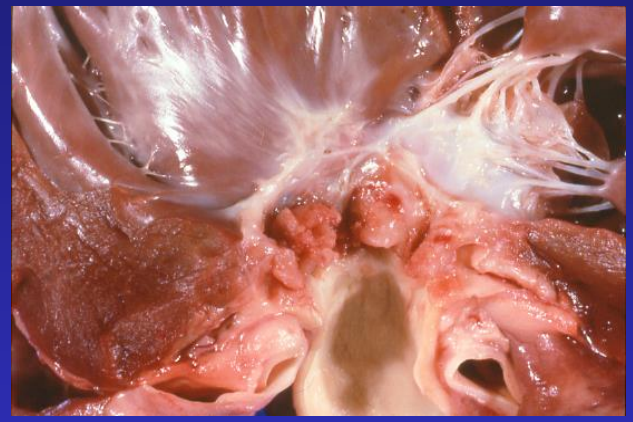
2nd European Crypto-infections Conference,
Catherine Mc Auley Centre, Dublin, Ireland, September 26-27, 2020.

Endocarditis, a common pathology caused by chronic Bartonella infections in both animals and humans



Bruno B. CHOMEL

Distinguished Professor of Zoonoses

Department of Population Health and Reproduction,
School of Veterinary Medicine,
University of California, Davis, CA, USA

Updated: 9/25/2020

UCDAVIS VETERINARY MEDICINE

Alpha-Proteobacteria

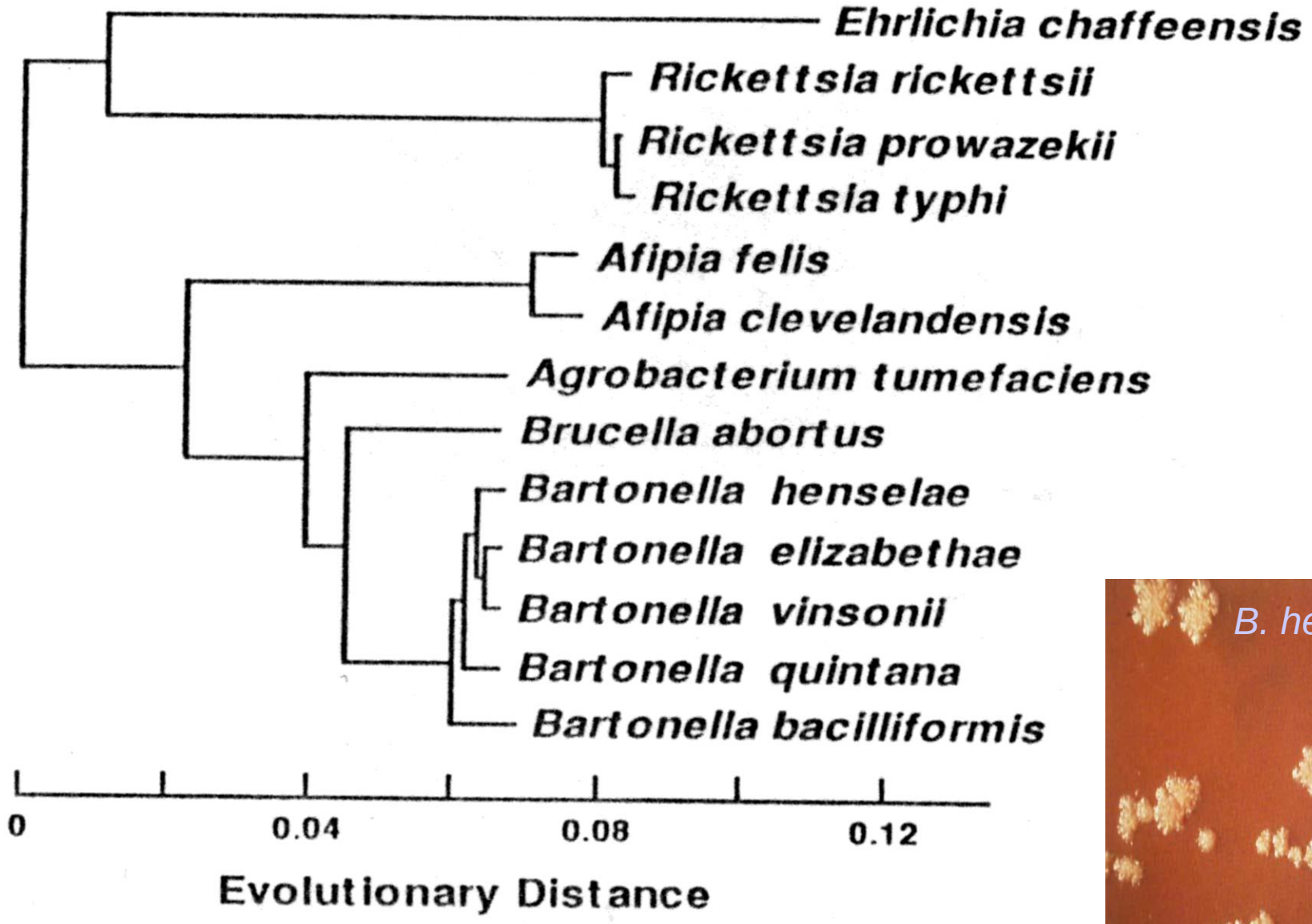


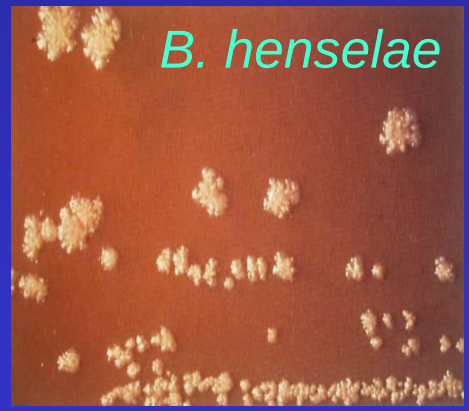
TABLE 1 Currently designated *Bartonella* species, their hosts, and associated human disease

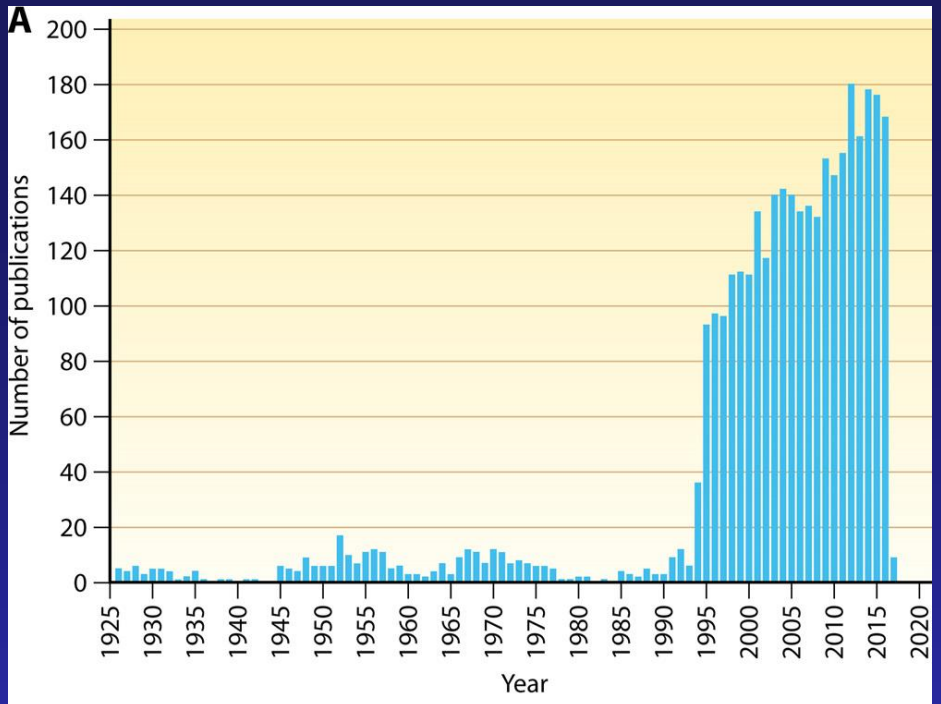
Species	Host(s)	Human disease association
B. acomydis	Golden spiny mouse (*Acomys russatus*) (398)	
B. alsatica	Rabbits (39)	Endocarditis (40)
B. ancashensis	Human patient (41)	Verruga peruana (41, 399)
B. apis	Honeybee symbiont (400)	
B. australis	Kangaroos (58)	
B. bacilliformis	Human (26, 401)	Oroya fever, verruga peruana, Carrion's disease (26)
B. birtlesii	Mice (402)	
B. bovis	Dairy cattle (403)	
B. callosciuri	Plantain squirrel (398)	
B. capreoli	Deer (403)	
B. chomelii	French cattle (404)	
B. clarridgeiae	Cat (187)	Lymphadenopathy, fever, papule, CSD (44, 187)
B. coopersplainsensis	Rat (58)	
B. doshiae	Voles (405)	
B. dromedarii	Camels (406)	
B. elizabethae	Rats (24)	Endocarditis, neuroretinitis (18, 407)
B. florenciae	Shrew, mouse (408)	
B. fuyuanensis	Field mouse (409)	
B. grahamii	Rodents, voles (405)	Neuroretinitis, CSD (51, 53)
B. heixiaziensis	Vole (409)	
B. henselae	Cat (31, 140)	CSD, endocarditis, bacillary angiomatosis, bacteremia (140)
B. jaculi	Greater Egyptian jerboa (398)	
B. japonica	Mice (410)	
B. koehlerae	Cat (411)	Endocarditis (19)
B. koehlerae subsp. *bothieri*	Bobcat (412)	
B. koehlerae subsp. *boulouisii*	Mountain lion (412)	
B. mayotimonensis	Bats (55)	Endocarditis (20)
B. melophagi	Sheep (413)	
B. naantaliensis	Bats (55)	
B. peromysci	Mouse (405)	
B. pachyuromydis	Fat-tail gerbil (398)	
B. phoceensis	Rat (414)	
B. queenslandensis	Rats (58)	
B. quintana	Human (415)	Trench fever, endocarditis, bacteremia, bacillary angiomatosis
B. rattaustraliani	Rats (416)	
B. rattimassiliensis	Rats (414)	
B. rochalimae	Foxes, raccoons, coyotes (57, 417)	Bacteremia, splenomegaly (57)
B. silvatica	Mice (410)	
B. schoenbuchensis	Deer (418)	
B. senegalensis	Tick (419)	
B. talpae	Moles (405)	
B. tamiae	Rodents, humans (58)	Fever (58, 59)
B. taylorii	Rats (405)	
B. tribocorum	Rats (420)	
B. vinsonii subsp. *arupensis*	Mice (65)	Endocarditis (21)
B. vinsonii subsp. *berkhoffii*	Dog, coyotes (181, 421)	Endocarditis (23)
B. vinsonii subsp. *vinsonii*	Voles (24)	
B. vinsonii subsp. *yucatanensis*	Rodents (5)	
B. weissii	Cat (181)	
B. washoensis	Dog (422)	

