stray). Data of surveys concerning cat populations are summarized in Tables I, II, III for

Table I. Surveys of *Bartonella* spp. infections (bacteremia or antibodies) in domestic cats in France, Germany and the Netherlands.

Country (location)	Survey	Cat population	Bartonella	Prevalence positive/total (%)	Reference
France (Paris)	B	Pets	B.spp.	72/436 (**16.5**)	[100]
			B.h.	H: 11/72 (**15.3**)	
				M: 36/72 (**50**)	
				H + M: 2/72 (**2.8**)	
			B.c.	15/72 (**20.8**)	
			B.h. + B.c.	8/72 (**2**)	
	S	Pets	B.h. + B.c.	179/436 (**41.1**)	
France (Lyon)	B	Pets	B.spp.	8/99 (**8.1**)	[199]
			B.h.	H: 6/8 (**75**)	
				M: 0/8 (**0**)	
			B.c.	2/8 (**25**)	
France (Nancy)	B	Strays	B.spp.	50/94 (**53**)	[106]
			B.h.	H: 17/50 (**34**)	
				M: 18/50 (**36**)	
			B.c.	15/50 (**30**)	
France (Marseille?)	B	Strays	B.spp.	38/61 (**62.3**)	[143]
			B.h.	H: 15/38 (**39.5**)	
				M: 7/38 (**18.4**)	
			B.c.	16/38 (**42.1**)	
Germany	S	Pets	B.h.	107/713 (**15**)	[103]
Germany (Freiburg)	B	Pets	B.h.	13/100 (**13**)	[203]
Germany (Berlin)	B	Pets/Strays	B.h.	20/193 (**10.4**)	[7]
				Pets: 1/97 (**1**)	
				Stray: 19/96 (**18.7**)	
				H: 1/20 (**5**)	
				M: 18/20 (**90**)	
			B.c.	1/20 (a stray cat) (**5**)	
The Netherlands	B	Shelter	B.h.	25/113 (**22**)	[17]
				H: 6/25 (**24**)	
				M: 10/25 (**40**)	
			B.h./B.c.	5/25 (**20**)	
			B.c.	4/25 (**16**)	
	S	Shelter/Pets	B.h.	Not given (**35–60**)	
				Pets: 28/50 (**56**)	
				Shelter: 56/113 (**50**)	

S: seroprevalence, B: bacteremia prevalence, B.h.: *Bartonella henselae*, B.c.: *Bartonella clarridgeiae*, B.spp.: *Bartonella* species, H: type I (Houston I), M: type II (Marseille).

Table II. Surveys of *Bartonella* spp. infections (bacteremia or antibodies) in domestic cats in northern and central Europe.

Country	Survey	Cat population	Bartonella	Prevalence positive/total (%)	Reference
Austria	S	Pets	B.h.	32/96 (**33.3**)	[3]
Czech Republic	B	Pets/Shelter/ Stray	B.h.	5/61 (**8**) M: 5/5 (**100**) Pets: 0/34 (**0**) Shelter: 1/21 (**5**) Stray: 4/6 (**66.6**)	[170]
Denmark	B	Pets/Shelter	B.h.	21/93 (**22.6**) H: 1/21 (**5**) M: 20/21 (**95**) Pets: 8/44 (**18.2**) Shelter: 13/49 (**26.5**)	[49]
	S	Pets/Shelter	B.h.	42/92 (**45.6**)	
Denmark (North Zealand)	B	Strays	B.h.	11/25 (**44**) M: 11/11 (**100**)	[75]
Norway	B	Pets	B.spp.	0/100 (**0**)	[15]
	S	Pets	B.h. (EIA)	1/100 (**1**)	
			B.h. (IFA)	0/100 (**0**)	
Poland	S	Shelters	B.h.	31/36 (**86**)	[184]
Sweden	S	Pets	B.h.	3/292 (**1**)	[108]
Sweden (Stockholm and southern Sweden)	B	Pets	B.h.	2/91 (**2.2**) M: 2/2 (**100**)	[76]
Switzerland	S	Pets	B.h.	60/728 (**8.3**)	[92]
United Kingdom (Bristol and Southwest UK)	B	Pets	B.h.	34/360 (**9.4**) H: 2/34 (**6**) M: 30/34 (**88**) H + M: 2/34 (**6**)	[22]
United Kingdom	S	Pets	B.h.	28/69 (**40.6**)	[13]
	S	Feral	B.h.	33/79 (**41.8**)	
United Kingdom	B	Pets	B.h.	40/351 (**11.4**)	[147]

S: seroprevalence, B: bacteremia prevalence, B.h.: *Bartonella henselae*, B.c.: *Bartonella clarridgeiae*, B.spp.: *Bartonella* species, EIA: ELISA, IFA: immunofluorescence, H: type I (Houston I), M: type II (Marseille).

Table III. Surveys of *Bartonella* spp. infections (bacteremia or antibodies) in domestic cats in Italy and Portugal.

Country	Survey	Cat population	Bartonella	Prevalence positive/total (%)	Reference
Italy (Lombardia)	B	Stray	B.spp.	140/769 (**18**)	[81]
(3 urban, 3 rural areas)			B.h.	H: 27/131 (**20.6**)	
				M: 80/131 (**61.1**)	
				H + M: 24/131 (**18**)	
	S	Stray	B.h.	207/540 (**38**)	
Italy (northern)	B	Stray	B.h.	361/1585 (**23**)	[82]
				Not given (**26**)	
				Not given (**52**)	
			B.c.	Not given (**5**)	
	S	Stray	B.h.	553/1416 (**39**)	
Italy (Tuscany)	B	Pets/catteries	B.spp.	0/28 (**0**)	[73]
	S	Pets/catteries	B.h.	98/427 (**23**)	
Italy (Reggio Emilia)	B	Pets	B.h.	24/248 (**9.7**)	[33]
Portugal	S	Pets	B.h.	1/14 (**6.7**)	[41]

S: seroprevalence, B: bacteremia prevalence, B.h.: *Bartonella henselae*, B.c.: *Bartonella clarridgeiae*, B.spp.: *Bartonella* species, H: type I (Houston I), M: type II (Marseille).

Europe, Table IV for Asia and Oceania, Table V for the Americas and Table VI for Africa and the Middle East. Cats are usually bacteremic for several weeks, based on experimental infections; but some cats can be bacteremic for more than a year, as shown in natural settings [132, 133] or experimentally [1, 131, 135, 137]. However, prevalence and level (number of colony forming units per millilitre of blood) of bacteremia are usually higher in young cats (< 1 year) than in adult cats [45]. Two main genotypes/serotypes of *B. henselae* have been described [16, 70, 144], and major regional variations in the respective prevalence of *B. henselae* type I (Houston) and type II (Marseille) have been reported in domestic cat populations (Tabs. I–VI). Co-infection of cats with these two genotypes has also been reported [17, 99]. Transmission of infection among cats requires the presence of fleas [46]. However, it is strongly suggested that infection among cats is occurring through inoculation of flea feces rather than flea bites [83, 84]. *Bartonella clarridgeiae* is unevenly distributed in cat populations worldwide, with a prevalence of 30% to 36% of all *Bartonella* isolates in some studies (France, the Netherlands or Philippines) to no more than 10% in the southeastern USA and Japan or Taiwan and lack of isolation in several studies in Europe, Australia and North America [52, 95]. *Bartonella koehlerae* has been isolated only from two cats in California, one cat in France and recently in one cat in Israel [8, 72, 196]. Furthermore, *Bartonella* infection has been reported in wild felids, such as pumas and bobcats in the New World [53].

Bartonella vinsonii subsp. *berkhoffii* was identified in a human case of endocarditis

Table IV. Surveys on *Bartonella* spp. infections (bacteremia or antibodies) in domestic cats in Asia and Oceania.

Country	Survey	Cat Population	Bartonella	Prevalence positive/total (%)	Reference
Australia (Sydney)	B	Pets/Feral	B.h.	27/77 (**35**)	[24]
				Pets: 3/18 (**16**)	
				Feral: 24/59 (**40**)	
Australia (Melbourne)	B	Pets	B.h.	45/342 (**13.2**)	[174]
New Zealand (Auckland)	B	Pets	B.h.	8/48 (17)	[117]
Japan	S	Pets	B.h.	30/199 (**15.1**)	[221]
Japan (Kanagawa, Saitama Prefectures)	S	Pets	B.h.	43/471 (**9.1**)	[165]
Japan	S	Pets	B.h.	128/1447 (**8.8**)	[168]
Japan	B	Pets/Pound	B.h.	3/33 (**9.1**)	[164]
Japan	B	Pets	B.spp.	50/690 (**7.2**)	[166]
			B.h.	H: 43/45 (**95.5**)	
				M: 1/45 (**2.2**)	
			B.c.	4/50 (**8**)	
			B.c. + B.h.	1/50 (**2**)	
Indonesia (Jakarta)	B	Stray	B.h.	6/14 (**43**)	[163]
			B.c.	3/14 (**21**)	
	S	Stray	B.h.	40/74 (**54**)	
Philippines (Manilla)	B	Stray	B.spp.	19/31 (**61**)	[47]
			B.h.	H: 13/19 (**68.4**)	
			B.c.	2/19 (**10.5**)	
			B.h. + B.c.	4/19 (**21**)	
	S	Stray	B.h.	73/107 (**68**)	
			B.c.	70/107 (**65**)	
Singapore	S	Stray	B.h.	38/80 (**47.5**)	[173]
Thailand	B	Pets/Stray	B.spp.	76/275 (**27.6**)	[167]
			B.h.	63/76 (**83**)	
			B.c.	9/76 (**11.8**)	
			B.h. + B.c.	4/76 (**5.3**)	
			B.h.	H: 48/67 (**71.6**)	
				M: 13/67 (**19.4**)	

S: seroprevalence, B: Bacteremia prevalence, B.h.: *Bartonella henselae*, B.c.: *Bartonella clarridgeiae*, B.spp.: *Bartonella* species, H: type I (Houston I), M: type II (Marseille).

Table V. Surveys on *Bartonella* spp. infections (bacteremia or antibodies) in domestic cats in the Americas.

Country	Survey	Cat population	Bartonella	Prevalence positive/total (%)	Reference
Brazil	S	Pets?	B.h.	Not given (**46**)	cited in [224]
Chile (Valdivia)	S	Pets	B.h.	54/76 (**71**)	[236]
			B.c.	Not given (**18.6**)	
Canada	S	Pets	B.h.	43/242 (**17.8**)	[149]
USA/Canada	S	Pets	B.h.	175/628 (**27.9**)	[116]
USA	S	Pets/Shelter	B.h.	370/1314 (**28.2**)	[41]
USA (Baltimore)	S	Stray/Vet. Hosp.	B.h.	77/592 (**13**)	[40]
USA (North Carolina)	S	Pets	B.h.	46/114 (**40.4**)	[12]
USA (Florida)	S	Feral/Stray	B.h.	186/553 (**33.6**)	[153]
USA	S	Feral	B.h.	93/100 (**93**)	[176]
(North Carolina)	S	Pets	B.h	57/76 (**75**)	
USA (California)	B	Pets/Stray	B.h.	81/205 (**39.5**)	[45]
				Pets: 24/112 (**21.4**)	
				Stray: 57/93 (**61.3**)	
	S	Pets/Stray	B.h.	165/205 (**81**)	
USA	B	Pets	B.h.	65/271 (**24**)	[98]
				H: 14/49 (**28.6**)	
				M: 32/49 (**65.3**)	
				H + M: 3/49 (**6.1**)	
			B.c.	(**0**)	
	S	Pets	B.h.	138/271 (**51**)	

S: seroprevalence, B: Bacteremia prevalence, B.h.: *Bartonella henselae*, B.c.: *Bartonella clarridgeiae*, B.spp.: *Bartonella* species, H: type I (Houston I), M: type II (Marseille).

Table VI. Serosurveys on *Bartonella* spp. infection in domestic cats in Africa and the Middle East.

Country	Survey	Cat population	Bartonella	Prevalence positive/total (%)	Reference
Egypt	S	Pets	B.h.	5/42 (**12**)	[41]
Israel	S	Pets	B.h.	45/114 (**39.5**)	[12]
Israel	B	Stray	B.h.	40/48 (**83**)	[8]
			B.c.	7/48 (**15**)	
			B.k.	1/48 (**2**)	
Jordan	S	Pets	B.h.	55/153 (**36**) true prevalence (**32**)	[4]
South Africa	S	Shelter	B.h.	11/52 (**21**)	[120]
	B	Pets	B.h.	1/31 (**3.2**) (H: 1/1)	[187]
Zimbabwe	S	Pets/Shelter	B.h.	28/119 (**24**)	[120]
	B	Pets	B.h.	2/25 (**8**)	[121]

S: seroprevalence, B: Bacteremia prevalence, B.h.: *Bartonella henselae*, B.c.: *Bartonella clarridgeiae*, B.k.: *Bartonella koehlerae*, B.spp.: *Bartonella* species, H: type I (Houston I), M: type II (Marseille).

