NATIONAL VETERINARY LABORATORY

P.O. Box 239, 1Tice Road
Franklin Lakes, NJ 07417
877-NVL-LABS (877-685-5227)
www.natvetlab.com

NEWSLETTER

Do *Bartonella* Cause Disease in Cats? I. Experimental Support©

Evelyn E. Zuckerman, Editor **Winter 2010** **Vol. 9, Number 1**

In This Issue:

In the winter 2010 issue of the NVL Newsletter we will once again discuss the experimental evidence that *Bartonella* **DEFINITELY** cause disease in domestic cats. There is still continuing controversy regarding the pathogenicity of feline *Bartonella* in cats. Several academic feline clinicians and researchers on the VIN message boards and in scientific seminars, continue to question the ability of feline *Bartonella* to cause disease in domestic cats and to fulfill Koch's Postulates. There are 11 experimental studies, 6 of which show that *Bartonella* cause inflammatory diseases in many tissues in cats.[1-11]

Robert Koch in his laboratory

Koch's Postulates:

For more than 100 years science and medicine have relied on Koch's Postulates to determine the microbial cause of diseases.[12] In their simplest form, Koch's Postulates state: 1) Universal presence of the microbe, 2) Isolation of the microbe in pure culture, 3) Inoculation of the microbe into a susceptible host must recreate the disease, and 4) Observe the same disease and re-isolate the microbe in pure culture.

Introduction:

There is ample evidence that *Bartonella* cause inflammatory diseases in humans, dogs, and cats. Experimental inoculation of *Bartonella* in cats has been shown to cause inflammatory diseases in 6 of the 11 published studies.[1-6] Despite these publications several critics continue to insist, on VIN and in national lectures, that *Bartonella* do not cause disease in pet cats. In addition to these experimental studies there are publications of naturally occurring *Bartonella* diseases in pet cats which will be discussed in a future Newsletter.

There are 11 published studies of the experimental induction of *Bartonella* diseases in cats.

Experimental Studies:

There have been conflicting results from the 11 *Bartonella* experimental infection studies with regard to clinical signs and disease outcome (Tables 1 & 2).[1-11] Necropsy findings were reported in only 3 of the 11 studies and, in these publications, there is clear evidence of inflammatory disease occurring in most of the *Bartonella* inoculated cats. In the studies where necropsies were performed, evidence of inflammatory disease in the skin, lymph nodes, liver, spleen, muscle, heart and kidney were documented. In 5 of the 7 studies, where necropsies were not performed, no evidence of disease was noted. These discrepant results are difficult to compare because of different *Bartonella* strains used, infected blood versus pure *Bartonella* cultures used in some studies, different routes and size of inoculations used, the genetics of the cats used in the studies and variable use of necropsies.

There is solid experimental evidence (summarized in Tables 1 & 2) that *Bartonella* induce inflammatory diseases which fulfill Koch's Postulates.[12-13] The continuing controversy may boil down to semantics: is inflammation a disease or a "disease process?" Inflammation of the liver is the disease "hepatitis"; inflammation in the eye can be "uveitis or chorioretinitis". In addition, the critics continue to ask "how can *Bartonella* cause so many diseases?" *Bartonella* only cause one disease "process" which is inflammation that can occur in any tissue. Thus *Bartonella* are multi tissue pathogens which cause inflammation in numerous organ systems of cats, dogs and people.

Summary of Experimental Findings:

We have posted full text PDF files of the following experimental disease publications on our web site: www.natvetlab.com.

The first paper describing experimental *Bartonella* diseases was published by Greene et al. in 1996 where they found skin papules at the inoculation site and lymphadenopathy in 8 of the 8 inoculated cats.[1] In addition they found that proper long term high dose antibiotic therapy cleared the *Bartonella* infections. This observation, and a similar successful therapy of naturally infected cats by Koehler and her colleagues, have been overlooked by those who continue to say that therapy for *Bartonella* infection is not possible.[14]

Guptill and her colleagues reported, in 1997, a study with necropsy findings: 12 of 12 cats developed lymphadenopathy, 12 of 12 splenic follicular hyperplasia, 8 of 12 fever, 3 of 12 hepatitis and liver granulomas, 1 of 12 myocarditis, and 1 of 12 pyogranulomatous nephrtis.[2] Despite these observations, the authors stated "there are few or no clinical signs of disease." This is a case of subclinical disease in a group of SPF cats only observed for 8 months.