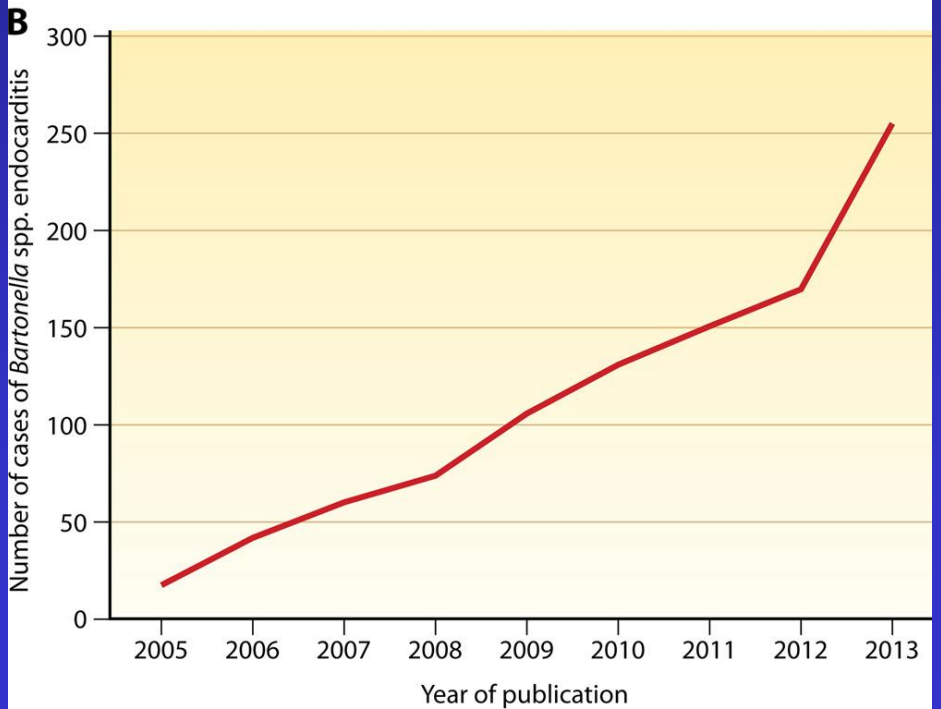
Okaro et al.,
Clin Microbiol Rev.
2017l;30:709-746

Conditions caused by *Bartonella* species in Humans

Bartonella sp.	N	Condition (s)
B. bacilliformis	10^3	Carrion's disease (Oroya fever or verruga peruana), Andes, Peru [Not Z]
B. quintana (Z)	10^2	Trench fever, endocarditis, chronic bacteremia, bacillary angiomatosis Worldwide
B. henselae (Z)	10^4	Cat scratch disease, endocarditis, myocarditis, chronic bacteremia, neuroretinitis, arthritis, status epilepticus, bacillary angiomatosis, peliosis hepatis, prolonged fever, weight loss, glomerulonephritis, osteomyelitis… (Worldwide)
B. clarridgeiae (Z)	<5	CSD?, health blood donor, endocarditis (Brazil, USA)
B. elizabethae (Z)	<5	Endocarditis, Neuroretinitis
B. v. berkhoffii (Z)	<5	Endocarditis (USA)
B. grahamii (Z)	<5	Uveitis, bilateral occlusion of retinal artery (The Nehterlands)
B. v. arupensis (Z)	<10	Fever, confusion, underlying valvulopathy, (Thailand)
B. washoensis(Z)	<5	Fever, Myocarditis (USA)
B. koehlerae (Z)	<5	Endocarditis, (Israel)
B. alsatica (Z)	<5	Endocarditis, lymphadenopathy, (France)
B. rochalimae (Z)	<5	Fever, enlarged spleen, (Peru/USA)
B. tamiae (Z??)	<5	Fever, ocular symptoms, fatigue, myalgia, (Thailand)
B.volans-like (Z)	<5	Joint pain, memory loss, and incoordination, (USA)
B. mayotimonensis (Z)	<5	Endocarditis, (USA)
B. rattimassiliensis (Z)	<5	Febrile patient, (Thailand)
B. vinsonii vinsonii (Z)	<5	Febrile patient, (Thailand)
B. tribocorum (Z)	<5	Chronic fatigue, Lyme negative, tick exposure, (France)
B. doshiae (Z)	<5	Chronic fatigue, Lyme negative, tick exposure, (France)
B. schoenbuchensis (Z)	<5	Chronic fatigue, Lyme negative, tick exposure, (France)





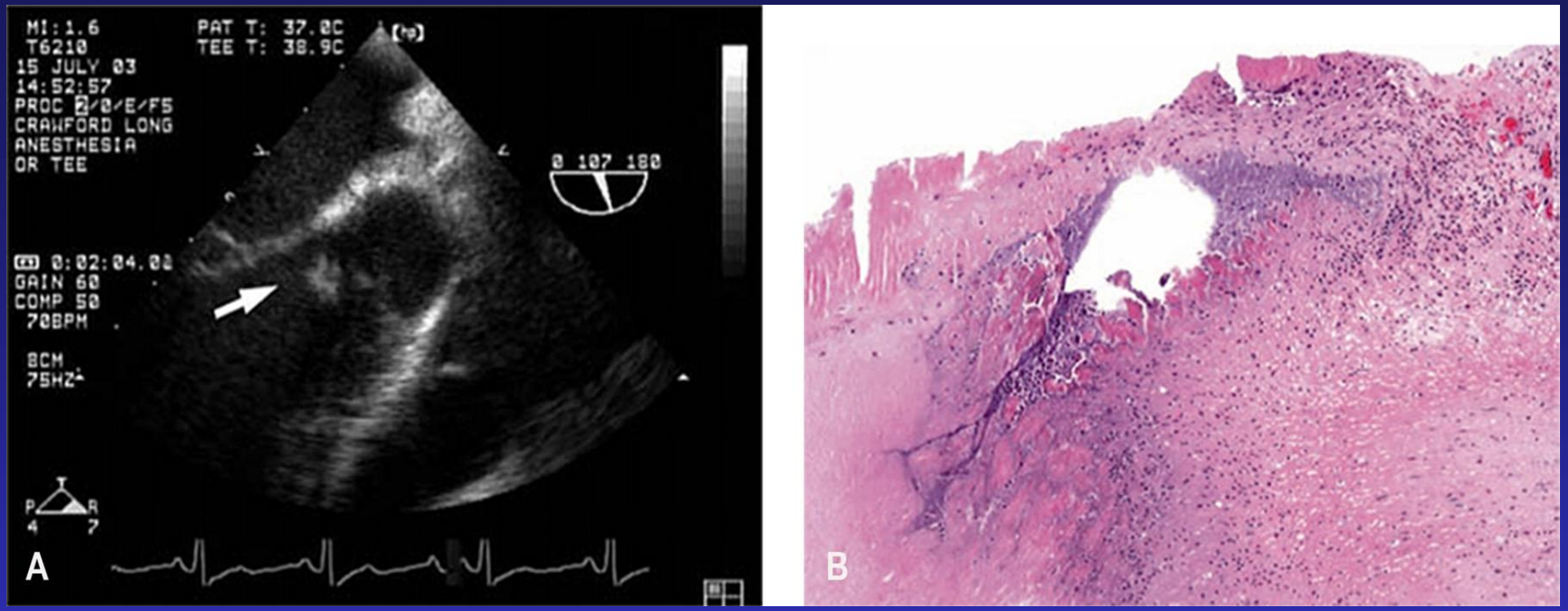


" In France, approximately 20% to 30% of all documented cases of Blood Culture Negative Endocarditis (BCNE) are *Bartonella* endocarditis, representing the second most common cause of endocarditis following *Coxiella burnetii*"

(A) Number of publications on *Bartonella* in PubMed. Source: https://www.ncbi.nlm.nih.gov/pubmed/?term bartonella.

(B) Increase in reported *Bartonella* endocarditis cases. (Adapted from Edouard et al.