[200]. This subspecies appears to be the most common *Bartonella* species/subspecies causing endocarditis in dogs [25]; however, other *Bartonella* species, including *B. clarridgeiae*, *B. washoensis* have been identified in canine endocarditis cases [48, 50, 154]. Overall, the prevalence of *B. vinsonii* subsp. *berkhoffii* antibodies in pet dogs is quite low (< 5%) [107, 181, 212], but can be higher in specific populations [11, 111] and in free-roaming dogs in the tropics ranging from 19% (5/26) for dogs from French Guyana and Martinique to 65% (33/51) for native dogs from Sudan[1]. In the western USA, coyotes (*Canis latrans*) constitute a major reservoir for *Bartonella vinsonii* subsp. *berkhoffii* [37, 38]. Limited data is available about the seroprevalence of *B. henselae* in dogs [13, 65, 107] which was found to also be quite low. However, a recent study reported higher prevalence of *B. henselae* antibodies in healthy (10.1%) and sick (27.2%) dogs from the southeastern USA [212].

4.2. Rodent-borne zoonotic *Bartonellae*

At present, only a limited number of human infections caused by rodent-borne *Bartonella* species or subspecies have been described in the scientific literature. There are still many unknown risk factors associated with such infections (i.e. mode of

[1] Davoust B., Drancourt M., Boni M., et al., Survey of seroprevalence of *Bartonella vinsonii*, *Ehrlichia canis* and *Coxiella burnetii* in dogs in southeast France, French Guyana, Martinique, Senegal, Ivory Coast and Sudan, EUWOG-ASR Joint Meeting, Marseille, France, 14–16 June 1999, Abstract 232B.

infection, vector involved, source of infection). Among the rodent-borne *Bartonellae*, *B. elizabethae* infection seems to be quite prevalent in intravenous (IV) drug users and homeless people in various parts of the USA and also in Sweden [56, 57, 156], based on serological studies. In IV drug users, *B. elizabethae* seroprevalence ranged from 33% in Baltimore [56] to 39% in Stockholm [156] and 46% in New York [57]. In homeless people from Los Angeles, California, the seroprevalence was 12.5% [210]. Furthermore, 31% of 1 136 Swedish orienteers were seropositive for *B. elizabethae* [155]. Infections caused by *B. elizabethae* in humans have been associated with endocarditis and neuroretinitis [60, 177]. However, such studies based only on serological data need to be confirmed by identification of this pathogen either by PCR methods or isolation. Rats (*Rattus norvegicus*) constitute the main reservoir of *B. elizabethae* [42, 77]. This *Bartonella* species has been isolated from urban rats from various parts of the world, including the USA (Louisiana, Maryland), Portugal and Peru [19, 77]. In China, Yunnan rats are infected with a large number of *Bartonella* strains that are genetically related to *B. elizabethae* [234]. In Thailand, a number of the *Bartonella* isolates from Thai rodents are closely related to *B. grahamii* and *B. elizabethae*, two species that have been associated with human illness [36].

Bartonella grahamii has been mainly isolated from bank voles (*Clethrionomys glareolus*) in the United Kingdom [20] and Poland [10] and from yellow-necked mice (*Apodemus flavicollis*) in Sweden [110], but has also been isolated from rats in the USA and a domestic mouse captured in California [77]. The rodent flea *Ctenophthalmus nobilis* was recently shown to be a competent vector of at least two *Bartonella* species, *B. grahamii*, which has previously been associated with human ocular infection (neuroretinitis and retinal artery occlusion) [123, 208], and *B. taylorii* [23]. White-footed mice (*Peromyscus leucopus*) are the reservoir of *B. vinsonii* subspecies *arupensis*, which has been isolated from 5% of 81 mice tested from Minnesota and Wisconsin and associated with one human infection (fever, bacteremia, neurological symptoms) [109, 228]. California ground squirrels (*Spermophilus beecheyi*) are the main reservoir of *B. washoensis*, which has been identified in a human case of myocarditis [139] and in a case of endocarditis in a dog [50]. Finally, isolation of *B. henselae* type Houston I from three long-tailed field mice (*Apodemus sylvaticus*) was very recently reported [75] and raises an interesting question about the possibility of natural infection of wild rodents with *B. henselae*. Further studies will be required to determine if rodents could be another natural reservoir of this bacterium beside its feline reservoir.

The epidemiological importance of rodent-borne *Bartonella* spp. as a cause of disease in animals and man is emerging, as suggested for a novel rodent *Bartonella*-associated febrile illness in the rural southwestern USA, based on serological evidence[2]. A few patients had high antibody titers against a strain of *Bartonella* isolated from a white-throaded wood rat (*Neotoma albigula*). Many new *Bartonella* species have been identified in South East Asia [36, 234] and some of them could be a source of human infection (Kosoy M., personal communication).

5. CLINICAL FEATURES

5.1. Humans

Classical Cat Scratch Disease: CSD caused by *B. henselae* is mainly characterized by a benign regional lympadenopathy [35, 43, 63, 157]. Usually after a cat scratch, a papule and then a pustule develops within

[2] Kosoy M., Ying B., Koster F., Gage K., Ecological and epidemiological implications of high genetic and antigenic diversity of rodent-borne *Bartonella* strains in the US West, American Society for Rickettsiology – *Bartonella* as an emerging pathogen group. 2001 joint conference, Big Sky, Montana, USA, 18–22 August 2001, Abstract 108.

Table VII. Miscellanous manifestations of *Bartonella henselae* infection in humans.

Clinical manifestations	References
Tumoral and Pseudotumoral manifestations of CSD	
Mimicking breast tumor, breast mass	[93, 160]
Granulomatous hepatitis and necrotizing splenitis	[150]
Simulating lymphoma	[90, 183, 231]
Gammopathy	[140]
Simulating rhabdomyosarcoma	[161]
Mimicking parotid malignancy	[122]
Pseudotumoral presentation	[74]
Simulating a malignant process of the chest wall	[172]
Peripheral lymphadenopathy	[14]
Myelodysplastic syndrome	[225]
Joint and/or bone localisation	
Arthritis, arthralgy	[5, 105]
Osteomyelitis	[148]
Skin localisation	
Skin nodules, cutaneous vasculitis	[206]
Erythema nodosum, granuloma annulare	[211]
Petechial, papular and vasculitic skin lesions,	[225]
Unusual eruption	[146]
Paronychia	[202]
Miscellaneous	
Endocarditis	[31, 70, 85, 101, 189, 223]
Henoch-Schonlein purpura	[9]
Purpura with leukocytoclasic vasculitis	[206]
Glomerulonephritis	[223]
Periodontitis	[55]

7 to 12 days at the inoculation site [35, 115, 157]. A regional lymphadenopathy (usually involving a single lymph node) develops one to three weeks after the inoculation and can persist a few weeks to several months [35]. Abscessed lymph nodes are reported occasionally in 12% [35] up to 48% of the cases [62]. Low-grade fever, malaise and aching are often reported; and in some instances, headache, anorexia and splenomegaly can occur. The various clinical manifestations of *B. henselae* infection are summarized in Table VII.

Atypical CSD: From 5% to 9% of CSD cases may develop atypical manifestations, including Parinaud's oculoglandular syndrome, encephalitis, endocarditis, hemolytic anemia, hepatosplenomegaly, glomerulonephritis, pneumonia, relapsing bacteremia, and osteomyelitis [157]. Cat scratch disease encephalopathy (CSDE), possibly associated with an immune-mediated response to *B. henselae* infection, is one of the most severe complications of CSD [175]. Patients with CSDE usually completely recover within one year without any sequelae. However,

Table VIII. Neurologic manifestations of *Bartonella henselae* infection in humans.

Clinical signs	References
Epilepsia partialis continua	[188]
Encephalopathy	[102, 162, 175]
Status epilepticus	[6, 79, 102]
Peripheral facial nerve paralysis	[227]
Coma	[102]
Fatal meningitis and encephalitis	[89, 162]
Meningoencephalitis	[216]
Meningitis	[230]
Hemiplegia	[195]

one case of fatal meningitis and encephalitis was reported in a 4-year-old child [89].

An expanding clinical spectrum associated with *B. henselae* infection: *B. henselae* has been identified as a frequent cause of prolonged fever and fever of unknown origin in children [114, 217, 218].

Besides a wider spectrum of neurological symptoms (Tab. VIII), many ocular lesions have also been associated with *Bartonella* infection, such as uveitis, focal retinal phlebitis, neuroretinitis, retinal and optical nerve neovascularization, retinal artery and vein occlusion (Tab. IX). It is important to indicate that most of these observations have mainly been based on the presence of *Bartonella* antibodies or a proven seroconversion rather than by isolation or positive PCR.

Tumoral and pseudo-tumoral lesions have also been reported, such as lesions mimicking breast tumor or rhabdomyosarcoma, lymphoma and gammopathy, as well as granulomatous hepatitis and necrotizing splenitis (Tab. VII). Rheumatic manifestations (arthralgia, arthritis) of *Bartonella* infection have been described both in children and adults (Tab. VII), as well as erythema nodosum [35, 211], leukocytoclastic vasculitis [104], fever of unknown origin with myalgia [114] and arthralgia [5, 35, 105]. Cases of osteomyelitis have also been described [148]. A causative role for *B. henselae* in Henoch-Schonlein purpura (HSP) was suggested based on serological evidence, as 12 (67%) of 18 HSP patients were seropositive versus only 8 (14%) of 57 controls [9]. HSP is an immune-mediated vasculitis that is characterized by excessive IgA production and frequently associated with thrombocytopenia. Monoclonal and biclonal

Table IX. Ocular manifestations of *Bartonella* spp. infection in humans.

Clinical signs	References
Uveitis	[71, 179]
Multifocal retinitis, neuroretinitis/stellate neuroretinitis (Leber's neuroretinitis) macular star/neovascularization	[18, 58, 59, 126, 169, 179, 180]
Parinaud's oculoglandular syndrome	[58, 80]
Retinal artery and vein occlusion, neovascular glaucoma, severe vision loss.	[94]
Optic disk edema with peripapillary serous retinal detachment	[226]
Peripapillary angioma,	[94]
Retinochoroidal exsudate, retinal phlebitis	[67]
Disciform keratitis	[88]
Retinal and optic nerve neovascularization	[169]
Focal retinochoroiditis, unifocal helioid choroiditis	[58, 186]
Posterior segment involvement	[125]

gammopathy in two patients infected with *Bartonella henselae* has also been described [140]. *Bartonella* have also been suggested as a cause of granulum annulare [211] and glomerulonephritis associated with negative culture endocarditis [223]. The first case of spontaneous splenic rupture caused by infection with *B. henselae* was recently reported, leading to massive hemoperitoneum [61]. Lesion of the spleen is common in disseminated infection with *B. henselae* [213], but massive spontaneous hemoperitoneum was only reported in association with hepatic bacillary peliosis in an HIV-infected patient [151].

Bartonella spp. were first described as a cause of human endocarditis in three separate reports in 1993, one caused by *B. quintana* in an immunocompromised individual [214], one caused by *B. elizabethae* in an immunocompetent patient [60] and the third caused by *B.* (*Rochalimaea*) *henselae* [101]. *Bartonella* species, mainly *B. quintana* and *B. henselae*, account for approximately 3% of human endocarditis cases, with more than 100 human cases reported in the international literature since 1993 [85, 189, 190]. In most human cases of *Bartonella* endocarditis, the vegetative lesions are preferentially located on the aortic valve [189] and most patients have high antibody titers [86]. Furthermore, most cases of *B. henselae* endocarditis are culture negative but positive by DNA amplification [85]. *Bartonella henselae* and *B. quintana* DNA were also detected in the cardiac tissue of four young Swedish orienteers who died of unexpected sudden cardiac death [229].