In 1999 Kordick and Breitschwerdt reported 13 of 13 inoculated cats developed lymphadenopathy, 9 of 13 splenic follicular hyperplasia, 9 of 13 cholangiohepatitis, 8 of 13 myocarditis, and 4 of 13 interstitial nephritis.[3] **They concluded "Detection of histologic changes in these cats supports a potential etiological role for *Bartonella* species in several idiopathic disease processes in cats."**

The last 2 studies that we will summarize were by O'Reilly and her colleagues.[4,5] They found overwhelming evidence that *Bartonella* cause disease in cats. In the first study, using various sources of *Bartonella* (pure culture, infected blood or infected flea feces), they found 17 of 17 cats developed fever and anorexia, 16 of 17 lymphadenopathy, 17 of 17 lethargy, 13 of 17 myalgia, 5 of 17 became aggressive.[4] They concluded that: "The LSU16 strain of *B. henselae* caused a reproducible clinically characteristic disease in cats. These signs are compatible with those reported for human patients with moderate to severe CSD." Their second study found that *Bartonella* induced lymphadenopathy, fever, and lethargy in all 9 kittens, neurological signs of aggression in 7 of 9, papules at the injection sites in 5 of 9, anorexia in 6 of 9, and myositis in 3 of 9 kittens.[5] They state "In this study reported here, *B. henselae* strain LSU16 causes reproducible, clinically characteristic disease in kittens." They suggest "Kittens that are febrile, anorectic, lethargic, and that have lymphadenopathy should be tested for *Bartonella* organisms, and contact with immunocompromised owners should be discouraged."

Editor's Note:

These studies conclusively demonstrate that *Bartonella* cause inflammatory disease processes in various tissues and organs in cats and that *Bartonella* infected cats can be treated successfully to eliminate their infections. It is time for the veterinary profession to end this controversy and get on with trying to prevent *Bartonella* diseases in cats and the zoonotic spread to people.[14-16]

Table 1

Bartonella Experimental Disease Studies (References 1-11)

Ref	Year	*Bartonella* Inoculum	Cat Inoculated: Source	Age	Length of Observation	Necropsy	Diseases Observed
Studies with Disease Induction:							
1	1996	*B. henselae*	Random Source	1-12 months	1 month	No	8/8 skin papules at inoculation site 8/8 lymphadenopathy
2	1997	*B. henselae*	SPF	3 months	8 months	Yes	12/12 lymphadenopathy 12/12 splenic follicular hyperplasia 8/12 fever 3/12 hepatitis & liver granulomas 1/12 myocarditis 1/12 pyogranulomatous nephritis
3	1999	*B. henselae*	SPF	4 months	15 months	Yes	13/13 lymphadenopathy 9/13 splenic follicular hyperplasia 9/13 cholangiohepatitis 8/13 myocarditis 4/13 interstitial nephritis
4	1999	*B. henselae*	SPF & Pound	7-15 months	2 months	No	SEE TABLE 2 BELOW
5	2000	*B. henselae* LSU 16 strain	SPF	3 months	6 months	Yes	9/9 fever 9/9 lymphadenopathy 9/9 lethargy 7/9 neurological signs- aggression 6/9 anorexia 5/9 skin papules at inoculation site 3/9 myositis
6	2001	*B. henselae* LSU 16 strain	SPF	10 months	2.5 months	No	6/6 skin lesions 4/6 fever
Studies without Disease Induction:							
7	1996	*B. henselae*	SPF	3-5 months	12 months	No	0/5 no clinical disease
8	1996	*B. henselae* Houston-1 strain	SPF	8 months	8 months	No	0*/31 no clinical disease * 2 skin swellings
9	1997	*B. henselae*	SPF	2-18 months	9 months	No	0/13 no clinical disease
10	2001	*B. henselae* Houston-1 strain	Random Source	Not specified	2-24 months	No	0/5 no clinical disease
11	2002	*B. koehlerae*	Random Source	10-12 months	6 months	No	0/4 no clinical disease

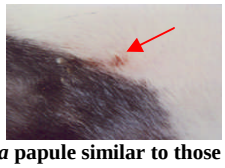
Table 2

Adverse clinical signs in cats inoculated with *B. henselae* (Strain LSU16)

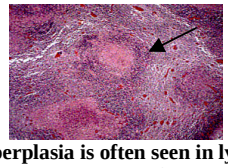
Reproduced from reference 4, O'Reilly et al.

Sign	No. of cats exhibiting sign/total no. (%) inoculated with[a]: Uninfected Controls	Pure culture LSU16	Infected blood	Infected flea feces
Fever[b]	0/15 (0%)	9/9 (100%)	3/3 (100%)	5/5 (100%)
Lethargy	0/15 (0%)	9/9 (100%)	3/3 (100%)	5/5 (100%)
Swelling and/or redness at inoculation site	0/15 (0%)	9/9 (100%)	3/3 (100%)	4/5 (80%)
Pustule at inoculation site	0/15 (0%)	3/9 (33%)	0/3 (0%)	0/3 (0%)
Anorexia	0/15 (0%)	9/9 (100%)	3/3 (100%)	5/5 (100%)
Anorexia requiring force feeding and/or fluids	0/15 (0%)	3/6 (50%)	0/3 (0%)	5/5 (100%)
Vomiting	0/15 (0%)	1/9 (11%)	0/3 (0%)	0/5 (0%)
Muscle pain or stiffness	0/15 (0%)	8/9 (89%)	2/3 (67%)	3/5 (60%)
Abnormal or aggressive behavior	0/15 (0%)	5/9 (56%)	0/3 (0%)	0/5 (0%)
Lymphadenopathy	7/15 (47%)	5/6[c] (83%)	3/3 (100%)	5/5 (100%)