Okaro et al.,
Clin Microbiol Rev.
2017l;30(3):709-746

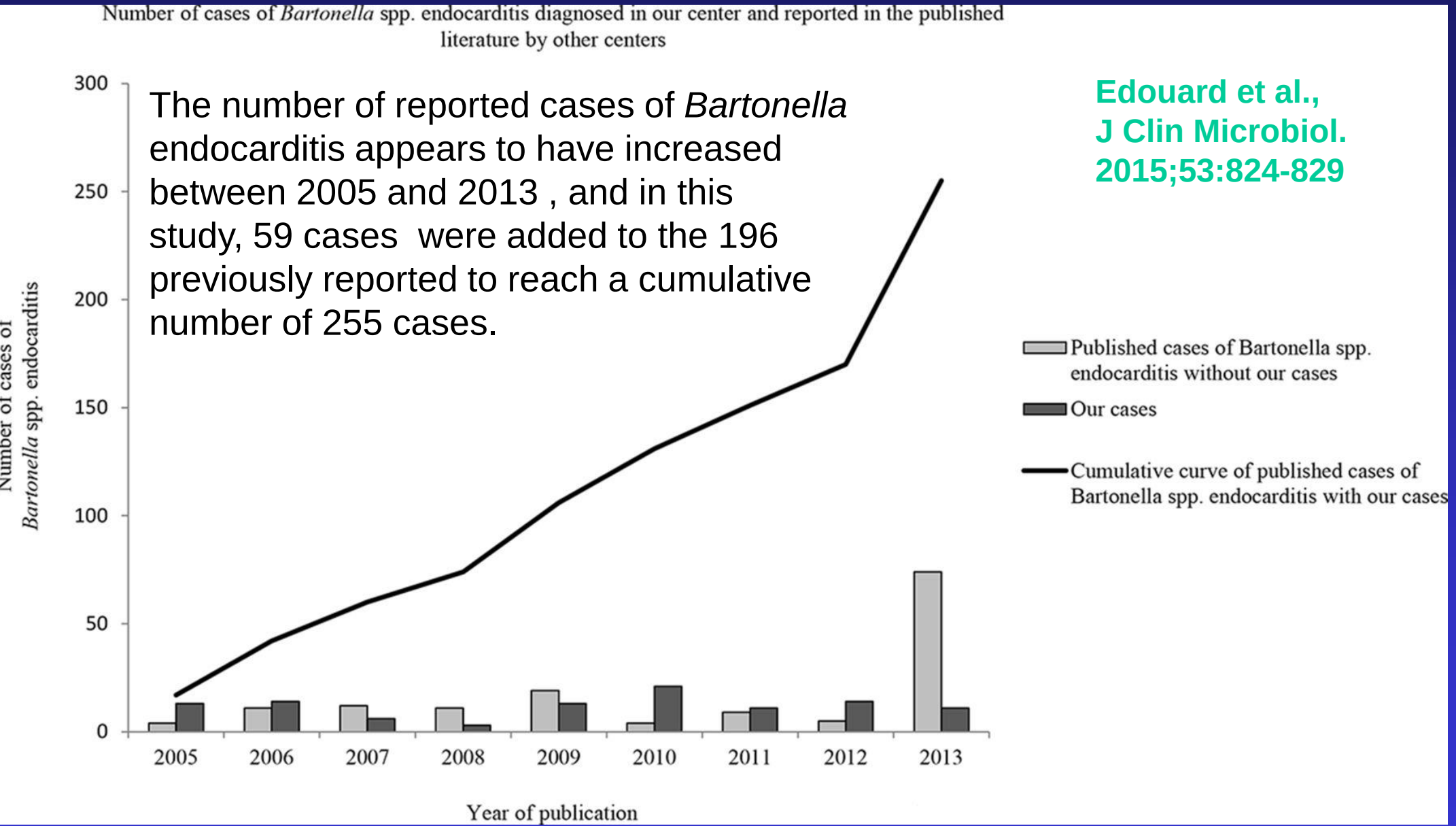


(A) Transoesophageal echocardiogram from a patient with BCNE caused by *B. henselae*. Bicuspid aortic valve with left coronary leaflet almost entirely replaced by a large vegetation (arrow).

(B) Giemsa stain of the patient in panel A showing extensive fibrosis and coccobacilli on the aortic valve that were confirmed to be *B. henselae*

Okaro et al., Clin Microbiol Rev. 2017l;30(3):709-746

Bartonella, a Common cause of endocarditis: a Report on 106 Cases and Review



The number of reported cases of *Bartonella* endocarditis appears to have increased between 2005 and 2013 , and in this study, 59 cases were added to the 196 previously reported to reach a cumulative number of 255 cases.

Edouard et al., J Clin Microbiol. 2015;53:824-829

Bartonella, a Common cause of endocarditis: a Report on 106 Cases and Review

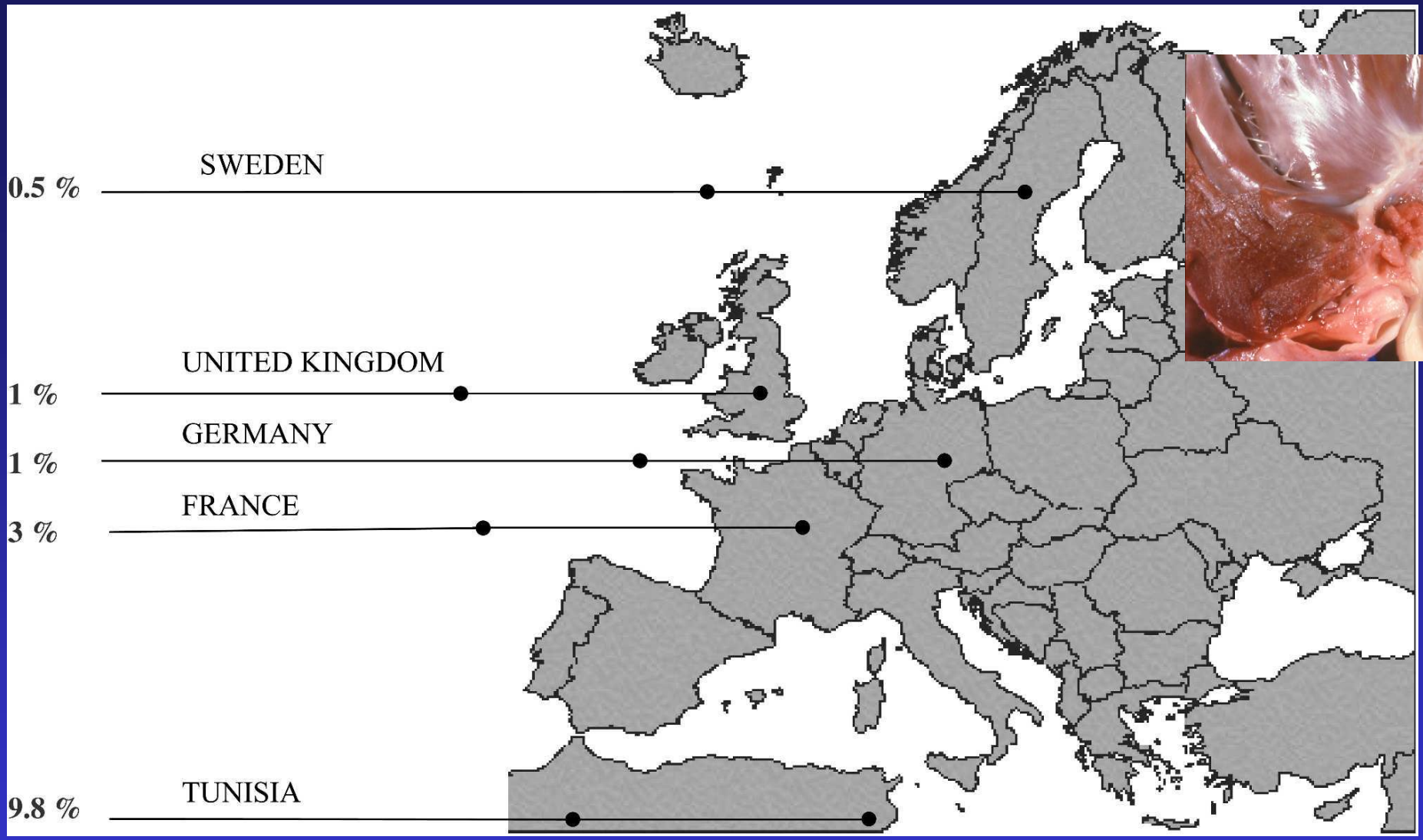
Edouard et al., J Clin Microbiol. 2015;53:824-829.

TABLE 1 Microbiologic diagnosis of 106 patients with *Bartonella* endocarditis

Test type and criteria	No. of positive samples/no. of samples tested (%)
IFA	
IFA with IgG titer ≥ 100	93/102 (91)
IFA with IgG titer ≥ 800	59/93 (63)
IFA with IgG titer from 1:100 to 1:800	34/93 (37)
Negative IFA	9/102 (9)
Western blotting	
Total	73/73 (100)
Patient with IgG titer ≥ 1:800	40/40 (100)
Patient with IgG titer from 1:100 to 1:800	25/25 (100)
Patient with negative IFA	8/8 (100)
Specific RT-PCR for *Bartonella* spp.	
Cardiac valves	48/52 (92)
Blood	20/60 (33)
Serum	25/70 (36)
16S RNA amplification	
Cardiac valves	21/35 (60)
Blood	0/15 (0)

TABLE 3 Epidemiologic features and biological data of the 91 patients with endocarditis induced by *Bartonella* spp. identified to the species level

Species	No. of cases	Mean age (yr)	Sex ratio (no. male/no. female)	No. of samples positive in the indicated test/total no. of samples tested				
				IFA with IgG ≥ 1:800	Western blotting	PCR on valve sample	PCR on blood sample	PCR on serum sample
B. quintana	48	54	43/5	28/47	35/35	26/27	13/28	13/32
B. henselae	39	49	26/13	19/36	28/28	19/20	6/24	12/24
B. alsatica	3	64	2/1	0/3	3/3	1/1	0/3	0/1
B. vinsonii	1	19	1/0	1/1	1/1	ND	1/1	0/1



Proportion of *Bartonella* endocarditis among Infectious Endocarditis in Europe and North Africa.

Source: Znazen et al., Am. J. Trop Med 2005;72: 503-507.

Bartonella endocarditis in patients from the U. K.

Table 1. *Clinical and diagnostic data for the 14 patients from whom tissue was submitted for PCR*

Patient no.	Sample date	Age/sex	Valve tissue examined	IFAT results*				Species detected by PCR	Comments
				Bh IgM	*Bh* IgG	*Bq* IgM	*Bq* IgG		
1	Jan. 2006	39 F	Aortic	<20	>512	<20	>512	*B. quintana*	Recent immigrant from Russia
2	6 Feb. 2006	35 M	Aortic	<20	>512	20	>512	*B. quintana*	Recent immigrant from Russia: itinerant builder [23]
3	22 Feb. 2006	56 M	Aortic	<20	>512	80	>512	*B. quintana*	No known risk factors
4	16 May 2006	40 M	Valve†	<20	>512	<20	>512	*B. quintana*	No known risk factors
5	11 Feb. 2007	39 M	Aortic	<20	>512	<20	>512	*B. quintana*	Recent immigrant from Lithuania: handyman, known to have lived 'rough' for a few months
6	19 Sept. 2007	58 F	Aortic	<20	256	<20	256	*B. quintana*	No known risk factors
7	8 Sept. 2007	33 M	Aortic	<20	512	<20	512	*B. quintana*	Recent immigrant from Czech Republic
8	11 Feb. 2008	18 M	Aortic & mitral‡	80	>512	<20	>512	*B. quintana*	Recent immigrant from Iran: history of congenital heart disease
9	23 June 2008	36 M	Aortic & mitral	<20	>512	<20	64	*B. henselae*	No known risk factors [24]
10	22 July 2008	30 M	Mitral	<20	>512	40	>512	*B. quintana*	No known risk factors
11	1 Sept. 2009	61 F	Aortic	<20	>512	<20	>512	*B. quintana*	No known risk factors
12	22 Feb. 2010	34 M	Mitral	80	>512	80	>512	*B. quintana*	Recent immigrant from Poland, lived in squat, heavy drinker
13	May 2010	69 F	Mitral	<20	>512	<20	>512	*B. quintana*	No known risk factors
14	11 May 2007	62 M	Heart material§	<20	>512	<20	>512	Not detected	Had BCNE and severe pneumonia

Bh, *B. henselae*; *Bq*, *B. quintana*.