In immunocompromised individuals, bacillary angiomatosis (BA) is one of the most common clinical manifestations of *Bartonella* infections [127]. The presence of chronic vascular proliferative lesions is observed. HIV infected patients with $CD4^+$ cell counts of less than $50/mm^3$ are more likely to develop BA lesions. Histopathologically, cutaneous BA is characterized by a tumor-like growth pattern with proliferation of capillaries having protuberant epitheloid endothelial cells [127, 193]. In transplant patients, various clinical manifestations or pathological lesions have been reported, such as pulmonary nodules [34] or sternal abscess [32], disseminated infection with granulomatous hepatitis [112], acute organ rejection [66], bacillary peliosis [2] and bacillary angiomatosis [118]. A case of hemophagocytic syndrome in a transplant patient was recently associated with *B. henselae* infection [119]. Hemophagocytic syndrome (HPS) combines febrile hepatosplenomegaly, pancytopenia, hypofibrinemia, and liver dysfunction.

5.2. Cats

Cats usually appear to be healthy carriers of *B. henselae*, as limited pathology has been associated with natural infection. However, due to the high prevalence of infection in cat populations, it has been difficult to attribute specific clinical signs to cats naturally infected with *B. henselae* [43, 45]. Based on serological results, naturally infected cats were more likely to have lymphadenitis and gingivitis, especially those co-infected with the feline immunodeficiency virus [222]. Such an association was also demonstrated between *B. henselae* seropositivity and presence of stomatitis or urological diseases [92]. *Bartonella henselae* has been implicated as a potential cause of anterior uveitis in cats [141] and a PCR confirmed case of *B. henselae* endocarditis was described in a cat from California [51].

In experimental conditions, cats infected with *B. henselae* (mainly type II, feline isolates) have developed various clinical signs [96, 137, 178]. The most commonly reported sign is fever, which usually does not last for more than a week [95]. Local inflammation (erythema, swelling) at the site of inoculation and localized or generalized lymphadenopathy have also been observed. Some other signs include lethargy and anorexia. Some cats also developed mild neurological signs, such as nystagmus, tremors, focal motor seizures, and behavior changes [95]. Reproductive disorders (stillbirths, lack of

pregnancy or pregnancy only after repeated breedings) were reported in experimentally infected queens [97]. Variation in pathogenicity of strains has been suggested for differences in clinical signs observed in experimental conditions [178].

5.3. Dogs

The first isolation of *Bartonella* from a dog occurred in a case of endocarditis in 1993 [26, 134]. Since then, *Bartonella vinsonii* subsp. *berkhoffii* has been identified as an important cause of canine endocarditis [26, 28], and was determined as the cause of one human endocarditis case [200]. As in humans, the clinical spectrum of *Bartonella* infection in dogs is expanding, as it is now associated with cardiac arrhythmias, endocarditis and myocarditis [28], as well as granulomatous lymphadenitis and granulomatous rhinitis [182]. In both humans and dogs, *Bartonella* associated cases of endocarditis usually involve the aortic valve and are characterized by massive vegetative lesions [154]. At one veterinary teaching hospital, *Bartonella* infection was implicated in almost one third of the endocarditis cases diagnosed over a two-year period [154]. Based upon serological evidence, infection with *B. vinsonii* subsp. *berkhoffii* may also cause immune-mediated hemolytic anemia, neutrophilic or granulomatous meningo encephalitis, neutrophilic polyarthritis, cutaneous vasculitis, and uveitis in dogs [29]. A case-control study of clinical diagnosis associated with dogs seropositive for *Bartonella* spp. suggests an association with lameness, arthritis-related lameness, splenomegaly and nasal discharge/epistaxis [107]. However, *B. vinsonii* subsp. *berkhoffii* has also been isolated from clinically healthy dogs, which may be long-term carriers of the bacterium [132]. Dogs can be infected by several other zoonotic *Bartonella* species, including *B. clarridgeiae* isolated from the blood of a dog with endocarditis [48] and detected by PCR in a dog with hepatic lymphocytic hepatitis [91]. *B. henselae* DNA has been detected in a dog with peliosis hepatis [124] and more recently in a dog with granulomatous hepatopathy [91]. *Bartonella henselae* DNA was amplified from the blood of three dogs with various clinical entities [171]. *Bartonella elizabethae* DNA was also detected in the blood of a sick dog [171]. Finally, *B. washoensis*, a rodent borne zoonotic *Bartonella*, was isolated from a dog suffering from mitral endocarditis [50].

6. DIAGNOSIS

6.1. Clinical diagnosis

In humans, clinical diagnosis of cat scratch disease is based on detection of an enlarged lymph node and possibly the presence of a small vesicle or granuloma at the inoculation site. However, clinical diagnosis of atypical forms of CSD and other emerging syndromes associated with *B. henselae* infection or other zoonotic *Bartonella* species is not easy and requires laboratory diagnostic means. In culture negative cases, using classical isolation media, the presence of epidemiological factors such a cat scratch or bite, owning a cat, possible contact with rodent, with fleas, ticks or other blood sucking arthropods may suggest such an etiology and should lead to *Bartonella* specific testing (serology, culture or PCR).

In dogs and cats, clinical diagnosis is usually not easy, as the clinical spectrum of *Bartonella* infection is not fully elucidated. *Bartonella* infection should be suspected in dogs with endocarditis, especially if affecting the aortic valve [154]. It also should be suspected in dogs with prolonged or intermittent fever, lethargy, unexplained lameness, or unexplained granulomatous disease. Similarly, veterinarians should consider performing a diagnostic test for *Bartonella* infection in sick dogs, when there is clinical or epidemiological suspicion of tick exposure. Thrombocytopenia, anemia, neutrophilic leukocytosis, and eosinophilia are the most commonly detected hematologic abnormalities in dogs seropositive for *B. vinsonii*

subsp. *berkhoffii* [29]. In all cases, suspicion of *Bartonella* infection is mainly established through serological testing, which provides evidence of *Bartonella* exposure [113, 115].

6.2. Serologic testing

In humans, serologic testing (mainly IFA testing) is the reference test for diagnosis of cat scratch disease [86, 115]. An IgG anti-*B. henselae* antibody titer ≥ 1:64 is considered as positive for infection when patients are tested at least two to three weeks after a suspected infection. *Bartonella*-associated endocarditis in humans and animals is usually associated with much higher IFA antibody titers (> 1:800) [86, 115]. Commercially prepared IFA slides for *B. henselae* and *B. quintana* antigens are available. Zangwill et al. [235] estimated the sensitivity and specificity of a *B. henselae*-based IFA to be 84% and 96%, respectively. A study comparing two commercially available IFA tests reported that the tests for IgG antibodies to *B. henselae* had higher sensitivities (100% and 85%, respectively) than specificities (70% and 73%, respectively), although this may have been the result of previous exposure to *B. henselae* among the healthy controls designated as the non-infected group [204]. Furthermore, a limiting diagnostic factor in humans is the lack of commercial tests for most rodent-borne zoonotic *Bartonella* species.

In cats, serologic testing is of limited diagnostic value, as many cats (especially stray cats) are likely to be seropositive against *B. henselae* [45]. Testing is indicated in kittens or recently adopted cats, because seronegative cats are more likely not to be bacteremic. Similarly, persons who may have immunocompromising conditions should require that an IFA test detecting antibodies against *B. henselae* be performed on cats prior to adoption. However, bacteremia in seronegative cats has been reported in a few instances and the antibodies usually cross-react with several *Bartonella* antigens [52]. As shown in one of our studies, serological screening for *Bartonella* antibodies may not be useful for the identification of bacteremic cats (positive predicite value = 46.4%), but the lack of antibodies to *B. henselae* was highly predictive of the absence of bacteremia (negative predicite value = 89.7%) [45]. Because of these limitations for serologic testing, bacterial isolation or PCR assay are necessary to identify the infecting *Bartonella* spp.

In dogs, as for humans, diagnosis of *Bartonella* infection is largely based on the presence of specific antibodies. Testing for various antigens seems to be appropriate, including *B. vinsonii berkhoffii* and *B. henselae* [107, 212].

No formal test evaluation studies have been undertaken to estimate the sensitivities and specificities of the serological tests commonly used for the diagnosis of *Bartonella* infection in cats and dogs. One study investigating the seroprevalence of *B. henselae* and *B. quintana* among pet cats in Jordan did provide estimates of sensitivity and specificity for the IFA used in the study [4]. That author reported that the sensitivities of the *B. henselae* IgG and *B. quintana* IgG IFA tests were 99% and 88%, respectively, while the specificities were 94% and 90%, respectively. These results will have to be validated, however, as it is unclear how infection status of cats was determined and whether they were representative of a population of naturally infected cats.

6.3. Bacterial isolation or PCR assay

Isolation of *Bartonella* spp. from cats or from humans with bacillary angiomatosis (for whom serologic testing may not be useful, because patients often do not mount detectable antibodies) is much easier than isolation of those organisms from other animal species or non-immunocompromised individuals. A positive blood culture or culture of other tissue is the most reliable test for definitive diagnosis of active *Bartonella* infection [95]. However, in cats, multiple blood cultures may be necessary because of

the relapsing nature of feline *Bartonella* bacteremia [137]. In humans with cat scratch disease or dogs with *Bartonella* infection, isolation of these bacteria is rarely successful. Isolation of *Bartonella* from blood samples is performed usually by using either pediatric lysis-centrifugation tubes or more commonly plastic tubes containing EDTA. The use of plastic EDTA tubes has the advantage to prevent breakage of the blood tube when subjected to low temperature freezing and avoid the risk of sample contamination during transfer from glass to plastic tubes prior to freezing. Anticoagulated blood is plated (usually after freezing to induce RBC lysis) onto fresh rabbit blood agar and incubated for at least four weeks at 35 °C with an atmosphere containing 5% carbon dioxide. Identification of the isolate is performed using molecular techniques, such as PCR or partial sequencing of selected genes.

Compared with bacteriologic culture, extraction of DNA from tissue samples and PCR testing has been more successful as a method of diagnosis of *Bartonella* infection in humans and dogs [115, 127, 154, 191]. Frozen tissue samples or fresh biopsy specimens can be easily tested. Polymerase chain reaction assay of paraffin-embedded tissues is more cumbersome, but possible. Testing should be performed by laboratory personnals who are familiar with processing these fastidious organisms; laboratories should be contacted for specific instructions for sample collection and submission.

7. TREATMENT

In humans, infected with *B. henselae*, treatment is different for immunocompetent patients having classical symptoms of cat scratch disease than for immunocompromised patients with angiomatous proliferative diseases [127]. For immunocompetent patients, numerous antimicrobial agents have been advocated for the treatment of typical CSD. However, in most instances, antibiotics do not appear to shorten or improve the course of the infection [198]. In human cases of *Bartonella* endocarditis, effective antibiotic therapy should include an aminoglycoside prescribed for a minimum of two weeks [190]. In immunocompromised patients with bacillary angiomatosis or bacillary peliosis, the effectiveness of treatments with various antimicrobial substances has been evaluated [127]. Overall, tetracyclines, erythromycin, rifampin, azithromycin, doxycycline or a combination of these antibiotics are effective and should be administered in these patients for at least six weeks and be continued for 4 to 6 months in those who have relapses [158, 198].

In cats, antimicrobial agents are not commonly used or recommended for treatment or prevention of *B. henselae*, as antibiotic treatments tested to date may reduce the level of bacteremia but do not clear the cats from their infection [135, 194]. Additionally, the minimal effectiveness of these antimicrobial agents could be explained by the fact that *Bartonella* species are intracellular organisms.

In dogs, no study has been performed to determine the efficacy of antibiotics for treatment of *Bartonella* infection. However, it is likely that antibiotics such as doxycycline (10 mg/kg/day) or tetracycline could reduce the level of bacteremia during chronic infections, but should be administered for prolonged periods of time (4–6 weeks). Fluoroquinolones alone or in combination with amoxicillin have also elicited a positive therapeutic response in dogs [29], as repeated *B. vinsonii* subsp. *berkhoffii* antibody titers became negative after treatment. However, antibiotic therapy may not be very effective when the lesions of endocarditis are already well established.

8. PREVENTION

Domestic cats represent the main reservoir for *B. henselae* and cat ownership is now surpassing dog ownership in many industrialized countries [52]. Selecting an appropriate pet cat is important to avoid such a

risk. In most instances, seronegative cats are more likely not to be bacteremic and to be safe for ownership [52]. Conversely, young kittens, especially impounded kittens and flea-infested kittens, are more likely to be bacteremic [45, 128]. It has also been shown that multiple cat ownership was associated with an increased risk for *Bartonella* infection [100]. Therefore, potential pet cat owners, especially if they are immunocompromised, should seek a cat raised in a "clean", flea-controlled environment. In case of adoption, especially when the cat origin is not well defined, it is recommended that serological testing be performed. Only seronegative cats should be adopted when immunocompromised individuals may be exposed to the adopted cat. Flea control is also one of the major control measures to prevent cat infection and its spread from cat to cat and potentially the spread from cats to humans [43]. Overall, effective means of preventing *B. henselae* infection are common sense, hygiene, and, possibly, modification of behavior of the cat owners themselves. Wash hands after handling pets, and clean any cuts, bites or scratches promptly with soap and water. Development of a feline vaccine to prevent the spread of infection in cat populations and reduce human risk of infection is being considered. However, the wide diversity of *Bartonella* isolates even within the same genotype has been of concern for development of an effective feline vaccine. The lack of cross-protectivity between *B. henselae* genotype Marseille and *B. henselae* genotype Houston I was demonstrated a few years ago [232]. Nevertheless, a more recent study was able to demonstrate an unidirectional protective effect using a *B. henselae* Houston I strain against a *B. henselae* Marseille strain challenge [233].