[a] Number of cats that showed the indicated sign at any time in the study.
[b] Rectal temperature of >103.0°F (39.4°C).
[c] 3 cats receiving pure-culture were not monitored for lymphadenopathy during the first 4 weeks postinfection and were excluded.



***Bartonella* papule similar to those seen at experimental injection sites.**



Follicular hyperplasia is often seen in lymphoid organs of experimentally infected cats.

References:

1. Greene, CE, McDermott, M, Jameson, PH, Atkins, CL, and Marks, AM: *Bartonella henselae* infection in cats: evaluation during primary infection, treatment, and rechallenge infection. J Clin Microbiol 34:1682-1685, 1996.
2. Guptill L, *et al*. Experimental infection of young specific pathogen-free cats with *Bartonella henselae*. J Infect Dis 176:206-216, 1997.
3. Kordick DL et al.: Clinical and pathologic evaluation of chronic *Bartonella henselae* or *Bartonella clarridgeiae* infection in cats. J Clin Microbiol 37:1536-1547, 1999.
4. O'Reilly, KL *et al*.: Acute clinical disease in cats following infection with a pathogenic strain of *Bartonella henselae* (LSU16). Infect Immun 67:3066-3072, 1999.
5. Mikolajczyk MG, O'Reilly KL: Clinical disease in kittens inoculated with a pathogenic strain of *Bartonella henselae*. Am J Vet Res 61:375-379, 2000.
6. O'Reilly KL et al.: Passive antibody to *Bartonella henselae* protects against clinical disease following homologous challenge but does not prevent bacteremia in cats. Infect Immun 69:1880-1882, 2001.
7. Chomel, BB, *et al*. Experimental transmission of *Bartonella henselae* by the cat flea. J Clin Microbiol 34:1952-1956, 1996.
8. Regnery RL, *et al*. Experimentally induced *Bartonella henselae* infections followed by challenge exposure and antimicrobial therapy in cats. Am J Vet Res 57:1714-1719, 1996
9. Abbott RC, Chomel BB, Kasten, *et al*.: Experimental and natural infection with *Bartonella henselae* in domestic cats.Comp Immunol Microbiol Infect Dis 20:41-51, 1997.
10.. Zanutto MS, *et al*.: Experimental infection and horizontal transmission of *Bartonella henselae* in domestic cats. Rev Inst Med Trop S Paulo 43:257-261, 2001.
11. Yamamoto, K, *et al*.: Experimental infection of domestic cats with *Bartonella koehlerae* and comparison of protein and DNA profiles with those of other *Bartonella* species infecting felines. J Clin Microbiol 40:466-474, 2002.
12. Koch R.: Uber bakteriologische Forschung Verhandlung des X Internationalen Medichinischen Congresses, Berlin, 1890, 1, 35. August Hirschwald, Berlin. (In German.) Xth International Congress of Medicine, Berlin, 1981.
13. Jacomo, V., Kelly, P.J. Raoult, D. Natural history of *Bartonella* infections (an exception to Koch's Postulate). Cl. Diag. Lab. Immunol. 9: 8-18, 2002.
14. Koehler JE, Glaser CA, Tappero JW: *Rochalimaea henselae* infection: a new zoonosis with the domestic cat as reservoir. JAMA 271:531-535, 1994..
15. Hardy, WD, Jr., Zuckerman, E, Corbishley, J. Seroprevalence of *Bartonella*-infection in healthy and diseased cats in the United States and Caribbean: Evidence for *Bartonella*-induced diseases in cats. Internat Conf American Society for Rickettsiology, Big Sky, Montana, August 17-22, 2001.
16. Hardy, WD, Jr., Zuckerman, EE, Corbishley, J, Gold, JWM[3], Baron, P, Polsky, B, Gilhuley, K, Kiehn, TE, and Armstrong, DA. Efficacy of high dose, long duration Doxycycline or Azithromycin treatment for *Bartonella* infections in pet cats. International Conference of the American Society for Rickettsiology, Big Sky, Montana, August 17-22, 2001.

Web sites with full text articles available:

Below are several web sites where full text scientific articles are available free of charge:

www.nlm.gov click on PubMed
www.scholar.google.com
www.highwire.stanford.edu
www.natvetlab.com