* Titres are given as the highest serum dilution yielding a positive result except: <20=a negative result at the screening dilution of 1:20, >512=strongly positive at the highest dilution tested (1:512).

† Recorded as 'heart valve'.

‡ Also a sample of brain tissue, which was negative for *Bartonella* spp.

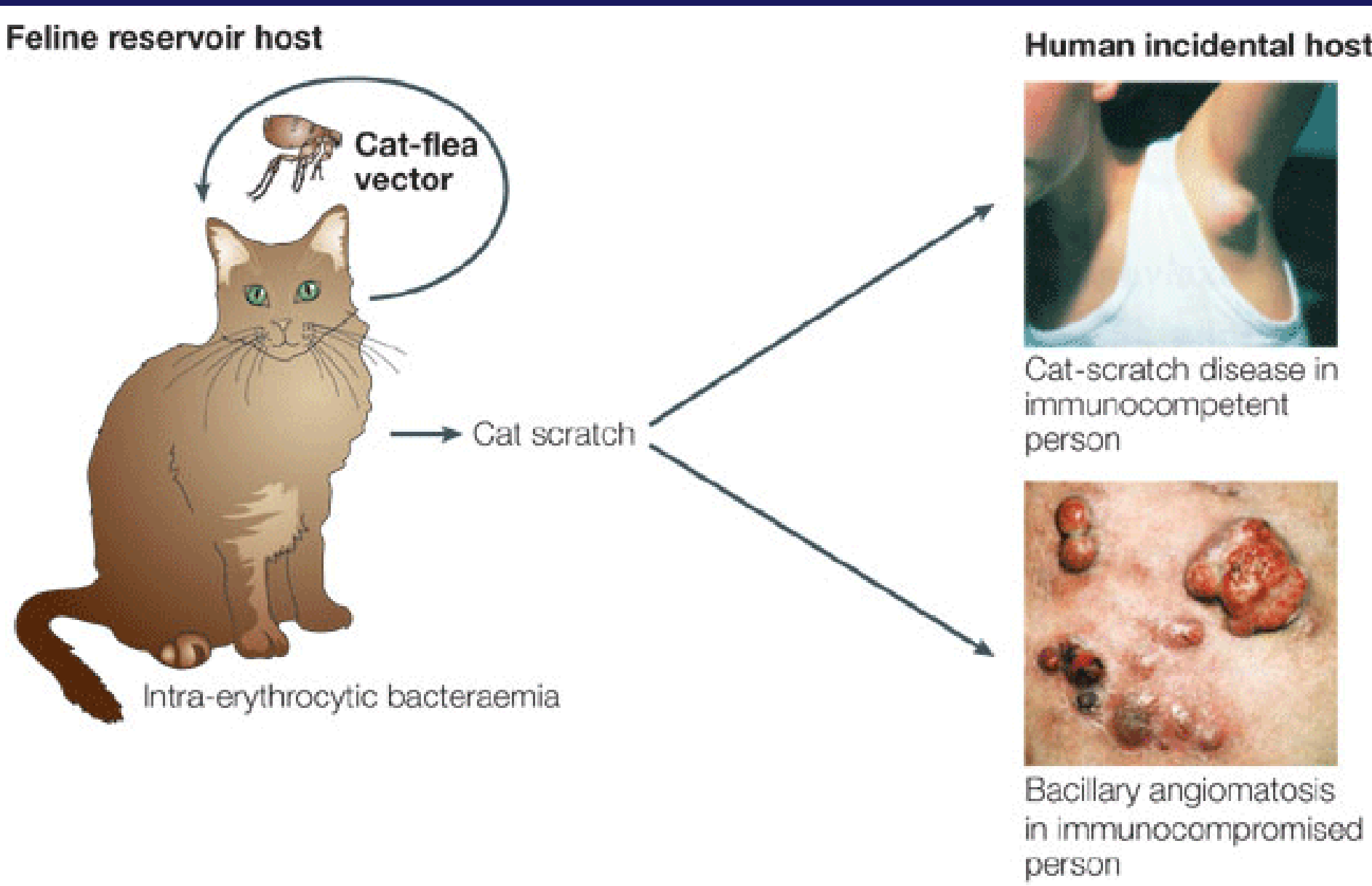
§ Heart tissue taken from the left atrium.

Between November 2005 and October 2010,samples from 685 endocarditis patients were submitted to the Health Protection Agency, U. K. for *Bartonella* serology. Serological evidence of infection was obtained for 57 (8.3%) patients.

PCR-based evidence of infection obtained from 13/14 patients for whom heart valve tissue was available.

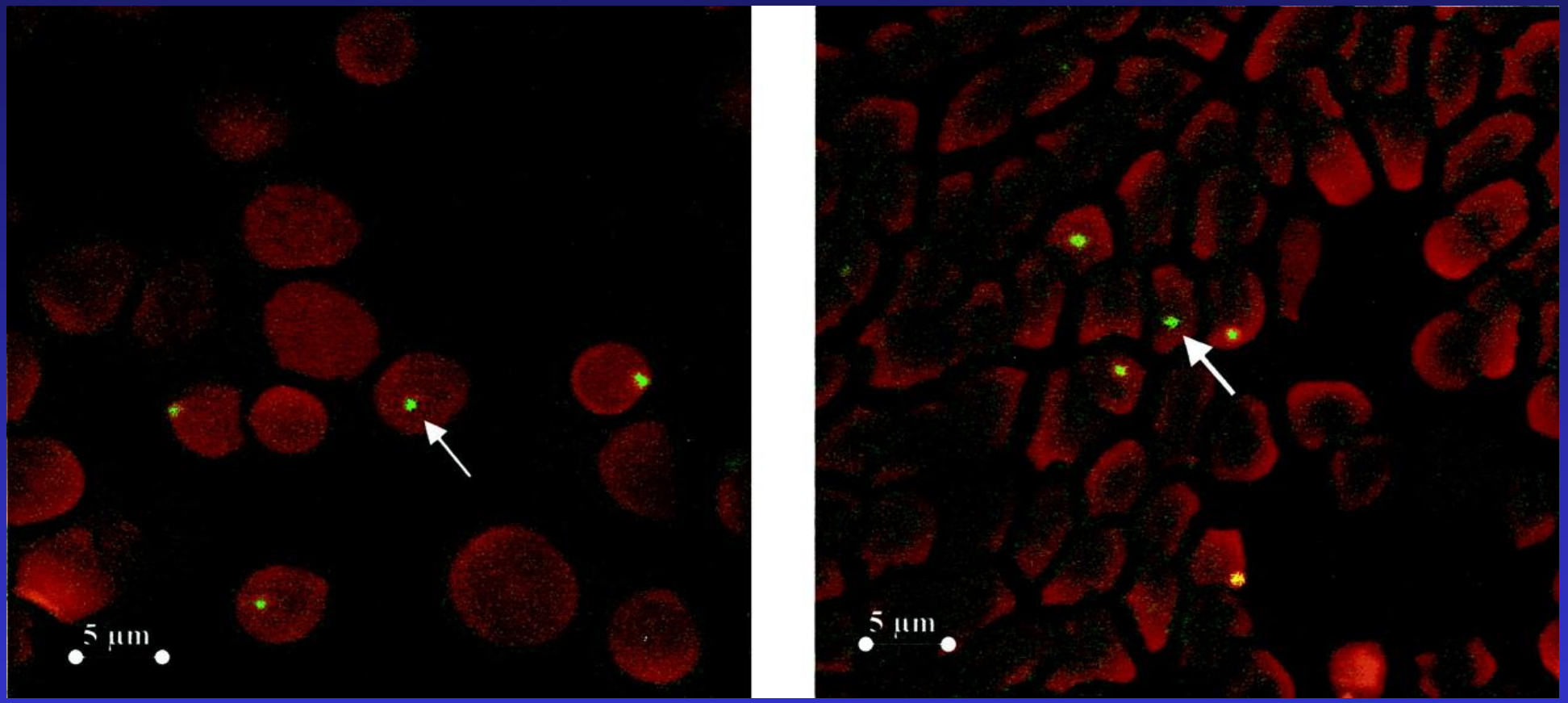
Six patients with *B. quintana* endocarditis were recent immigrants into the UK, of whom four lived in poor socioeconomic conditions. Therefore, *Bartonella* is a not uncommon cause of endocarditis in the UK.

Chaloner *et al*., Epidemiol. Infect. (2013), 141, 841–846.



Nature Reviews | Microbiology

Digital sections of feline red blood cells infected with *B. henselae* as viewed by laser scanning confocal microscopy.



Rolain J M et al. J. Clin. Microbiol. 2001;39:2978-2980

Journal of Clinical Microbiology

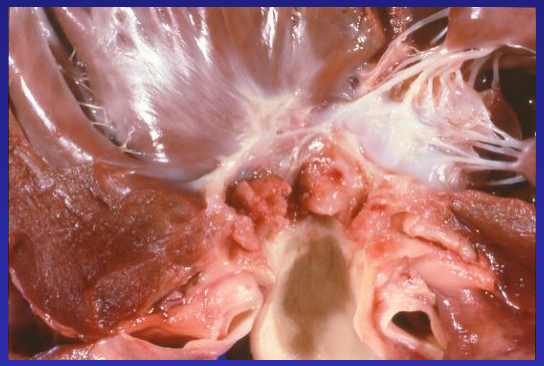
Domestic dogs can be infected with a wide range of *Bartonella spp.* or subspecies, including:

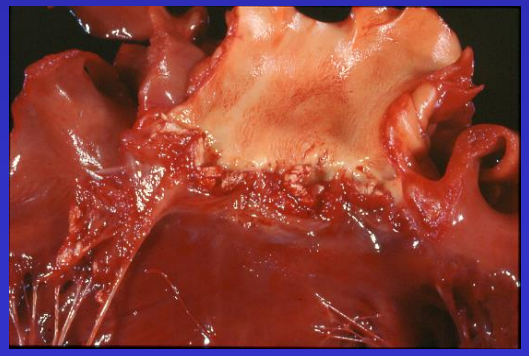
B. vinsonii subsp. *berkhoffii,* (Z)
B. henselae,(Z)
B. rochalimae, (Z)
B. clarridgeiae, (Z)
B. washoensis, (Z)
B. elizabethae,(Z)
B. vinsonii subsp. *arupensis* (Z)
B. quintana, (Z)
B. koehlerae, (Z)
B. bovis,
B. grahamii, (Z)
B. taylorii
B. vinsonii subsp. *vinsonii*

and new candidate species,
B. volans-like (Z)
Candidatus B. merieuxii (formerly HMD)
three novel genotypes (BK1 (Bangkok), KK1 (Khon Kaen) and KK2)