Canine *Bartonella* infections are also likely to be vector-borne and ticks have been suggested as possible vectors of *B. vinsonii* subsp. *berkhoffii* [27, 39, 181]. Therefore, prevention of tick infestation should be one of the main control measures that are employed in the clinical setting. Use of tick repellents and cleaning of the dog after a walk in high-risk terrain should be done systematically to prevent not only *Bartonella,* but also other tick-borne infections. Flea control measures are also important, as dogs may become infected with *B. henselae* [212], possibly when exposed to cat fleas, which are known to transmit the infection among cats.

9. CONCLUSION

Beside cat scratch disease, a well-known zoonosis for which the etiological agent was finally identified at the end of the XXth Century, several new zoonotic *Bartonella* infections have recently been recognized. Most of these zoonotic pathogens have a rodent reservoir and it is likely that new rodent-borne *Bartonella* species will be identified in the near future, some of which will likely be zoonotic. Most *Bartonella* species are vector borne and such vectors still need to be identified for several emerging zoonotic *Bartonella* species. Finally, the clinical spectrum of *Bartonella* infections in both humans and dogs has greatly widened since better tools for identification of these bacteria became available.

REFERENCES

[1] Abbott R.C., Chomel B.B., Kasten R.W., Floyd-Hawkins K.A., Kikuchi Y., Koehler J.E., Pedersen N.C., Experimental and natural infection with *Bartonella henselae* in domestic cats, Comp. Immunol. Microbiol. Infect. Dis. 20 (1997) 41–51.

[2] Ahsan N., Holman M.J., Riley T.R., Abendroth C.S., Langhoff E.G., Yang H.C., Peliosis hepatis due to *Bartonella henselae* in transplantation: a hemato-hepato-renal syndrome,Transplantation 65 (1998) 1000–1003.

[3] Allerberger F., Schonbauer M., Zangerle R., Dierich M., Prevalence of antibody to *Rochalimaea henselae* among Austrian cats, Eur. J. Pediatr. 154 (1995) 165.

[4] Al-Majali A.M., Seroprevalence of and risk factors for *Bartonella henselae* and *Bartonella quintana* infections among pet cats in Jordan, Prev. Vet. Med. 64 (2004) 63–71.

[5] Al-Matar M.J., Petty R.E., Cabral D.A., Tucker L.B., Peyvandi B., Prendiville J., Forbes J., Cairns R., Rothstein R., Rheumatic manifestations of *Bartonella* infection in two children, J. Rheumatol. 29 (2002) 184–186.

[6] Armengol C.E., Hendley J.O., Cat-scratch disease encephalopathy: a cause of status epilepticus in school-aged children, J. Pediatr. 134 (1999) 635–638.

[7] Arvand M., Klose A.J., 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. 39 (2001) 743–746.

[8] Avidor B., Graidy M., Efrat G., Leibowitz C., Shapira G., Schattner A., Zimhony O., Giladi M., *Bartonella koehlerae*, a new cat-associated agent of culture-negative human endocarditis, J. Clin. Microbiol. 42 (2004) 3462–3468.

[9] Ayoub E.M., McBride J., Schmiederer M., Anderson B., Role of *Bartonella henselae* in the etiology of Henoch-Schonlein purpura, Pediatr. Infect. Dis. J. 21 (2002) 28–31.

[10] Bajer A., Pawelczyk A., Behnke J.M., Gilbert F.S., Sinski E., Factors affecting the component community structure of haemoparasites in bank voles (*Clethrionomys glareolus*) from the Mazury Lake District region of Poland, Parasitology 122 (2001) 43–54.

[11] Baneth G., Breitschwerdt E.B., Hegarty B.C., Pappalardo B., Ryan J., A survey of tick-borne bacteria and protozoa in naturally exposed dogs from Israel, Vet. Parasitol. 74 (1998) 133–142.

[12] Baneth G., Kordick D.L., Hegarty B.C., Breitschwerdt E.B., Comparative seroreactivity to *Bartonella henselae* and *Bartonella quintana* among cats from Israel and North Carolina, Vet. Microbiol. 50 (1996) 95–103.

[13] Barnes A., Bell S.C., Isherwood D.R., Bennett M., Carter S.D., Evidence of *Bartonella henselae* infection in cats and dogs in the United Kingdom, Vet. Rec. 147 (2000) 673–677.

[14] Benesch M., Kerbl R., Wirnsberger A., Stunzner D., Mangge H., Schenkeli R., Deutsch J., Peripheral lymphadenopathy in childhood – recommendations for diagnostic evaluation, Klin. Pädiatr. 212 (2000) 277–282.

[15] Bergh K., Bevanger L., Hanssen I., Loseth K., Low prevalence of *Bartonella henselae* infections in Norwegian domestic and feral cats, APMIS 110 (2002) 309–314.

[16] Bergmans A.M., Schellekens J.F., van Embden J.D., Schouls L.M., Predominance of two *Bartonella henselae* variants among cat-scratch disease patients in the Netherlands, J. Clin. Microbiol. 34 (1996) 254–260.

[17] Bergmans A.M., de Jong C.M., van Amerongen G., Schot C.S., Schouls L.M., Prevalence of *Bartonella* species in domestic cats in The Netherlands, J. Clin. Microbiol. 35 (1997) 2256–2261.

[18] Bhatti M.T., Asif R., Bhatti L.B., Macular star in neuroretinitis, Arch. Neurol. 58 (2001) 1008–1009.

[19] Birtles R.J., Raoult D., Comparison of partial citrate synthase gene (gltA) sequences for phylogenetic analysis of *Bartonella* species, Int. J. Syst. Bacteriol. 46 (1996) 891–897.

[20] Birtles R.J., Harrison T.G., Molyneux D.H., *Grahamella* in small woodland mammals in the UK: isolation, prevalence and host specificity, Ann. Trop. Med. Parasitol. 88 (1994) 317–327.

[21] Birtles R.J., Harrison T.G., Saunders N.A., Molyneux D.H., Proposals to unify the genera *Grahamella* and *Bartonella*, with descriptions of *Bartonella talpae* comb. nov., *Bartonella peromysci* comb. nov., and three new species, *Bartonella grahamii* sp. nov., *Bartonella taylorii* sp. nov., and *Bartonella doshiae* sp. nov., Int. J. Syst. Bacteriol. 45 (1995) 1–8.

[22] Birtles R.J., Laycock G., Kenny M.J., Shaw S.E., Day M.J., Prevalence of *Bartonella* species causing bacteraemia in domesticated and companion animals in the United Kingdom, Vet. Rec. 151 (2002) 225–229.

[23] Bown K.J., Bennet M., Begon M., Flea-borne *Bartonella grahamii* and *Bartonella taylorii* in bank voles, Emerg. Infect. Dis. 10 (2004) 684–687.

[24] 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 28 (1996) 262–265.

[25] Breitschwerdt E.B., Kordick D.L., *Bartonella* infection in animals: Carriership, reservoir potential, pathogenicity, and zoonotic potential for human infection, Clin. Microbiol. Rev. 13 (2000) 428–438.

[26] Breitschwerdt E.B., Kordick D.L., Malarkey D.E., Keene B., Hadfield T.L., Wilson K., Endocarditis in a dog due to infection with a novel *Bartonella* subspecies, J. Clin. Microbiol. 33 (1995) 154–160.

[27] Breitschwerdt E.B., Hegarty B.C., Hancock S.I., Sequential evaluation of dogs naturally infected with *Ehrlichia canis*, *Ehrlichia chaffeensis*, *Ehrlichia equi*, *Ehrlichia ewingii*, or *Bartonella vinsonii*, J. Clin. Microbiol. 36 (1998) 2645–2651.

[28] Breitschwerdt E.B., Atkins C.E., Brown T.T., Kordick D.L., Snyder P.S., *Bartonella vinsonii* subsp. *berkhoffii* and related members of the alpha subdivision of the *Proteobacteria* in dogs with cardiac arrhythmias, endocarditis or myocarditis, J. Clin. Microbiol. 37 (1999) 3618–3626.

[29] Breitschwerdt E.B., Blann K.R., Stebbins M.E., Munana K.R., Davidson M.G., Jackson H.A., Willard M.D., Clinicopathological abnormalities and treatment response in 24 dogs seroreactive to *Bartonella vinsonii* (*berkhoffii*) antigens, J. Am. Anim. Hosp. Assoc. 40 (2004) 92–101.

[30] Brenner D.J., O'Connor S.P., Winkler H.H., Steigerwalt A.G., Proposals to unify the genera *Bartonella* and *Rochalimaea*, with descriptions of *Bartonella quintana* comb. nov., *Bartonella vinsonii* comb. nov., *Bartonella henselae* comb. nov., and *Bartonella elizabethae* comb. nov., and

to remove the family Bartonellaceae from the order Rickettsiales, Int. J. Syst. Bacteriol. 43 (1993) 777–786.

[31] Brouqui P., Raoult D., Endocarditis due to rare and fastidious bacteria, Clin. Microbiol. Rev. 14 (2001) 177–207.

[32] Bruckert F., de Kerviler E., Zagdanski A.M., Molina J.M., Casin I., Guermazi A., Bedrossian J., Frija J., Sternal abscess due to *Bartonella* (*Rochalimaea*) *henselae* in a renal transplant patient, Skeletal Radiol. 26 (1997) 431–433.

[33] Cabassi C.S., Farnetti E., Casali B., Taddei S., Donofrio G., Galvani G., Cavirani S., Isolation of *Bartonella henselae* from domestic cats in an Italian urban area, New Microbiol. 25 (2002) 253–257.

[34] Caniza M.A., Granger D.L., Wilson K.H., Washington M.K., Kordick D.L., Frush D.P., Blitchington R.B., *Bartonella henselae*: etiology of pulmonary nodules in a patient with depressed cell-mediated immunity, Clin. Infect. Dis. 20 (1995) 1505–1511.

[35] Carithers H.A., Cat-scratch disease. An overview based on a study of 1 200 patients, Am. J. Dis. Child. 139 (1985) 1124–1133.

[36] Castle K.T., Kosoy M., Lerdthusnee K., Phelan L., Bai Y., Gage K.L., Leepitakrat W., Monkanna T., Khlaimanee N., Chandranoi K., Jones J.W., Coleman R.E., Prevalence and diversity of *Bartonella* in rodents of northern Thailand: a comparison with *Bartonella* in rodents from southern China, Am. J. Trop. Med. Hyg. 70 (2004) 429–433.

[37] Chang C.C., Yamamoto K., Chomel B.B., et al., Sero-epidemiology of *Bartonella vinsonii* subsp. berkhoffii infection in California coyotes, 1994–1998, Emerg. Infect. Dis. 5 (1999) 711–715.

[38] Chang C.C., Kasten R.W., Chomel B.B., Simpson D.C., Hew C.M., Kordick D.L., Heller R., Piemont Y., Breitschwerdt E.B., 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. 38 (2000) 4193–4200.

[39] Chang C.C., Chomel B.B., Kasten R.W., Romano V., Tietze N., Molecular evidence of *Bartonella* spp. in questing adult *Ixodes pacificus* ticks in California, J. Clin. Microbiol. 39 (2001) 1221–1226.

[40] Childs J.E., Rooney J.A., Cooper J.L., Olson J.G., Regnery R.L., Epidemiologic observations on infection with *Rochalimaea* species among cats living in Baltimore, Md, J. Am. Vet. Med. Assoc. 204 (1994) 1775–1778.

[41] Childs J.E., Olson J.G., Wolf A., Cohen N., Fakile Y., Rooney J.A., Bacellar F., Regnery R.L., Prevalence of antibodies to *Rochalimaea* species (cat-scratch disease agent) in cats, Vet. Rec. 136 (1995) 519–520.