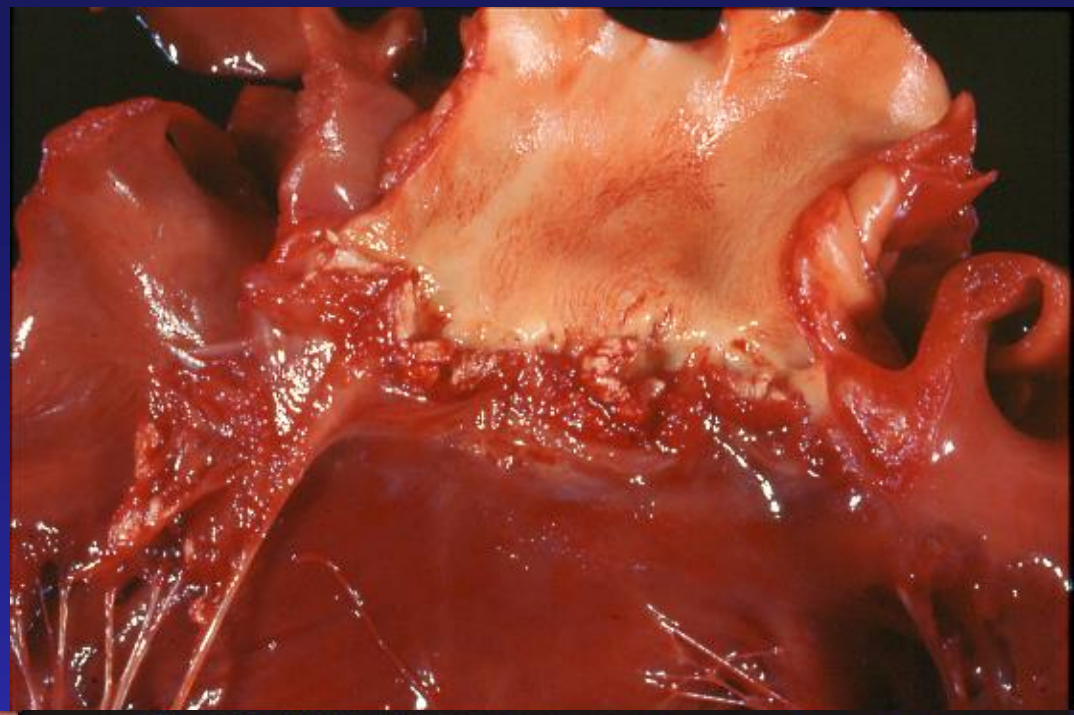
Clinical features of *Bartonella* infection in Domestic Dogs

***Bartonella* species**	**Clinical signs**
B. vinsonii subsp. *berkhoffii*	Endocarditis, arrhythmias, Myocarditis, granulomatous rhinitis and lymphadenitis, anterior uveitis, chorioretinitis, meningo-encephalitis, anemia/thrombocytopenia
B. henselae	Endocarditis, peliosis hepatis,granulomatous hepatitis, polyarthritis, idiopathic effusions, lymphadenitis, panniculitis
B. henselae & *B. elizabethae*	Non specific clinical abnormalities (severe weight loss, protracted lethargy, anorexia & chronic disease course)
***B**. clarridgeiae*	Endocarditis, hepatic lesions
B. washoensis	Endocarditis
B. quintana	Endocarditis
B. koehlerae	Endocarditis
B. rochalimae	Endocarditis, seizures, lameness

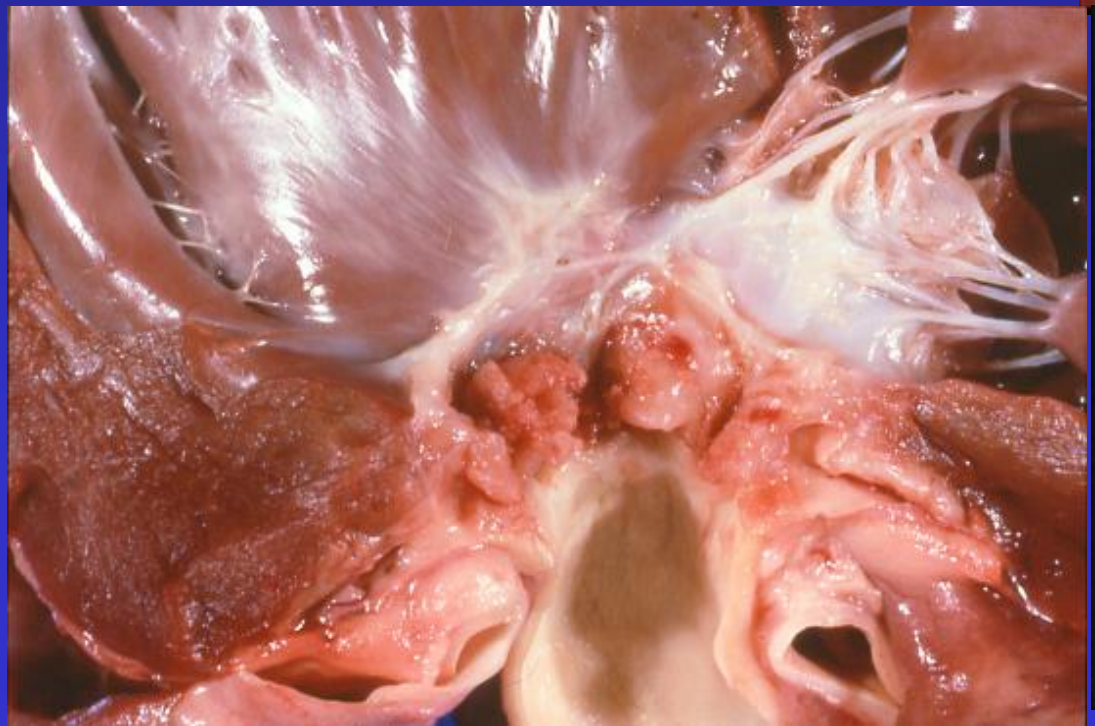




Dog endocarditis
Caused by *Bartonell*a spp.



B. clarridgeiae detected
By PCR in this dog



Clinical Symptoms and Etiology of Dog Endocarditis Cases, U.C. Davis, VMTH, 1999-2001.

18 dogs, all medium to large breed, median weight		N (%)
Presenting complaint:	lameness	8 (44%)
	lethargy	6 (33%)
	anorexia	6 (33%)
	respiratory problems	4 (22%)
	weakness	3 (17%)
Valve involvement:	aortic	9 (50%)
	mitral	8 (44%)
	aortic and mitral	1 (6%)
Etiology:	Unknown	6 (33%)
	Bartonella	5 (28%)
	Staphylococcus aureus	3 (17%)
	Streptococcus canis	2 (11%)
	Pseudomonas aeruginosa	1 (6%)
	Escherichia coli	1 (6%)

McDonald et al.,
J Vet Intern Med.
2004;18:56-64

Clinical Cases of Dog Endocarditis, U.C. Davis, 6/1999-5/2001

ID#	Date	Age	Sex	Breed	Valve	*Bartonella* serol	*Bartonella* Cult	*Bartonella* PCR	*A. phag* Serol
1	6/99	7 y	MN	Bernese	Aortic	Neg	Neg	NA	Neg
2	11/99	14 y	FS	Australian	Mitral	Neg	Neg	NA	Neg
3	12/99	14 y	FS	Shetland	Aortic	Neg	Neg	NA	Neg
4	1/00	9 y	MN	Shepherd	Aortic	1024	Neg	+ (Bc-l)	1:160
5	3/00	10y	MN	Labrador	Mitral	Neg	Neg	NA	Neg
6	4/00	2.5 y	MN	Boxer	Aortic	2048	+ (B.c.)	+ (B.c.)	1:100
7	6/00	9y	MN	Germ. Shep.	Mitral	Neg	Neg	NA	Neg
8	6/00	4 y	MN	Red Hound	Mitral	Neg	Neg	NA	Neg
9	10/00	8 y	FS	Germ. Shep.	Mitral	32/64	Neg	NA	Neg
10	10/00	5.5 y	M	Labrador	Aortic	Neg	Neg	NA	Neg
11	12/00	6 mo	F	Great Dane	Aortic	Neg	Neg	NA	Neg
12	1/01	7 y	M	Bull Mastiff	Aortic	1024	Neg	+ (Bvb)	1:640
13	1/01	6 y	MN	Airedale	Aortic	1024	Neg	+ (Bvb)	1:320
14	1/01	12 y	MN	Golden retr.	Mitral	Neg	Neg	NA	1:80
15	2/01	10 y	MN	Labrador mix	Aortic	4096	Neg.	+ (Bvb)	1:100
16	3/01	9y	MC	Shepherd mix	M&A	Neg	Neg	Neg	Neg
17	4/01	6.5y	FS	Bull Mastiff	Mitral	256 (Bc)	Neg	Neg	Neg
18	5/01	8y	FS	Golden retr.	Mitral	Neg	Neg	Neg	Neg

McDonald et al., J Vet Intern Med. 2004;18:56-64.

Bartonella spp. Endocarditis Case-Control Study in U.S. Army Working Dogs (from A.F.I.P. archives).

Materials and Methods:

- CASES: 26 dogs with histopathological diagnosis of endocarditis.
- CONTROLS: 28 dogs with history of hip dysplasia, no lymphoplasmatic changes on histopathology of cardiac tissue.

- Histopathology: H & E, Warthin-Starry silver staining
- DNA extraction (Qiagen Kits)
- PCR/RFLP of citrate synthase (*gtlA*) gene
  - (*Taq*I, *Hha*I, *Aci*I and *Mse*I endonucleases)
  - Partial sequencing of citrate synthase gene

Davis et al., J Vet Cardiol. 2020 Feb;27:1-9. doi: 10.1016/j.jvc.2019.11.005. Epub 2019 Nov 1

Bartonella spp. Endocarditis Case-Control Study in U.S. Army Dogs (from A.F.I.P. archives).

RESULTS:

- CASES: 73.0% (19/26 dogs) PCR Positive
- CONTROLS: 3.6% (1/28 dogs) PCR weak Positive

- Histopathology: 20% (4/20) had visible organisms with Warthin-Starry silver staining

- PCR/RFLP of *gltA* gene and partial sequencing of the gene: several profiles or sequences, including

6 *B. vinsonii berkhoffii* (2 from Thailand, 1974; 4 from USA (Bethesda,MD, 1978; San Antonio, TX, 1978 and 1986; Puerto Rico, 1987)

8 *B. henselae* (mainly Vietnam, 1970-1972)

1 *B. elizabethae* (Germany 1988)

2 *B. washoensis* (Guam, 1992; Germany, 1995)

2 mixed infections (Okinawa, 1970; Florida, 1986)

Davis et al., J Vet Cardiol. 2020 Feb;27:1-9. doi: 10.1016/j.jvc.2019.11.005. Epub 2019 Nov 1

Bartonella spp. Valvular Endocarditis in Dogs Necropsied at U.C. Davis (1997-2001).

(Pesavento et al., Vet Pathol. 2005;42:370-373)

- 31 necropsied dogs with valvular endocarditis during the 5-year period.

- Routine blood culture positive for 10 dogs, including *E. coli*, *Pseudomonas aeruginosa*, Beta-hemolytic *streptococci* and *Staphylococcus* spp.

- *Bartonella* DNA detected by PCR (primers directed at citrate synthase gene) on 12 (38.7%) of these 31 dogs.
  - 2 dogs also blood culture positive for other pathogens
  - 10 dogs blood culture negative.

  mean (range) age: 9 (1-16) yrs; 9/12 intact/neutered males
  5/12 had history of polyarthritis or swollen joints.

Bartonella endocarditis

Humans:

France: 3% (10/299) (Marseille) to 4.5% (Lyon) of all endocarditis cases

Germany: 3% (*B. henselae*: 2.6%; *B. quintana*: 0.4%)

Sweden: 1 case in 1997; 0/334 infective endocarditis

United Kingdom: 1.1%

Tunisia: almost 10% (mainly *B. quintana*)

(source: Brouqui & Raoult, FEMS Immunol Med Microbiol, 2006;47:1-13)

Dogs:

USA, California:	8/45 (18%) (Sykes et al., 2006),
	5/18 (28%) (MacDonald et al.,2004)
	6/31 (19%) (Pesavento et al., 2005)
USA, Colorado:	9/119 (7.6%) (Fenimore et al., 2011)

Published endocarditis cases in dogs from around the world

Bartonella species	Number of cases (46)	Country
B. v. berkhoffii		
type III	3	USA (Army) [N.Carol. tested]
type IV	1	Canada
N.S. (Not stated)	6	USA (Army) [U.C. Davis tested]
N.S.	6	USA (3 Calif.; 3 North Carol.)
N.S.	3	USA (Colorado* co-infect)
N.S.	2	Spain (1 co-infect with *B. rochalimae*)
B. henselae	8	USA (Army) [U.C. Davis tested]
	7*	USA (Colorado, Wyoming)
	1	Israel
B. quintana	2	USA, New Zealand
B. rochalimae	1	USA (Army, co-infect.; N. C. tested]
	1	USA (Calif.)
	5	USA (Virginia, N. Carol., Texas (2), Florida)
	6	Spain (1 co-infect with *B. v. berkhoffii*)
B. koehlerae	1	Israel
	1	Spain
B. clarridgeiae	1	USA (Calif.)
	1	Brazil
B. washoensis	1	USA (Calif)
	2	USA (Army) [U.C. Davis tested]
B. elizabethae	1	USA (Army) [U.C. Davis tested]
Unknown	2	USA (Army) [U.C. Davis tested]

Bartonella species associated with endocarditis in humans and dogs

***Bartonella* sp.**	**Human**	**Dogs**
B. quintana (Z)	+++	+ (2 cases)
B. henselae (Z)	++	+ +
B. clarridgeiae (Z)	1 case (USA)*	+ (2 cases)
B. rochalimae (Z)	1 case	++ (13 cases)
B. vinsonii berkhoffii (Z)	+ (2 cases, UK, USA)	+++
B. vinsonii arupensis (Z)	+ (1 case, France)	No
B. washoensis (Z)	+ (1 case, Germany)	+ (1 case)
B. koehlerae (Z)	+ (1 case, Israel)	+ (2 cases)
B. elizabethae (Z)	+ (1 case, USA)	+ (1 case)
*B. alsatica (*Z*)*	+ (3 cases, France)	No
*B. mayotimonensis (*Z*)*	+ (1 case, USA)	No

* UCSF, J. Koehler, unpublished.

Zoonotic Bartonella species in cardiac valves of healthy coyotes, California, USA.

Kehoe et al., Emerg Infect Dis. 2014;20:2133-6.

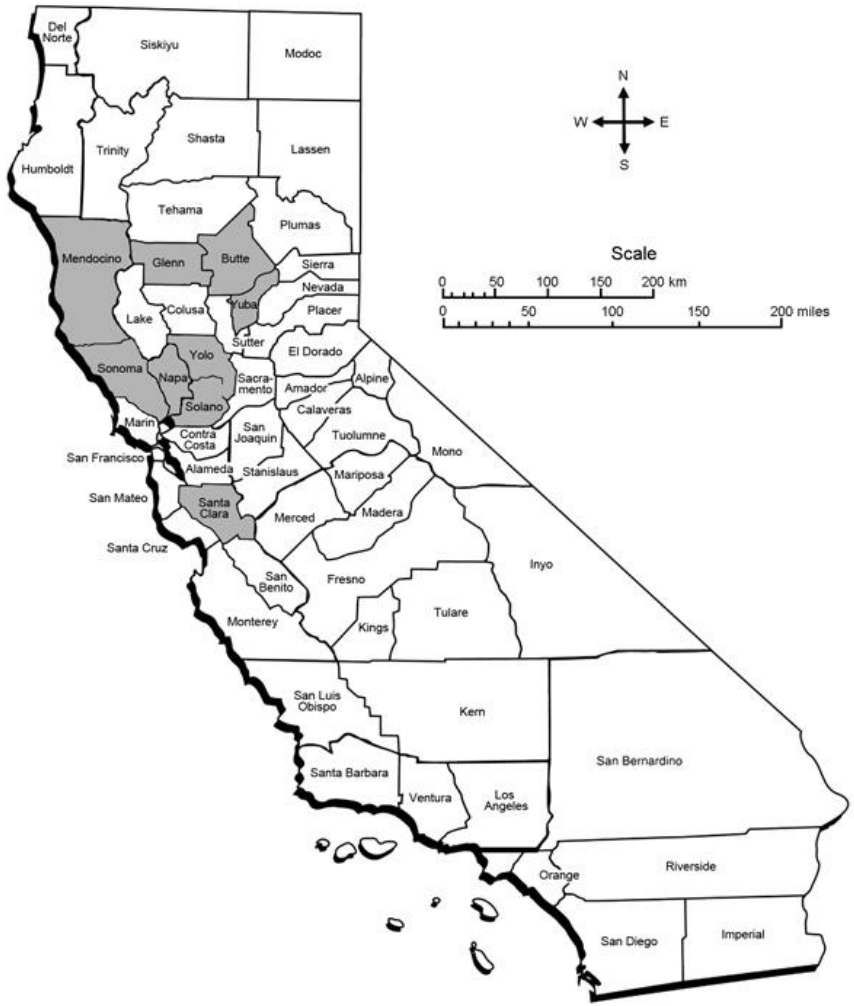
Table. Coyotes (*Canis latrans*) positive for *Bartonella* species by PCR, California, USA

Coyote no.	Sex/estimated age, y	Weight, kg	County	*Bartonella* PCR-positive tissue	*Bartonella* species by DNA sequencing
91	F/1	11.7	Yuba	Aortic valve	*B. vinsonii* subsp. *berkhoffii* type III
92	M/1	13	Yuba	Aortic valve	*B. vinsonii* subsp. *berkhoffii* type I
93	M/1	10.5	Mendocino	Aortic valve	*B. vinsonii* subsp. *berkhoffii* type I
				Mitral valve	*B. vinsonii* subsp. *berkhoffii**
99	M/<1	10.6	Yuba	Spleen	*B. rochalimae*
101	M/1	12.3	Yuba	Mitral valve	*B. vinsonii* subsp. *berkhoffii**
102	M/<1	10	Glenn	Spleen	*B. vinsonii* subsp. *berkhoffii* type II
106	F/1	12	Yuba	Aortic valve	*B. vinsonii* subsp. *berkhoffii**
110	M/<1	11	Yuba	Aortic valve, spleen	*B. vinsonii* subsp. *berkhoffii* type II
121	F/<1	8.6	Santa Clara	Aortic valve	*B. vinsonii* subsp. *berkhoffii**
124	F/9	10.4	Santa Clara	Aortic valve	*B. vinsonii* subsp. *berkhoffii**
137	M/<1	10.7	Mendocino	Mitral valve	*B. henselae*
146	M/3	16.6	Sonoma	Aortic valve	*B. vinsonii* subsp. *berkhoffii* type I
152	M/<1	9.7	Napa	Spleen	*B. vinsonii* subsp. *berkhoffii* type II
156	F/<1	8.1	Santa Clara	Mitral valve	*B. vinsonii* subsp. *berkhoffii**
164	F/<1	10.1	Napa	Mitral valve	*B. vinsonii* subsp. *berkhoffii* type I

*Type not amplified.

Despite the absence of gross vegetative endocardial lesions, *Bartonella* DNA was amplified and sequenced from >20% of the coyotes, mainly from cardiac valves [only 4 (6%) coyotes had PCR-positive spleens, compared with 12 (17%) coyotes with PCR-positive cardiac valves].

We hypothesize that *Bartonella* in the spleen indicated early or ongoing bacteremia, whereas bartonellae in the heart valves, in their absence in the spleen, indicated valvular bacterial localization, possibly facilitating persistent infection that could evolve through time to endocarditis.



Molecular prevalence of *Bartonella* species in 70 coyotes from 9 counties, California, USA. Shaded areas are counties where coyotes were trapped during the early 2000s. *Bartonella*-positive coyotes were identified from the 9 counties as follows: Yuba, 6 (33%) of 18 trapped coyotes; Santa Clara, 3/22 (14%); Mendocino, 2/11 (18%); Napa, 2/6 (33%); Sonoma, 1/5 (20%); Glenn, 1/4 (25%); Yolo, 0/1; Butte, 0/1; Solano, 0/2

Bacterial endocarditis and *Bartonella* endocarditis cases: Comparison in humans and dogs.