[42] Childs J.E., Ellis B.A., Nicholson W.L., Kosoy M., Sumner J.W., Shared vector-borne zoonoses of the Old World and New World: home grown or translocated? Schweiz. Med. Wochenschr. 129 (1999) 1099–1105.

[43] Chomel B.B., Cat Scratch Disease, Rev. Sci. Tech. Off. Int. Epizoot. 19 (2000) 136–150.

[44] Chomel B.B., Kasten R.W., Bartonellaceae, in: Hirsh D.C., MacLachlan N.J., Walker R.L. (Eds.), Veterinary Microbiology, second Edition, Blackwell Publishing, Ames, IA, USA, 2004, pp. 260–264.

[45] Chomel B.B., Abbott R.C., Kasten R.W., Floyd-Hawkins K.A., Kass P.H., Glaser C.A., Pedersen N.C., Koehler J.E., *Bartonella henselae* prevalence in domestic cats in California: Risk factors and association between bacteremia and antibody titers, J. Clin. Microbiol. 33 (1995) 2445–2450.

[46] Chomel B.B., Kasten R.W., Floyd-Hawkins K.A., Chi B., Yamamoto K., Roberts-Wilson J., Gurfield A.N., Abbott R.C., Pedersen N.C., Koehler J.E., Experimental transmission of *Bartonella henselae* by the cat flea, J. Clin. Microbiol. 34 (1996) 1952–1956.

[47] Chomel B.B., Carlos E.T., Kasten R.W., Yamamoto K., Chang C.C., Carlos R.S., Abenes M.V., Pajares C.M., *Bartonella henselae* and *Bartonella clarridgeiae* infection in domestic cats from The Philippines, Am. J. Trop. Med. Hyg. 60 (1999) 593–597.

[48] Chomel B.B., MacDonald K.A., Kasten R.W., Chang C.C., Wey A.C., Foley J.E., Thomals W.P., Kittleson M.D., Aortic valve endocarditis in a dog due to *Bartonella clarridgeiae*, J. Clin. Microbiol. 39 (2001) 3548–3554.

[49] Chomel B.B., Boulouis H.J., Petersen H., Kasten R.W., Yamamoto K., Chang C.C., Gandoin C., Bouillin C., Hew C.M., Prevalence of *Bartonella* infection in domestic cats in Denmark, Vet. Res. 33 (2002) 205–213.

[50] Chomel B.B., Wey A.C., Kasten R.W., Isolation of *Bartonella washoensis* from a dog with mitral valve endocarditis, J. Clin. Microbiol. 41 (2003) 5327–5332.

[51] Chomel B.B., Wey A.C., Kasten R.W., Stacy B.A., Labelle P., A fatal case of endocarditis in a domestic cat associated with *Bartonella henselae* type I infection, J. Clin. Microbiol. 41 (2003) 5337–5339.

[52] Chomel B.B., Boulouis H.J., Breitschwerdt E.B., Cat scratch disease and other zoonotic *Bartonella* infections, J. Am. Vet. Med. Assoc. 224 (2004) 1270–1279.

[53] Chomel B.B., Kikuchi Y., Martenson J.S., Roelke-Parker M.E., Chang C.C., Kasten R.W., Foley J.E., Laudre J., Murphy K., Swift P.K., Kramer V.L., O'Brien S.J., Seroprevalence of *Bartonella* infection in American free-ranging and captive pumas (*Felis concolor*) and bobcats (*Lynx rufus*), Vet Res. 35 (2004) 233–241.

[54] Chung C.Y., Kasten R.W., Paff S.M., Van Horn B.A., Vayssier-Taussat M., Boulouis H.J., Chomel B.B., *Bartonella* spp. DNA associated with biting flies from California, Emerg. Infect. Dis. 10 (2004) 1311–1313.

[55] Colombo A.P., Teles R.P., Torres M.C., Souto R., Rosalem W.J., Mendes M.C., Uzeda M., Subgingival microbiota of Brazilian subjects with untreated chronic periodontitis, J. Periodontol. 73 (2002) 360–369.

[56] Comer J.A., Flynn C., Regnery R.L., Vlahov D., Childs J.E., Antibodies to *Bartonella* species in inner-city intravenous drug users in Baltimore, MD, Arch. Intern. Med. 156 (1996) 2491–2495.

[57] Comer J.A., Diaz T., Vlahov D., Monterroso E., Childs J.E., Evidence of rodent-associated *Bartonella* and *Rickettsia* infections among intravenous drug users from Central and East Harlem, New York City, Am. J. Trop. Med. Hyg. 65 (2001) 855–860.

[58] Cunningham E.T., Koehler J.E., Ocular bartonellosis, Am. J. Ophthalmol. 130 (2000) 340–349.

[59] Cunningham E.T. Jr., Schatz H., McDonald H.R., Johnson R.N., Acute multifocal retinitis, Am. J. Ophthalmol. 123 (1997) 347–357.

[60] Daly J.S., Worthington M.G., Brenner D.J., Moss C.W., Hollis D.G., Weyant R.S., Steigerwalt A.G., Weaver R.E., Daneshvar M.I., O'Connor S.P., *Rochalimaea elizabethae* sp. nov. isolated from a patient with endocarditis, J. Clin. Microbiol. 31 (1993) 872–881.

[61] Daybell D., Paddock C.D., Zaki S.R., Comer J.A., Woodruff D., Hansen K.J., Peacock J.E. Jr., Disseminated infection with *Bartonella henselae* as a cause of spontaneous splenic rupture, Clin. Infect. Dis. 39 (2004) 21–24.

[62] Debré R., Job J.C., La maladie des griffes de chat, Acta Paediatr. Scand. Suppl. 43 (1954) 1–86.

[63] Debré R., Lamy M., Jammet M.L., Costil L., Mozziconacci P., La maladie des griffes de chat, Bull. Memb. Soc. Méd. Hosp. Paris 66 (1950) 76–79.

[64] Dehio C., Molecular and cellular basis of *Bartonella* pathogenesis, Annu. Rev. Microbiol. 58 (2004) 365–390.

[65] Demers D.M., Bass J.W., Vincent J.M., Person D.A., Noyes D.K., Staege C.M., Samlaska C.P., Lockwood N.H., Regnery R.L., Anderson B.E., Cat-scratch disease in Hawaii: etiology and seroepidemiology, J. Pediatr. 127 (1995) 23–26.

[66] Dharnidharka V.R., Richard G.A., Neiberger R.E., Fennell R.S. 3rd, Cat scratch disease and acute rejection after pediatric renal transplantation, Pediatr. Transplant. 6 (2002) 327–331.

[67] Diaz-Valle D., Toledano Fernandez N., Arteaga Sanchez A., Miguelez Sanchez R., Pascual Allen D., Severe retinal phlebitis in ocular bartonellosis, Arch. Soc. Esp. Oftalmol. 78 (2003) 223–226.

[68] Dillon B., Valenzuela J., Don R., Blanckenberg D., Wigney D.I., Malik R., Morris A.J., Robson J.M., Iredell J., Limited diversity among human isolates of *Bartonella henselae*, J. Clin. Microbiol. 40 (2002) 4691–4699.

[69] Dolan M.J., Wong M.T., Regnery R.L., Jorgensen J.H., Garcia M., Peters J., Drehner D., Syndrome of *Rochalimaea henselae* adenitis suggesting cat scratch disease, Ann. Intern. Med. 118 (1993) 331–336.

[70] Drancourt M., Birtles R., Chaumentin G., Vandenesch F., Etienne J., Raoult D., New serotype of *Bartonella henselae* in endocarditis and cat-scratch disease, Lancet 347 (1996) 441–443.

[71] Drancourt M., Bodaghi B., Lepidi H., Le Hoang P., Raoult D., Intraocular detection of *Bartonella henselae* in a patient with HLA-B27 uveitis, J. Clin. Microbiol. 42 (2004) 1822–1825.

[72] Droz S., Chi B., Horn E., Steigerwalt A.G., Whitney A.M., Brenner D.J., *Bartonella koehlerae* sp. nov., isolated from cats, J. Clin. Microbiol. 37 (1999) 1117–1122.

[73] Ebani V.V., Cerri D., Andreani E., Cat scratch disease. Survey on the presence of *Bartonella henselae* among cats of Tuscany, New Microbiol. 25 (2002) 307–313.

[74] Eckart P., Tournade G., Amiour M., Guillot M., Courtheoux P., Rousselot P., Pseudotumoral presentation of cat scratch disease, Arch. Pediatr. 8 (2001) 393–396.

[75] Engbaek K., Lawson P.A., Identification of *Bartonella* species in rodents, shrews and cats in Denmark: detection of two *B. henselae* variants, one in cats and the other in the long-tailed field mouse, APMIS 112 (2004) 336–341.

[76] Engvall E.O., Brandstrom B., Fermer C., Blomqvist G., Englund L., Prevalence of *Bartonella henselae* in young, healthy cats in Sweden, Vet. Rec. 152 (2003) 366–369.

[77] Ellis B.A., Regnery R.L., Beati L., Bacellar F., Rood M., Glass G.G., Marston E., Ksiazek T.G., Jones D., Childs J.E., Rats of the genus *Rattus* are reservoir hosts for pathogenic *Bartonella* species: an Old World origin for a New World disease? J. Infect. Dis. 180 (1999) 220–224.

[78] Eskow E., Rao R.V., Mordechai E., Concurrent infection of the central nervous system by *Borrelia burgdorferi* and *Bartonella henselae*: evidence for a novel tick-borne disease complex, Arch. Neurol. 58 (2001) 1357–1363.

[79] Easley R.B., Cooperstock M.S., Tobias J.D., Cat-scratch disease causing status epilepticus in children, South Med. J. 92 (1999) 73–76.

[80] Escarmelle A., Delbrassine N., De Potter P., Cat scratch disease and Parinaud's oculoglandular syndrome, J. Fr. Ophtalmol. 27 (2004) 179–183.

[81] Fabbi M., De Giuli L., Tranquillo M., Bragoni R., Casiraghi M., Genchi C., Prevalence of *Bartonella henselae* in Italian stray cats: evaluation of serology to assess the risk of transmission of *Bartonella* to humans, J. Clin. Microbiol. 42 (2004) 264–268.

[82] Fabbi M., Vicari N., Tranquillo M., Pozzi C., Prati P., De Meneghi D., Bertoletti I., Lauzi S., Guiso P., Genchi C., 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 46 (2004) 127–129.

[83] Finkelstein J.L., Brown T.P., O'Reilly K.L., Wedincamp J. Jr., Foil L.D., Studies on the growth of *Bartonella henselae* in the cat flea (Siphonaptera: Pulicidae), J. Med. Entomol. 39 (2002) 915–919.

[84] Foil L., Andress E., Freeland R.L., Roy A.F., Rutledge R., Triche P.C., O'Reilly K.L., Experimental infection of domestic cats with *Bartonella henselae* by inoculation of *Ctenocephalides felis* (Siphonaptera: Pulicidae) feces, J. Med. Entomol. 35 (1998) 625–628.

[85] Fournier P.E., Lelievre H., Eykyn S.J., Mainardi J.L., Marrie T.J., Bruneel F., Roure C., Nash J., Clave D., James E., Benoit-Lemercier C., Deforges L., Tissot-Dupont H., Raoult D., Epidemiologic and clinical characteristics of *Bartonella quintana* and *Bartonella henselae* endocarditis: a study of 48 patients, Medicine (Baltimore) 80 (2001) 245–251.

[86] Fournier P.E., Mainardi J.L., Raoult D., Value of microimmunofluorescence for diagnosis and follow-up of *Bartonella* endocarditis, Clin. Diagn. Lab. Immunol. 9 (2002) 795–801.

[87] Frean J., Arndt S., Spencer D., High rate of *Bartonella henselae* infection in HIV-positive outpatients in Johannesburg, South Africa, Trans. R. Soc. Trop. Med. Hyg. 96 (2002) 549–550.

[88] Gabler B., Linde H.J., Reischl U., Lohmann C.P., Disciform keratitis caused by *Bartonella henselae* infection: detection of a rare ocular complication of cat-scratch disease with PCR, Klin. Monatsbl. Augenheilkd. 217 (2000) 299–302.

[89] Gerber J.E., Johnson J.E., Scott M.A., Madhusudhan K.T., Fatal meningitis and encephalitis due to *Bartonella henselae* bacteria, J. Forensic. Sci. 47 (2002) 640–644.

[90] Ghez D., Bernard L., Bayou E., Bani-Sadr F., Vallee C., Perronne C., *Bartonella henselae* infection mimicking a splenic lymphoma, Scand. J. Infect. Dis. 33 (2001) 935–936.