	Humans %	Dogs %
Bacterial endocarditis		
Culture neg. infect. endoc.	14 (88/620)	27
Aortic Valve	43-47	23
Mitral Valve	47-57	67
Pre-existing valvular disease	30	unlikely
Bartonella positive endocarditis		
Aortic	88 (29/33)	71.4 (5/7)
Mitral	12 (4/33)	14.3 (1/7)
Mixed	6 (2/33)	14.3 (1/7)
Pre-existing valvular disease	53 (8/15)	unlikely

Serology & PCR results from 61 *Bartonella*-infected dogs

(blood & other fluid samples tested by BAPGM enrichment culture)

Between 2003 and 2009, 924 samples from 663 sick dogs submitted to North Carolina State University, College of Veterinary Medicine for diagnostic testing with the *Bartonella* α-Proteobacteria growth medium (BAPGM) platform .

61 (9.2%) of 663 dogs were culture positive or had *Bartonella* DNA detected by PCR.

BAPGM culture was required for PCR detection in 32 (52.5%) cases

Pérez et al. J Vet Intern Med 2011;25:805–810

Serology & PCR results from 61 *Bartonella*-infected dogs

(blood & other fluid samples tested by BAPGM enrichment culture)

	***Bartonella* IFA (N +/N tested)**			***Bartonella* PCR (N+ /N Tested)**		
Bart. species (N, %)	*B. henselae*	*B.v. berkhoffii*	BAPGM culture	Plate Isolate after BAPGM culture	BAPGM and plate culture combined	Only detected by BAPGM
B.h., 30 (49%)	7/19 (37%)	4/17 (24%)	14/30 (47%)	5/30 (17%)	19/30 (63%)	15/30 (50%)
B.v.b., 17 (28%)	4/10 (40%)	4/10 (40%)	6/17 (35%)	6/17 (35%)	10/17 (59%)	9/17 (53%)
B.h.,B.v.b., 7 (11%)	0/2	0/2	6/7 (86%)	3/7 (43%)	6/7 (86%)	5/7 (71%)
B.k., 2 (3 %)	NP	NP	1/2	0/2	1/2	1/2
B.v.-l., 2 (3%)	0/1	NP	0/2	2/2	2/2	2/2
B. bovis, 1 (1.6%)	NP	NP	0/1	0/1	0/1	0/1
B.v.b., B.k, 1 (1.6%)	NP	NP	1/1	0/1	1/1	0/1
B.v.b., B.vl, 1 (1.6%)	0/1	0/1	1/1	0/1	1/1	0/1
Total, 61 (100%)	11/33 (33%)	8/30 (27%)	29/61 (48%)	16/61 (26%)	40/61 (66%)	32/61 (53%)

BAPGM, Bartonella α-Proteobacteria growth medium; *B. bovis, Bartonella bovis; B.h., Bartonella henselae; B.k., Bartonella koehlerae; B.v.b., Bartonella vinsonii* subsp. *berkhoffii; B.v.-l., Bartonella volans-like*; IFA, immunofluorescent antibody assays.

Pérez et al. J Vet Intern Med 2011;25:805–810

Bartonella species associated with endocarditis in domestic animals

Bartonella sp.		Animal species (location)	Isolation/ PCR/serology
B. quintana (Z)		Dogs (USA, New Zeal.)	PCR
B. clarridgeiae (Z?)		Dogs (USA, Brazil)	Isolation/PCR
B. rochalimae (Z)		Dogs (USA, Spain)	PCR/Isolation
B. vinsonii berkhoffii (Z)	type 1	Dogs (USA)	Isolation/PCR
	type 2	Dogs (USA)	Isolation/PCR
	type 3	Dogs (USA)	PCR
	type 4	Dogs (Canada, Col.)	PCR
B. washoensis (Z)		Dog (USA: Calif.)	Isolation
B. koehlerae (Z)		Dog (Israel, Spain)	PCR
B. elizabethae (Z)		Dog (USA, Army)	PCR
B. henselae (Z)		Cats (USA, Australia)	Isolation,
		Dog (Netherlands)	PCR (dog, NCSU),
		(USA)	serol. (dogs, NCSU)
B. bovis		Cows (France)	PCR

Treatment of *Bartonella rochalimae* endocarditis in dogs

Doxycycline (Vibramycin, Pfizer): 6.6 mg/kg PO in the mornings and 3.3 mg/kg in the evenings/ or 5.3 mg/kg twice daily
and
Enrofloxacin (Baytril, Bayer) 5.7 mg/kg PO once a day [up to 21 months) or 9.7 mg/kg once daily.

Other treatment option:
Azithromycin (Zithromax, Pfizer): 8 mg/kg PO every 24 hours for 7 days and then every 48 hours + Doxycycline (Vibramycin, Pfizer) 8 mg/kg PO every 12 hours.

Ernst et al., J. Vet. Intern Med. 2020;34:1447-1453.

Vegetative endocarditis associated with natural *Bartonella* infection in domestic cats.

Malik et al., 1999 J. Fel. Med. Surg.. 1:171-180.

Between 1990 and 1997, vegetative endocarditis diagnosed in six neutered cats aged between 3 and 9 years.

Diagnosis made using echocardiography (5 cases) or at necropsy (1 case).

Case	Age	Sex	Breed	Valve Affected	Culture/Histology
A	3	FN	DSH	aortic, mitral	ND
B	9	FN	DSH	aortic	*Bartonella* spp.
C	6	MN	Persian	aortic, mitral	*Bartonella* spp.
D	8	MN	DSH	aortic, ? Mitral	ND
E	6	MN	DSH	mitral, aortic	Streptococcus
F	6	FN	Tonkinese	tricuspid	Gram + cocci

No confirmation of *Bartonella* by PCR, only based on cultural aspect

Bartonella endocarditis in cats

Fatal Case of Endocarditis Associated with *Bartonella henselae* Type I Infection in a Domestic Cat

Bruno B. Chomel,[1]* Aaron C. Wey,[2]† Rickie W. Kasten,[1] Brian A. Stacy,[3] and Philippe Labelle[3]

Department of Population Health and Reproduction[1] and Department of Pathology, Microbiology and Immunology, Veterinary Medicine Teaching Hospital,[3] School of Veterinary Medicine, University of California, Davis, California 95616, and Veterinary Centers of America, Emergency Animal Hospital & Referral Center, San Diego, California 92108[2]

Received 3 March 2003/Returned for modification 21 June 2003/Accepted 11 August 2003

We report the first feline case of *Bartonella henselae* endocarditis. Despite negative blood cultures, the cat had high *Bartonella* antibody titers and *B. henselae* type I DNA was detected in the damaged aortic valve. Microscopic examination of the valve revealed endocarditis with small silver positive coccoid structures in endothelial cells.

Ann N Y Acad Sci. 2009 May;1166:120-6. doi: 10.1111/j.1749-6632.2009.04523.x.

Bartonella endocarditis: a pathology shared by animal reservoirs and patients.

Chomel BB et al Kasten RW, Williams C, Wey AC, Henn JB, Maggi R, Carrasco S, Mazet J, Boulouis HJ, Maillard R, Breitschwerdt EB.

Bartonellae were first recognized to cause endocarditis in humans in 1993 when cases caused by Bartonella quintana, B. elizabethae, and B. henselae were reported..

“A few Bartonella endocarditis cases, including B. henselae, have been reported in cats in the USA and Australia. The second case of B. henselae type Houston I identified in the USA is presented. “

Veterinary Microbiology 168 (2014) 169–176

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Experimental infection of dogs with various *Bartonella* species or subspecies isolated from their natural reservoir

Bruno B. Chomel [a,*], Richard W. Ermel [b], Rickie W. Kasten [a], Jennifer B. Henn [c], Drew A. Fleischman [a], Chao-Chin Chang [d]

[a] Department of Population Health and Reproduction, School of Veterinary Medicine, University of California, Davis, CA 95616, USA
[b] Division of Comparative Medicine, Animal Resources Center, Beckman Research Institute City of Hope, 1500 East Duarte Road, Duarte, CA 91010-3000, USA
[c] Napa County Health and Human Services, Napa, CA, USA
[d] Graduate Institute of Microbiology and Public Health, National Chung Hsing University, Taichung 402, Taiwan

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ABSTRACT

Dogs can be infected by a wide variety of *Bartonella* species. However, limited data is available on experimental infection of dogs with *Bartonella* strains isolated from domestic animals or wildlife. We report the inoculation of six dogs with *Bartonella henselae* (feline strain 94022, 16S rRNA type II) in three sets of two dogs, each receiving a different inoculum dose), four dogs inoculated with *B. vinsonii* subsp. *berkhoffii* type I (ATCC strain, one mongrel dog) or type II (coyote strain, two beagles and one mongrel) and *B. rochalimae* (coyote strain, two beagles). None of the dogs inoculated with *B. henselae* became bacteremic, as detected by classical blood culture. However, several dogs developed severe necrotic lesions at the inoculation site and all six dogs seroconverted within one to two weeks. All dogs inoculated with the *B. v. berkhoffii* and *B. rochalimae* strains became bacteremic at levels comparable to previous experimental infections with either a dog isolate or a human isolate. Our data support that dogs are likely accidental hosts for *B. henselae*, just like humans, and are efficient reservoirs for both *B. v. berkhoffii* and *B. rochalimae*.

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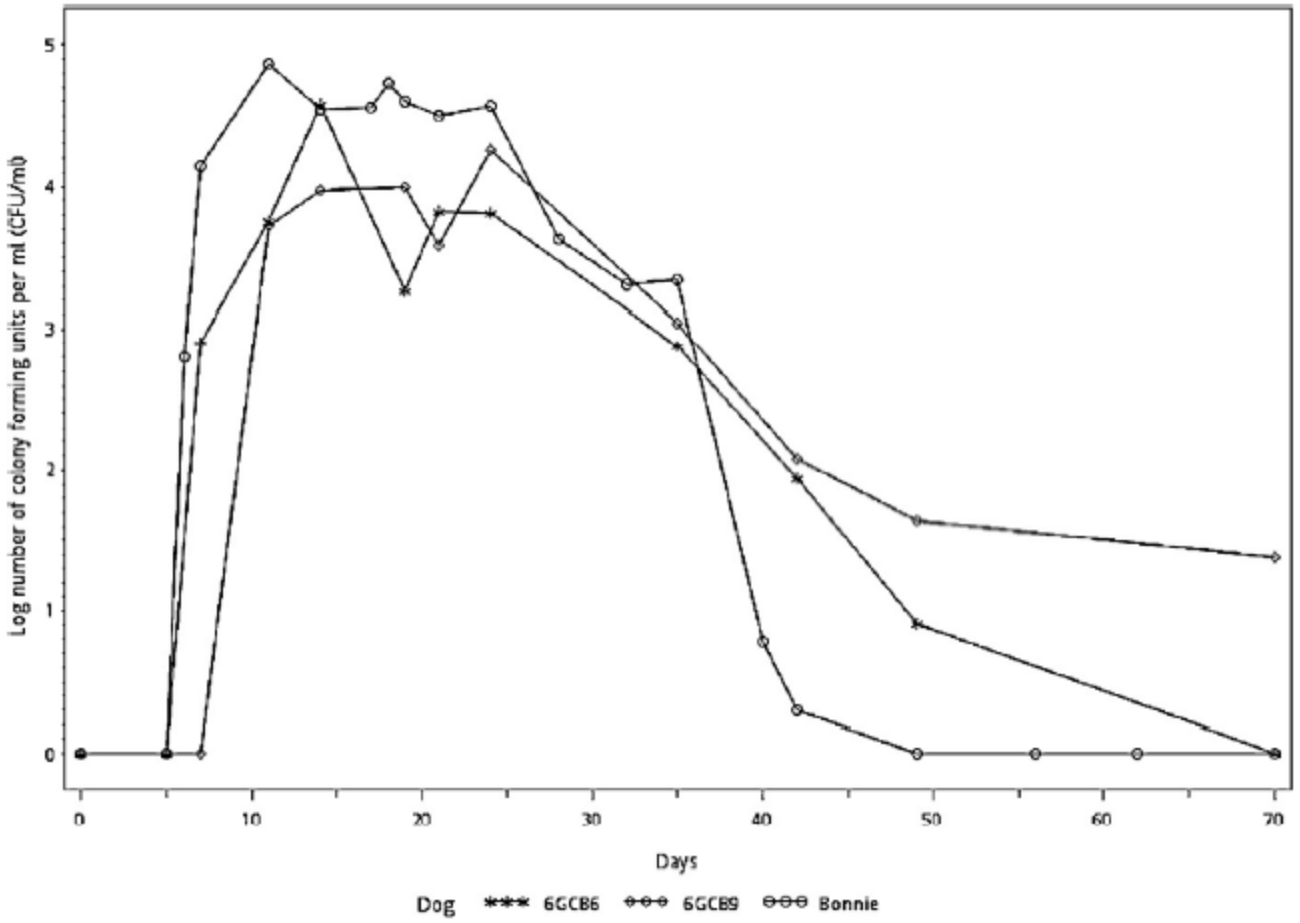


Fig. 2. *Bartonella vinsonii* subsp. *berkhoffii* type II (coyote strain) bacteremia in three dogs inoculated by intradermal route.

Chomel et al. Vet Microbiol. 2014; 168:169-176.

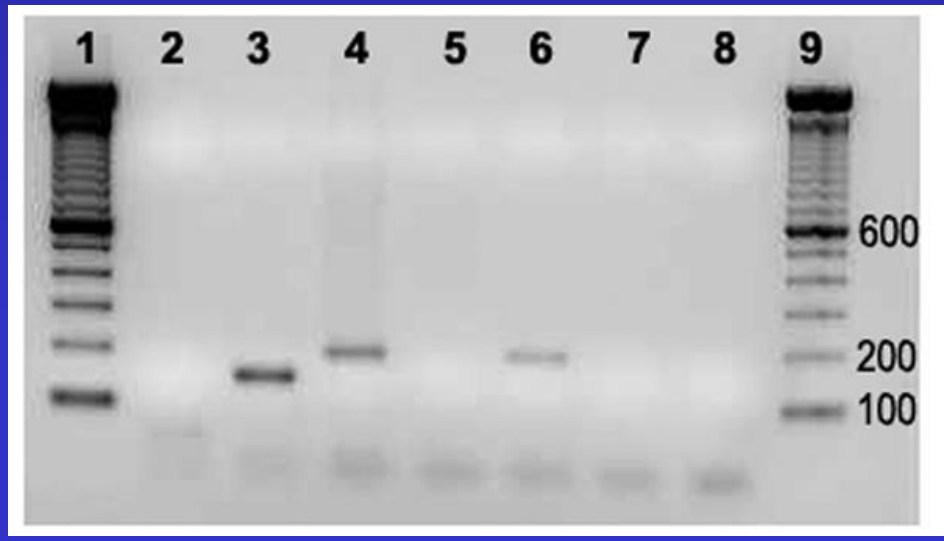
Conditions caused by *Bartonella henselae* in humans, cats and dogs, and by *B. vinsonii berkhoffii* in dogs.

Conditions	Humans	Cats	Dogs
Chronic bacteremia	+	++	+
Lymphadenitis,granulomatous rhinitis and lymphadenitis	++	+	++
Bacillary angiomatosis/peliosis	++	-	+
Endo/Myocarditis, Arrhythmia	++	+	++
Prolonged fever	+	-	+/-
Lethargy, weight loss, anorexia	+	+/-	+
Neurological symptoms	++	+/-	+
Encephalitis	+	?	+/-
Arthritis, joint pain, Lameness	+	?	+
Glomerulonephritis	+	+/-	?
Uveitis and ocular lesions	+	+	+
Reproductive disorders	? +/-	+	?

Endocarditis in Cattle Caused by *Bartonella bovis*

Maillard et al., Emerg. Infect. Dis. 2007; 13:1383-1385.

This study aimed to determine the role of *Bartonella* as an endocarditis agent in cattle. *Bartonella bovis* was identified by PCR, gene sequences analysis, and specific internal transcribed spacer (ITS) amplicon product size in two bovine endocarditis cases with high antibody titers, which demonstrates that *B. bovis* is a pathogen for cattle.



PCR amplification of 16S–23S ITS on vegetative and normal-appearing valves of cows A and B.

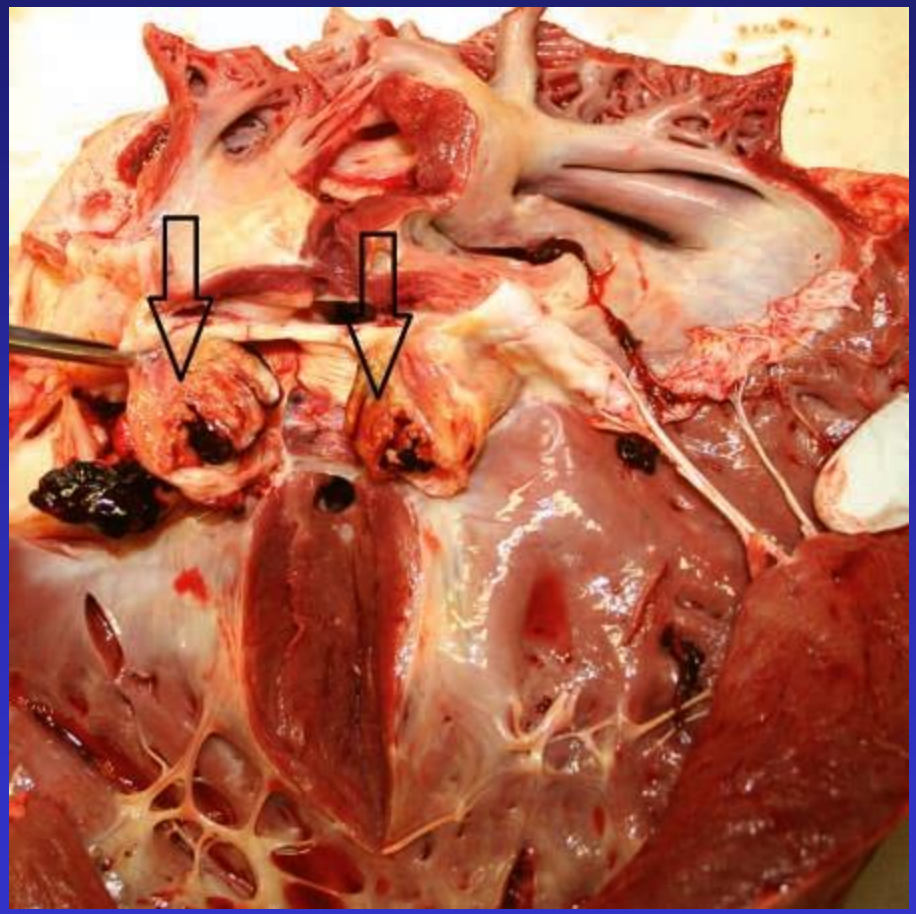
1, Molecular weight marker; 2, negative control;
3, *Bartonella quintana*; 4, *B. bovis*;
5 and 6, normal and vegetative valves (Cow A);
7 and 8, normal and vegetative valves (Cow B);
9, molecular weight marker.

Endocarditis in Angus Cow Caused by *Bartonella bovis*

Erol et al., J. Vet. Diagn Invest. 2013;25(2):288-290.

A 7-year-old pregnant Angus cow was found dead in the field. At necropsy, the aortic valve was expanded by moderate fibrous connective tissue and acidophilic coagulum containing multifocal marked bacteria, mineral, neutrophils, and red blood cells.

Amplicons were sequenced, and the *glt*A, ribC, ssrA, and 16S ribosomal RNA gene sequences were found to have 100% homology to *Bartonella bovis*, whereas the ftsZ and *rpo*B sequences showed 99.9% and 99.6% homology, respectively, to the type strain of *B. bovis*.



Valvular endocarditis in an Angus cow. hemorrhage present in the aortic valve cusp (arrows).

Endocarditis caused by *Bartonella*, *Brucella* and *Coxiella* in humans.

	Bartonella sp.	*Brucella* sp.	*Coxiella burnetii*
Frequency (Europe)	3-4% >90% B.q.; B. h.	1-2% (6% Greece) (0.3-0.6% of all *Brucella* cases)	3-5% (8.7-11% worldwide)
Localization	aortic, mitral	aortic (85%)	aortic, mitral
Acute or Chronic	Chronic	Acute/Chronic	Chronic
Sex	Male (60-85%)	Male	Male (2/3)
Antibody titer	High to very High	(High) (culture+)	High to very high
Death	20%	80%	<30%? Up to 60% (before Rx available)

Bartonella in Sea Otters

Northern Sea otters (*Enhydra lutris kenyoni*).

(Carrasco et al., Vet Microbiol. 2014;170:325-34).

(Carrasco et al., Vector Borne Zoonotic Dis. 2014;14(12):831-7).

Bartonella DNA in a total of 23 (46%) of 50 Alaskan sea otters and 3 (10%) of 30 California sea otters

Positive with 3 different sets of primers (Sequencing done at UCD and NCSU)

Closest to DNA from a northern American river otter, *B. volans* and *B. washoensis* and some close to *B. henselae*

Seroprevalence:

Alaska: 34% (15/44) Live captured – 50% (25/50) stranded

(*B. washoensis - B. volans/B. henselae)*

California: 15.5% (25/161) stranded

Questions ?