[91] Gillespie T.N., Washabau R.J., Goldschmidt M.H., Cullen J.M., Rogala A.R., Breitschwerdt E.B., Detection of *Bartonella henselae* and *Bartonella clarridgeiae* DNA in hepatic specimens from two dogs with hepatic disease, J. Am. Vet. Med. Assoc. 222 (2003) 47–51.

[92] Glaus T., Hofmann-Lehmann R., Greene C., Glaus B., Wolfensberger C., Lutz H., Seroprevalence of *Bartonella henselae* infection and correlation with disease status in cats in Switzerland, J. Clin. Microbiol. 35 (1997) 2883–2885.

[93] Godet C., Roblot F., Le Moal G., Roblot P., Frat J.P., Becq-Giraudon B., Cat-scratch disease presenting as a breast mass, Scand. J. Infect. Dis. 36 (2004) 494–495.

[94] Gray A.V., Michels K.S., Lauer A.K., Samples J.R., *Bartonella henselae* infection associated with neuroretinitis, central retinal artery and vein occlusion, neovascular glaucoma, and severe vision loss, Am. J. Ophthalmol. 137 (2004) 187–189.

[95] Guptill L., Bartonellosis, Vet. Clin. North Am. Small Anim. Pract. 33 (2003) 809–825.

[96] Guptill L., Slater L., Wu C.C., Lin T.L., Glickman L.T., Welch D.F., HogenEsch H., Experimental infection of young specific pathogen-free cats with *Bartonella henselae*, J. Infect. Dis. 176 (1997) 206–216.

[97] Guptill L., Slater L.N., Wu C.C., Lin T.L., Glickman L.T., Welch D.F., Tobolski J., HogenEsch H., Evidence of reproductive failure and lack of perinatal transmission of *Bartonella henselae* in experimentally infected cats, Vet. Immunol. Immunopathol. 65 (1998) 177–189.

[98] Guptill L., Wu C.C., HogneEsch H., Slater L.N., Glickman N., Dunham A., Syme H., Glickman L., Prevalence, risk factors and genetic diversity of *Bartonella henselae* infections in pet cats in four regions of the United States, J. Clin. Microbiol. 42 (2004) 652–659.

[99] Gurfield A.N., Boulouis H.J., Chomel B.B., Heller R., Kasten R.W., Yamamoto K., Piemont Y., Coinfection with *Bartonella clarridgeiae* and *Bartonella henselae* and with different *Bartonella henselae* strains in domestic cats, J. Clin. Microbiol. 35 (1997) 2120–2123.

[100] Gurfield A.N., Boulouis H.J., Chomel B.B., Kasten R.W., Heller R., Bouillin C., Gandoin C., Thibault D., Chang C.C., Barrat F., Piemont Y., Epidemiology of *Bartonella* infection in domestic cats in France, Vet. Microbiol. 80 (2001) 185–198.

[101] Hadfield T.L., Warren R., Kass M., Brun E., Levy C., Endocarditis caused by *Rochalimaea henselae*, Hum. Pathol. 24 (1993) 1140–1141.

[102] Hadley S., Albrecht M.A., Tarsy D., Cat-scratch encephalopathy: a cause of status epilepticus and coma in a healthy young adult, Neurology 45 (1995) 196.

[103] Haimerl M., Tenter A.M., Simon K., Rommel M., Hilger J., Autenrieth I.B., Seroprevalence of *Bartonella henselae* in cats in Germany, J. Med. Microbiol. 48 (1999) 849–856.

[104] Hashkes P.J., Trabulsi A., Passo M.H., Systemic cat-scratch disease presenting as leukocytoclastic vasculitis, Pediatr. Infect. Dis. J. 15 (1996) 93–95.

[105] Hayem F., Chacar S., Hayem G., *Bartonella henselae* infection mimicking systemic onset juvenile chronic arthritis in a 2 1/2-year-old girl, J. Rheumatol. 23 (1996) 1263–1265.

[106] Heller R., Artois M., Xemar V., De Briel D., Gehin H., Jaulhac B., Monteil H., Piemont Y., Prevalence of *Bartonella henselae* and *Bartonella clarridgeiae* in stray cats, J. Clin. Microbiol. 35 (1997) 1327–1331.

[107] Henn J.B., Liu C.H., Kasten R.W., VanHorn B.A., Beckett L.A., Kass P.H., Chomel B.B., Seroprevalence of antibodies against *Bartonella* species and evaluation of risk factors and clinical signs associated with seropositivity in dogs, Am. J. Vet. Res. 66 (2005) in press.

[108] 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. 34 (2002) 192–196.

[109] Hofmeister E.K., Kolbert C.P., Abdulkarim A.S., Magera J.M., Hopkins M.K., Uhl J.R., Ambyaye A., Telford S.R. 3rd, Cockerill F.R. 3rd, Persing D.H., Cosegregation of a novel *Bartonella* species with *Borrelia burgdorferi* and *Babesia microti* in *Peromyscus leucopus*, J. Infect. Dis. 177 (1998) 409–416.

[110] Holmberg M., Mills J.N., McGill S., Benjamin G., Ellis B.A., *Bartonella* infection in sylvatic small mammals of central Sweden, Epidemiol. Infect. 130 (2003) 149–157.

[111] Honadel T.E., Chomel B.B., Yamamoto K., Chang C., Farver T.B., Seroepidemiology of *Bartonella vinsonii* subsp. *berkhoffii* exposure among healthy dogs, J. Am. Vet. Med. Assoc. 219 (2001) 480–484.

[112] Humar A., Salit I., Disseminated *Bartonella* infection with granulomatous hepatitis in a liver transplant recipient, Liver. Transpl. Surg. 5 (1999) 249–251.

[113] Jackson L.A., Perkins B.A., Wenger J.D., Cat scratch disease in the United States: An analysis of three national databases, Am. J. Public Health 83 (1993) 1707–1711.

[114] Jacobs R.F., Schutze G.E., *Bartonella henselae* as a cause of prolonged fever and fever of unknown origin in children, Clin. Infect. Dis. 26 (1998) 80–84.

[115] Jacomo V., Kelly P.J., Raoult D., Natural history of *Bartonella* infections (an exception to Koch's postulate), Clin. Diagn. Lab. Immunol. 9 (2002) 8–18.

[116] Jameson P., Green C., Regnery R., Dryden M., Marks A., Brown J., Cooper J., Glaus B., Greene R., Prevalence of *Bartonella henselae* antibodies in pet cats throughout regions of North America, J. Infect. Dis. 172 (1995) 1145–1149.

[117] Joseph A.K., Wood C.W., Robson J.M., Paul S.L., Morris A.J., *Bartonella henselae* bacteraemia in domestic cats from Auckland, N. Z. Vet. J. 45 (1997) 185–187.

[118] Juskevicius R., Vnencak-Jones C., Pathologic quiz case: a 17-year-old renal transplant patient with persistent fever, pancytopenia, and axillary lymphadenopathy. Bacillary angiomatosis of the lymph node in the renal transplant recipient, Arch. Pathol. Lab. Med. 128 (2004) e12–e14.

[119] Karras A., Thervet E., Legendre C., Groupe Cooperatif de transplantation d'Ile de France, Hemophagocytic syndrome in renal transplant recipients: report of 17 cases and review of literature, Transplantation 77 (2004) 238–243.

[120] Kelly P.J., Matthewman L.A., Hayter D., Downey S., Wray K., Bryson N.R., Raoult D., *Bartonella* (*Rochalimaea*) *henselae* in southern Africa – evidence for infections in domestic cats and implications for veterinarians, J. S. Afr. Vet. Assoc. 67 (1996) 182–187.

[121] Kelly P.J., Rooney J.J., Marston E.L., Jones D.C., Regnery R.L., *Bartonella henselae* isolated from cats in Zimbabwe, Lancet 351 (1998) 1706.

[122] Kempf V.A., Petzold H., Autenrieth I.B., Cat scratch disease due to *Bartonella henselae* infection mimicking parotid malignancy, Eur. J. Clin. Microbiol. Infect. Dis. 20 (2001) 732–733.

[123] Kerkhoff F.T., Bergmans A.M., van Der Zee A., Rothova A., Demonstration of *Bartonella grahamii* DNA in ocular fluids of a patient with neuroretinitis, J. Clin. Microbiol. 37 (1999) 4034–4038.

[124] Kitchell B.E., Fan T.M., Kordick D., Breitschwerdt E.B., Wollenberg G., Lichtensteiger C.A., Peliosis hepatis in a dog infected with *Bartonella henselae*, J. Am. Vet. Med. Assoc. 216 (2000) 519–523.

[125] Kobayashi K., Koga T., Oki T., Iwao K., Okumura A., Okinami S., Cat scratch disease with posterior segment involvement, Nippon Ganka Gakkai Zasshi 107 (2003) 99–104.

[126] Kodama T., Masuda H., Ohira A., Neuroretinitis associated with cat-scratch disease in Japanese patients, Acta Ophthalmol. Scand. 81 (2003) 653–657.

[127] Koehler J.E., Tappero J.W., Bacillary angiomatosis and bacillary peliosis in patients infected with human immunodeficiency virus, Clin. Infect. Dis. 17 (1993) 612–624.

[128] Koehler J.E., Glaser C.A., Tappero J.T., *Rochalimaea henselae* infection: A new zoonosis with the domestic cat as reservoir, JAMA 271 (1994) 531–535.

[129] Koehler J.E., Sanchez M.A., Garrido C.S., Whitfeld M.J., Chen F.M., Berger T.G., Rodriguez-Barradas M.C., LeBoit P.E., Tappero J.W., Molecular epidemiology of *Bartonella* infections in patients with bacillary angiomatosis-peliosis, N. Engl. J. Med. 337 (1997) 1876–1883.

[130] Koehler J.E., Sanchez M.A., Tye S., Garrido-Rowland C.S., Chen F.M., Maurer T., Cooper J.L., Olson J.G., Reingold A.L., Hadley W.K., Regnery R.R., Tappero J.W., Prevalence of *Bartonella* infection among human immunodeficiency virus-infected patients with fever, Clin. Infect. Dis. 37 (2003) 559–566.

[131] Kordick D.L., Breitschwerdt E.B., Relapsing bacteremia after blood transmission of *Bartonella henselae* to cats, Am. J. Vet. Res. 58 (1997) 492–497.

[132] Kordick D.L., Breitschwerdt E.B., Persistent infection of pets within a household with three *Bartonella* species, Emerg. Infect. Dis. 4 (1998) 325–328.

[133] Kordick D.L., Wilson K.H., Sexton D.J., Hadfield T.L., Berkhoff H.A., Breitschwerdt E.B., Prolonged *Bartonella* bacteremia in cats associated with cat-scratch disease patients, J. Clin. Microbiol. 33 (1995) 3245–3251.

[134] Kordick D.L., Swaminathan B., Greene C.E., Wilson K.H., Whitney A.M., O'Connor S., Hollis D.G., Matar G.M., Steigerwalt A.G., Malcolm G.B., Hayes P.S., Hadfield T.L., Breitschwerdt E.B., Brenner D.J., *Bartonella vinsonii* subsp. *berkhoffii* subsp. nov., isolated from dogs; *Bartonella vinsonii* subsp. *vinsonii*; and emended description of *Bartonella vinsonii*, Int. J. Syst. Bacteriol. 46 (1996) 704–709.

[135] Kordick D.L., Papich M.G., Breitschwerdt E.B., Efficacy of enrofloxacin or doxycycline for treatment of *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats, Antimicrob. Agents Chemother. 41 (1997) 2448–2455.

[136] Kordick D.L., Hilyard E.J., Hadfield T.L., Wilson K.H., Steigerwalt A.G., Brenner D.J.,

Breitschwerdt E.B., *Bartonella clarridgeiae*, a newly recognized zoonotic pathogen causing inoculation papules, fever, and lymphadenopathy (cat scratch disease), J. Clin. Microbiol. 35 (1997) 1813–1818.

[137] Kordick D.L., Brown T.T., Shin K., Breitschwerdt E.B., Clinical and pathologic evaluation of chronic *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats, J. Clin. Microbiol. 37 (1999) 1536–1547.

[138] Kordick S.K., Breitschwerdt E.B., Hegarty B.C., Southwick K.L., Colitz C.M., Hancock S.I., Bradley J.M., Rumbough R., Mcpherson J.T., MacCormack J.N., Coinfection with multiple tick-borne pathogens in a Walker Hound kennel in North Carolina, J. Clin. Microbiol. 37 (1999) 2631–2638.

[139] Kosoy M., Murray M., Gilmore R.D. Jr., Bai Y., Gage K.L., *Bartonella* strains from ground squirrels are identical to *Bartonella washoensis* isolated from a human patient, J. Clin. Microbiol. 41 (2003) 645–650.

[140] Krause R., Auner H.W., Daxbock F., Mulabecirovic A., Krejs G.J., Wenisch C., Reisinger E.C., Monoclonal and biclonal gammopathy in two patients infected with *Bartonella henselae*, Ann. Hematol. 82 (2003) 455–457.

[141] Lappin M.R., Kordick D.L., Breitschwerdt E.B., *Bartonella* spp. antibodies and DNA in aqueous humour of cats, J. Feline Med. Surg. 2 (2000) 61–68.

[142] La V.D., Clavel B., Leptez S., Aboudharam G., Raoult D., Drancourt M., Molecular detection of *Bartonella henselae* DNA in the dental pulp of 800-year-old French cats, Clin. Infect. Dis. 39 (2004) 1391–1394.

[143] La Scola B., Davoust B., Boni M., Raoult D., Lack of correlation between *Bartonella* DNA detection within fleas, serological results, and results of blood culture in a *Bartonella*-infected stray cat population, Clin. Microbiol. Infect. 8 (2002) 345–351.

[144] La Scola B., Liang Z., Zeaiter Z., Houpikian P., Grimont P.A., Raoult D., Genotypic characteristics of two serotypes of *Bartonella henselae*, J. Clin. Microbiol. 40 (2002) 2002–2008.

[145] La Scola B., Zeaiter Z., Khamis A., Raoult D., Gene-sequence-based criteria for species definition in bacteriology: the *Bartonella* paradigm, Trends Microbiol. 11 (2003) 318–321.

[146] Landau M., Kletter Y., Avidor B., Ephrat G., Ephros M., Brenner S., Giladi M., Unusual eruption as a presenting symptom of cat scratch disease, J. Am. Acad. Dermatol. 41 (1999) 833–836.

[147] Laycock G.M., Day M.J., Birtles R.J., Prevalence of *Bartonella henselae* in cats in the UK, Vet. Rec. 148 (2001) 219.

[148] Ledina D., Rincic J., Ivic I., Marasovic D., Ledina D., A child with *Bartonella henselae* osteomyelitis of the right humerus, Acta Dermatovenerol. Croat. 12 (2004) 92–95.

[149] Leighton F.A., Artsob H.A., Chu M.C., Olson J.G., A serological survey of rural dogs and cats on the southwestern Canadian prairie for zoonotic pathogens, Can. J. Public Health. 92 (2001) 67–71.

[150] Liston T.E., Koehler J.E., Granulomatous hepatitis and necrotizing splenitis due to *Bartonella henselae* in a patient with cancer: case report and review of hepatosplenic manifestations of *Bartonella* infection, Clin. Infect. Dis. 22 (1996) 951–957.

[151] Lozano F., Corzo J.E., Leon E.M., Rufo C., Loza A., Gomez-Mateos J.M., Massive hemoperitoneum: a new manifestation of bacillary peliosis in human immunodeficiency virus infection, Clin. Infect. Dis. 28 (1999) 911–912.

[152] Lucey D., Dolan M.J., Moss C.W., Garcia M., Hollis D.G., Wegner S., Morgan G., Almeida R., Leong D., Greisen K.S., Relapsing illness due to *Rochalimaea henselae* in immunocompetent hosts: implication for therapy and new epidemiological associations, Clin. Infect. Dis. 14 (1992) 683–688.

[153] Luria B.J., Levy J.K., Lappin M.R., Breitschwerdt E.B., Legendre A.M., Hernandez J.A., Gorman S.P., Lee I.T., Prevalence of infectious diseases in feral cats in Northern Florida, J. Feline Med. Surg. 6 (2004) 287–296.

[154] MacDonald K.A., Chomel B.B., Kittleson M.D., Kasten R.W., Thomas W.P., Pesavento P., A prospective study of canine infective endocarditis in northern California (1999–2001): emergence of *Bartonella* as a prevalent etiologic agent, J. Vet. Intern. Med. 18 (2004) 56–64.

[155] McGill S., Wesslen L., Hjelm E., Holmberg M., Rolf C., Friman G., Serological and epidemiological analysis of the prevalence of *Bartonella* spp. antibodies in Swedish elite orienteers 1992–1993, Scand. J. Infect. Dis. 33 (2001) 423–428.

[156] McGill S., Rajs J., Hjelm E., Lindquist O., Friman G., A study on forensic samples of *Bartonella* spp. antibodies in Swedish intravenous heroin addicts, APMIS 111 (2003) 507–513.

[157] Margileth A.M., Cat scratch disease, Adv. Pediatr. Infect. Dis. 8 (1993) 1–21.

[158] Margileth A.M., Recent advances in diagnosis and treatment of cat scratch disease, Curr. Infect. Dis. Rep. 2 (2000) 141–146.

[159] Margileth A.M., Baehren D.F., Chest-wall abscess due to cat-scratch disease (CSD) in an adult with antibodies to *Bartonella clarridgeiae*: case report and review of the thoracopulmonary manifestations of CSD, Clin. Infect. Dis. 27 (1998) 353–357.

[160] Markaki S., Sotiropoulou M., Papaspirou P., Lazaris D., Cat-scratch disease presenting as a solitary tumour in the breast: report of three cases, Eur. J. Obstet. Gynecol. Reprod. Biol. 106 (2003) 175–178.

[161] Marr B.P., Shields C.L., Shields J.A., Eagle R.C. Jr., Conjunctival cat-scratch disease simulating rhabdomyosarcoma, J. Pediatr. Ophthalmol. Strabismus 40 (2003) 302–303.

[162] Marra C.M., Neurologic complications of *Bartonella henselae* infection, Curr. Opin. Neurol. 8 (1995) 164–169.

[163] Marston E.L., Finkel B., Regnery R.L., Winoto I.L., Graham R.R., Wignal S., Simanjuntak G., Olson J.G., Prevalence of *Bartonella henselae* and *Bartonella clarridgeiae* in an urban Indonesian cat population, Clin. Diagn. Lab. Immunol. 6 (1999) 41–44.

[164] Maruyama S., Nogami S., Inoue I., Namba S., Asanome K., Katsube Y., Isolation of *Bartonella henselae* from domestic cats in Japan, J. Vet. Med. Sci. 58 (1996) 81–83.

[165] Maruyama S., Hiraga S., Yokoyama E., Naoi M., Tsuruoka Y., Ogura Y., Tamura K., Namba S., Kameyama Y., Nakamura S., Katsube Y., Seroprevalence of *Bartonella henselae* and *Toxoplasma gondii* infections among pet cats in Kanagawa and Saitama Prefectures, J. Vet. Med. Sci. 60 (1998) 997–1000.

[166] Maruyama S., Nakamura Y., Kabeya H., Tanaka S., Sakai T., Katsube Y., Prevalence of *Bartonella henselae*, *Bartonella clarridgeiae* and the 16S rRNA gene types of *Bartonella henselae* among pet cats in Japan, J. Vet. Med. Sci. 62 (2000) 273–279.

[167] Maruyama S., Sakai T., Morita Y., Tanaka S., Kabeya H., Boonmar S., Poapolathep A., Chalarmchaikit T., Chang C.C., Kasten R.W., Chomel B.B., Katsube Y., Prevalence of *Bartonella* species and 16s rRNA gene types of *Bartonella henselae* from domestic cats in Thailand, Am. J. Trop. Med. Hyg. 65 (2001) 783–787.

[168] Maruyama S., Kabeya H., Nakao R., Tanaka S., Sakai T., Xuan X., Katsube Y., Mikami T., Seroprevalence of *Bartonella henselae*, *Toxoplasma gondii*, FIV and FeLV infections in domestic cats in Japan, Microbiol. Immunol. 47 (2003) 147–153.

[169] Mason J.O. 3rd, Retinal and optic nerve neovascularization associated with cat scratch neuroretinitis, Retina 24 (2004) 176–178.

[170] Melter O., Hercik K., Weyant R.S., Janecek J., Nemec A., Mecera J., Gonzorova L., Branny P., Detection and characterization of feline *Bartonella henselae* in the Czech Republic, Vet. Microbiol. 93 (2003) 261–273.

[171] Mexas A.M., Hancock S.I., Breitschwerdt E.B., *Bartonella henselae* and *Bartonella elizabethae* as potential canine pathogens, J. Clin. Microbiol. 40 (2002) 4670–4674.

[172] Millot F., Tailboux L., Paccalin M., Barret D., Zelinsky A., Thomas E., Levillain P., Guilhot F., Cat-scratch disease simulating a malignant process of the chest wall, Eur. J. Pediatr. 158 (1999) 403–405.

[173] Nasirudeen A.M., Thong M.L., Prevalence of *Bartonella henselae* immunoglobulin G antibodies in Singaporean cats, Pediatr. Infect. Dis. J. 18 (1999) 276–278.

[174] Ng S.O., Yates M.T., Ease of isolation and semiquantitative culture of *Bartonella henselae* from cats in Melbourne, Pathology 29 (1997) 333–334.

[175] Noah D.L., Bresee J.S., Gorensek M.J., Rooney J.A., Cresanta J.L., Regnery R.L., Wong J., del Toro J., Olson J.G., Childs J.E., Cluster of five children with acute encephalopathy associated with cat-scratch disease in south Florida, Pediatr. Infect. Dis. J. 14 (1995) 866–869.

[176] Nutter F.B., Dubey J.P., Levine J.F., Breitschwerdt E.B., Ford R.B., Stoskopf M.K., Seroprevalences of antibodies against *Bartonella henselae* and *Toxoplasma gondii* and fecal shedding of *Cryptosporidium* spp., *Giardia* spp., and *Toxocara cati* in feral and pet domestic cats, J. Am. Vet. Med. Assoc. 225 (2004) 1394–1398.

[177] O'Halloran H.S., Draud K., Minix M., Rivard A.K., Pearson P.A., Leber's neuroretinitis in a patient with serologic evidence of *Bartonella elizabethae*, Retina 18 (1998) 276–278.

[178] O'Reilly K.L., Bauer R.W., Freeland R.L., Foil L.D., Hughes K.J., Rohde K.R., Roy A.F., Stout R.W., Triche P.C., Acute clinical disease in cats following infection with a pathogenic strain of *Bartonella henselae* (LSU16), Infect. Immun. 67 (1999) 3066–3072.

[179] Ormerod L.D., Dailey J.P., Ocular manifestations of cat-scratch disease, Curr. Opin. Ophthalmol. 10 (1999) 209–216.

[180] Ormerod L.D., Skolnick K.A., Menosky M.M., Pavan P.R., Pon D.M., Retinal and choroidal manifestations of cat-scratch disease, Ophthalmology 105 (1998) 1024–1031.

[181] Pappalardo B.L., Correa M.T., York C.C., Peat C.Y., Breitschwerdt E.B., Epidemiologic evaluation of the risk factors associated with exposure and seroreactivity to *Bartonella vinsonii* in dogs, Am. J. Vet. Res. 58 (1997) 467–471.

[182] Pappalardo B.L., Brown T., Gookin J.L., Morrill C.L., Breitschwerdt E.B., Granulomatous disease associated with *Bartonella* infection in two dogs, J. Vet. Intern. Med. 14 (2000) 37–42.

[183] Peter J.B., Boyle M., Patnaik M., Hadfield T.L., Barka N.E., Schwartzman W.A., Penny R.S., Persistent generalized lymphadenopathy and non-Hodgkin's lymphoma in AIDS: association with *Rochalimaea henselae* infection, Clin. Diagn. Lab. Immunol. 1 (1994) 115–116.

[184] Podsiadly E., Sokolowska E., Tylewska-Wierzbanowska S., Seroprevalence of *Bartonella henselae* and *Bartonella quintana* infections in Poland in 1998–2001, Ann. NY Acad. Sci. 990 (2003) 407–408.

[185] Podsiadly E., Chmielewski T., Tylewska-Wierzbanowska S., *Bartonella henselae* and *Borrelia burgdorferi* infections of the central nervous system, Ann. NY Acad. Sci. 990 (2003) 404–406.

[186] Pollock S.C., Kristinsson J., Cat-scratch disease manifesting as unifocal helioid choroiditis, Arch. Ophthalmol. 116 (1998) 1249–1251.

[187] Pretorius A.M., Kelly P.J., Birtles R.J., Raoult D., Isolation of *Bartonella henselae* from a serologically negative cat in Bloemfontein,

South Africa, J. S. Afr. Vet. Assoc. 70 (1999) 154–155.

[188] Puligheddu M., Giagheddu A., Genugu F., Giagheddu M., Marrosu F., Epilepsia partialis continua in cat scratch disease, Seizure 13 (2004) 191–195.

[189] Raoult D., Fournier P.E., Drancourt M., Marrie T.J., Etienne J., Cosserat J., Cacoub P., Poinsignon Y., Leclercq P., Sefton A.M., Diagnosis of 22 new cases of *Bartonella* endocarditis, Ann. Intern. Med. 125 (1996) 646–652.

[190] Raoult D., Fournier P.E., Vandenesch F., Mainardi J.L., Eykyn S.J., Nash J., James E., Benoit-Lemercier C., Marrie T.J., Outcome and treatment of *Bartonella* endocarditis, Arch. Intern. Med. 163 (2003) 226–230.

[191] Regnery R.L., Anderson B.E., Clarridge J.E. 3rd, Rodriguez-Barradas M.C., Jones D.C., Carr J.H., Characterization of a novel *Rochalimaea* species, *R. henselae* sp. nov., isolated from blood of a febrile, human immunodeficiency virus-positive patient, J. Clin. Microbiol. 30 (1992) 265–274.

[192] Regnery R., Martin M., Olson J., Naturally occurring "*Rochalimaea henselae*" infection in domestic cat, Lancet 340 (1992) 557–558.

[193] Regnery R.L., Childs J.E., Koehler J.E., Infections associated with *Bartonella* species in persons infected with human immunodeficiency virus, Clin. Infect. Dis. 21 (1995) S94–S98.

[194] Regnery R.L., Rooney J.A., Johnson A.M., Nesby S.L., Manzewitsch P., Beaver K., Olson J.G., Experimentally induced *Bartonella henselae* infections followed by challenge exposure and antimicrobial therapy in cats, Am. J. Vet. Res. 57 (1996) 1714–1719.

[195] Rocha J.L., Pellegrino L.N., Riella L.V., Martins L.T., Acute hemiplegia associated with cat-scratch disease, Braz. J. Infect. Dis. 8 (2004) 263–266.

[196] Rolain J.M., Fournier P.E., Raoult D., Bonerandi J.J., First isolation and detection by immunofluorescence assay of *Bartonella koehlerae* in erythrocytes from a French cat, J. Clin. Microbiol. 41 (2003) 4001–4002.

[197] 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. 9 (2003) 338–342.

[198] Rolain J.M., Brouqui P., Koehler J.E., Maguina C., Dolan M.J., Raoult D., Recommendations for treatment of human infections caused by *Bartonella* species, Antimicrob. Agents Chemother. 48 (2004) 1921–1933.

[199] 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. 11 (2004) 423–425.

[200] Roux V., Eykyn S.J., Wyllie S., Raoult D., *Bartonella vinsonii* subsp. *berkhoffii* as an agent of a febrile blood culture-negative endocarditis in a human, J. Clin. Microbiol. 38 (2000) 1698–1700.

[201] Roux V., Raoult D., Inter- and intraspecies identification of *Bartonella* (*Rochalimaea*) species, J. Clin. Microbiol. 33 (1995) 1573–1579.

[202] Sander A., Frank B., Paronychia caused by *Bartonella henselae*, Lancet 350 (1997) 1078.

[203] Sander A., Buhler C., Pelz K., von Cramm E., Bredt W., Detection and identification of two *Bartonella henselae* variants in domestic cats in Germany, J. Clin. Microbiol. 35 (1997) 584–587.

[204] Sander A., Posselt M., Oberle K., Bredt W., Seroprevalence of antibodies to *Bartonella henselae* in patients with cat scratch disease and in healthy controls: evaluation and comparison of two commercial serological tests, Clin. Diagn. Lab. Immunol. 5 (1998) 486–490.

[205] Sander A., Zagrosek A., Bredt W., Schiltz E., Piemont Y., Lanz C., Dehio C., Characterization of *Bartonella clarridgeiae* flagellin (FlaA) and detection of antiflagellin antibodies in patients with lymphadenopathy, J. Clin. Microbiol. 38 (2000) 2943–2948.

[206] Schmoor P., Darie H., Maccari F., Gros P., Millet P., Cutaneous vasculitis disclosing cat-scratch disease, Ann. Dermatol. Venereol. 125 (1998) 894–896.

[207] Schulein R., Seubert A., Gille C., Lanz C., Hansmann Y., Piemont Y., Dehio C., Invasion and persistent intracellular colonization of erythrocytes. A unique parasitic strategy of the emerging pathogen *Bartonella*, J. Exp. Med. 193 (2001) 1077–1086.

[208] Serratrice J., Rolain J.M., Granel B., Ene N., Conrath J., Avierinos J.F., Disdier P., Raoult D., Weiller P.J., Bilateral retinal artery branch occlusions revealing *Bartonella grahamii* infection, Rev. Med. Interne 24 (2003) 629–630.

[209] Signorini L., Simeone F., Tonegatti L., Colombini P., Cadeo B., Cristini F., Matteeli A., Viale P., Co-infection with Esptein-Barr virus and *Bartonella henselae* resulting in systemic bartonellosis, J. Infect. 45 (2002) 206–207.

[210] Smith H.M., Reporter R., Rood M.P., Linscott A.J., Mascola L.M., Hogrefe W., Purcell R.H., Prevalence study of antibody to rat-borne pathogens and other agents among patients using a free clinic in downtown Los Angeles, J. Infect. Dis. 186 (2002) 1673–1676.

[211] Smoller B.R., Madhusudhan K.T., Scott M.A., Horn T.D., Granuloma annulare – Another manifestation of *Bartonella* infection? Am. J. Dermatol. 23 (2001) 510–513.

[212] Solano-Gallego L., Bradley J., Hegarty B., Sigmon B., Breitschwerdt E., *Bartonella henselae* IgG antibodies are prevalent in dogs from southeastern USA, Vet. Res. 35 (2004) 585–595.

[213] Spach D.H., Koehler J.E., *Bartonella*-associated infections, Infect. Dis. Clin. North Am. 12 (1998) 137–155.

[214] Spach D.H., Callis K.P., Paauw D.S., Houze Y.B., Schoenknecht F.D., Welch D.F., Rosen H., Brenner D.J., Endocarditis caused by *Rochalimaea quintana* in a patient infected with human immunodeficiency virus, J. Clin. Microbiol. 31 (1993) 692–694.

[215] Suksawat J., Xuejie Y., Hancock S.I., Hegarty B.C., Nilkumhang P., Breitschwerdt E.B., Serologic and molecular evidence of coinfection with multiple vector-borne pathogens in dogs from Thailand, J. Vet. Intern. Med. 15 (2001) 453–462.

[216] Tattevin P., Lellouche F., Bruneel F., Regnier B., De Broucker T., *Bartonella henselae* meningoencephalitis, Rev. Neurol. (Paris) 157 (2001) 698–700.

[217] Tsujino K., Tsukahara M., Tsuneoka H., Ichihara K., Furuya T., Kawauchi S., Oga A., Sasaki K., Clinical implication of prolonged fever in children with cat scratch disease, J. Infect. Chemother. 10 (2004) 227–233.

[218] Tsukahara M., Tsuneoka H., Iino H., Murano I., Takahashi H., Uchida M., *Bartonella henselae* infection as a cause of fever of unknown origin, J. Clin. Microbiol. 38 (2000) 1990–1991.

[219] Tsuneoka H., Umeda A., Tsukahara M., Sasaki K., Evaluation of indirect fluorescence antibody assay for detection of *Bartonella clarridgeiae* and seroprevalence of *B. clarridgeiae* among patients with suspected cat scratch disease, J. Clin. Microbiol. 42 (2004) 3346–3349.

[220] Tuttle A.D., Birkenheuer A.J., Juopperi T., Levy M.G., Breitschwerdt E.B., Concurrent bartonellosis and babesiosis in a dog with persistent thrombocytopenia, J. Am. Vet. Med. Assoc. 223 (2003) 1306–1310, 1280–1281.

[221] Ueno H., Muramatsu Y., Chomel B.B., Hohdatsu T., Koyama H., Morita C., Seroepidemiological survey of *Bartonella* (*Rochalimaea*) *henselae* in domestic cats in Japan, Microbiol. Immunol. 39 (1995) 339–341.

[222] Ueno H., Hohdatsu T., Muramatsu Y., Koyama H., Morita C., Does coinfection of *Bartonella henselae* and FIV induce clinical disorders in cats? Microbiol. Immunol. 40 (1996) 617–620.

[223] Van Tooren R.M., Van Leusen R., Bosch F.H., Culture negative endocarditis combined with glomerulonephritis caused by *Bartonella* species in two immunocompetent adults, Neth. J. Med. 59 (2001) 218–224.

[224] Velho P.E., Cintra M.L., Uthida-Tanaka A.M., de Moraes A.M., Mariotto A., What do we (not) know about the human bartonelloses? Braz. J. Infect. Dis. 7 (2003) 1–6.

[225] Von Kobyletzki G., Nordmeier R., Stucker M., Sandmann M., Respondek M., Baier J., Altmeyer P., Acute generalized cat scratch disease in myelodysplastic syndrome, Hautarzt 52 (2001) 980–984.

[226] Wade N.K., Levi L., Jones M.R., Bhisitkul R., Fine L., Cunningham E.T. Jr., Optic disk edema associated with peripapillary serous retinal detachment: an early sign of systemic *Bartonella henselae* infection, Am. J. Ophthalmol. 130 (2000) 327–334.

[227] Walter R.S., Eppes S.C., Cat scratch disease presenting with peripheral facial nerve paralysis, Pediatrics 101 (1998) E13.

[228] Welch D.F., Carroll K.C., Hofmeister E.K., Persing D.H., Robison D.A., Steigerwalt A.G., Brenner D.J., Isolation of a new subspecies, *Bartonella vinsonii* subsp. *arupensis*, from a cattle rancher: identity with isolates found in conjunction with *Borrelia burgdorferi* and *Babesia microti* among naturally infected mice, J. Clin. Microbiol. 37 (1999) 2598–2601.

[229] Wesslen L., Ehrenborg C., Holmberg M., McGill S., Hjelm E., Lindquist O., Henriksen E., Rolf C., Larsson E., Friman G., Subacute *Bartonella* infection in Swedish orienteers succumbing to sudden unexpected cardiac death or having malignant arrhythmias, Scand. J. Infect. Dis. 33 (2001) 429–438.

[230] Wong M.T., Dolan M.J., Lattuada C.P. Jr., Regnery R.L., Garcia M.L., Mokulis E.C., LaBarre R.A., Ascher D.P., Delmar J.A., Kelly J.W. et al., Neuroretinitis, aseptic meningitis, and lymphadenitis associated with *Bartonella* (*Rochalimaea*) *henselae* infection in immunocompetent patients and patients infected with human immunodeficiency virus type 1, Clin. Infect. Dis. 21 (1995) 352–360.

[231] Wong T.Z., Kruskal J., Kane R.A., Trey G., Cat-scratch disease simulating lymphoma, J. Comput. Assist. Tomogr. 20 (1996) 165–166.

[232] Yamamoto K., Chomel B.B., Kasten R.W., Chang C.C., Tseggai T., Decker P.R., Mackowiak M., Floyd-Hawkins K.A., Pedersen N.C., Homologous protection but lack of heterologous-protection by various species and types of *Bartonella* in specific pathogen-free cats, Vet. Immunol. Immunopathol. 65 (1998) 191–204.

[233] Yamamoto K., Chomel B.B., Kasten R.W., Hew C.M., Weber D.K., Lee W.I., Koehler J.E., Pedersen N.C., Infection and re-infection of domestic cats with various *Bartonella* species or types: *B. henselae* type I is protective against heterologous challenge with *B. henselae* type II, Vet. Microbiol. 92 (2003) 73–86.

[234] Ying B., Kosoy M.Y., Maupin G.O., Tsuchiya K.R., Gage K.L., Genetic and ecologic characteristics of *Bartonella* communities in rodents in southern China, Am. J. Trop. Med. Hyg. 66 (2002) 622–627.

[235] Zangwill K.M., Hamilton D.H., Perkins B.A., Regnery R.L., Plikaytis B.D., Hadler J.L., Cartter M.L., Wenger J.D., Cat scratch disease in Connecticut. Epidemiology, risk factors, and evaluation of a new diagnostic test, N. Engl. J. Med. 329 (1993) 8–13.

[236] Zaror L., Ernst S., Navarrete M., Ballesteros A., Boroscheck D., Ferres M., Thibaut J., Serologic detection of *Bartonella henselae* in cats in the city of Valdivia, Chile, Arch. Med. Vet. 34 (2002) 103–110.