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NEWSLETTER

7th International Conference on *Bartonella* as Animal and Human Pathogens©

Evelyn E. Zuckerman, Editor **Spring 2012** **Vol. 11, Number 2**

In This Issue:

In the spring 2012 issue of the NVL Newsletter we will discuss new information presented at the 7th International Conference on *Bartonella* as Animal and Human Pathogens, April 25-28th 2012, held in Raleigh, NC. The Conference was originally scheduled to be held in Japan in 2011 but the earthquake and resulting tsunami necessitated a change in venue. The meeting was organized by Dr. Edward Breitschwerdt, Dr. Dorsey Kordick and their colleagues at NC State College of Veterinary Medicine. The meeting was a great success both scientifically and socially and was attended by more than 80 participants from 10 countries.

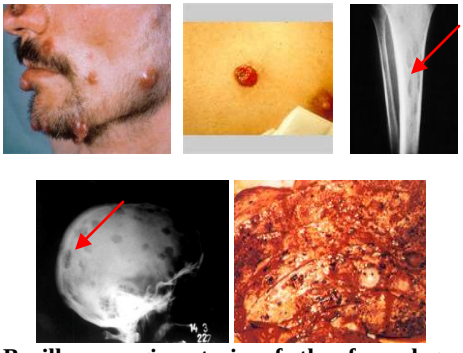
The Meeting:

The three-day meeting was divided into seven sessions: **Session 1**- Pathogenesis and Models of Disease, **Session 2**- Clinical Manifestations in Humans & Animals, **Session 3**- Laboratory Diagnostics, **Session 4**- Genomics and Evolution, **Session 5**- Vectors and Ecology, **Session 6**- *Bartonella* in Wildlife, **Session 7**- *Bartonella* Taxonomy and Species Variety.

Having attended all seven International *Bartonella* Meetings, I (Dr. Hardy) noted the change in subject matter from mostly clinical presentations of *Bartonella* diseases in the first 6 meetings to the present meeting that was heavily molecular and genetically oriented. Unfortunately, only a few of the presentations are of interest for the practicing veterinarian. In this regard, Dr. Jack Broadhurst, Cat Health Clinic. Pinehurst, NC was the only practicing veterinarian to attend the meeting. However, it is clear from this meeting that the *Bartonella* disease spectrum in all animals, especially in humans, is expanding and *Bartonella* are truly stealth pathogens responsible for an expanding list of chronic diseases.[1-9]

Keynote Lecture:

The keynote lecture was: **Functional Diversification of Virulence-Associated Type IV Secretion Systems of the Genus *Bartonella*. Christoph Dehio The Department of Focal Area Infection Biology, Biozentrum, University of Basel, Basel, Switzerland.** Dr. Dehio's research interests are the bacterial pathogens associated with the formation of tumors in humans.[5] In particular, he is studying the molecular and cellular mechanisms that lead to the formation of vascular tumors by the bacterium *Bartonella henselae*. Dr. Dehio described how the virulence associated type IV secretion system (T4SSs) of Gram-negative bacteria are ancestrally related to bacterial conjugation systems that allow for the transfer of DNA between bacteria. *Bartonella* have adapted this system in evolution for virulence and pathogenic factors that allow them to attach to cells and penetrate specific cell types. This enables them to cause inflammatory diseases in various tissues in many animals. In humans, this can lead to bacillary angiomatosis, a vascular tumor-like proliferation of endothelial cells (Figures below).

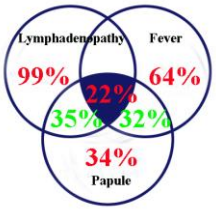


Bacillary angiomatosis of the face, leg, bone (tibia and skull), and liver.

Session 1: Pathogenesis and Models of Disease. The papers in this session were too molecular to be of interest to practicing veterinarians. In general, the speakers presented data on the molecular and genetic factors that enable *Bartonella* to be such a stealth pathogen and to establish persistent infections that are difficult to treat.[2] There was even information explaining their ability to exist in hostile environments such as the high iron content of erythrocytes and the cool temperatures experienced when they reside in the intestinal tracts of fleas before they are transmitted to their reservoir hosts.

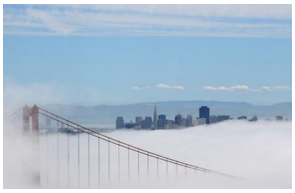
Session 2: Clinical Manifestations in Humans and Animals.
This session contained seven presentations regarding human *Bartonella* diseases including our presentation of the misconceptions about bartonellosis. One presentation discussed the relatively high prevalence of *Bartonella rochalimae* in dogs in Peru. Another presentation covered the therapeutic role of the *Bartonella quintana* lipopolysaccharide in inflammatory diseases. We will summarize only 2 of the presentations in this session since they are most relevant to veterinarians.

All *Bartonella* Diseases are not "Cat Scratch Disease": Misconceptions about Bartonellosis. WD Hardy & EE Zuckerman, National Veterinary Laboratory, Franklin Lakes, NJ. Common misconceptions about cat scratch disease (CSD) are that: 1) fleas or flea dirt must be present on cats in order to transmit the bacteria to people, 2) there is no need to test or treat healthy cats, 3) CSD is the only *Bartonella* disease, and 4) CSD is a benign self-limiting disease. With the assistance of many of our veterinary clients, we were able to interview more than 500 people who had reported developing a *Bartonella* disease. These individuals had their cats tested for *Bartonella* at our laboratory after they were diagnosed with a *Bartonella* disease. We identified 283 people with a *Bartonella* disease who were diagnosed with the infection. 61% had developed classic CSD with fever, lymphadenopathy, malaise, and a papule (see figure below).



Classic CSD Prodrome

23% developed CSD and sequelae consisting of chorioretinitis, cognitive dysfunction, psychoses, neurologic disorders, endocarditis, and hepatosplenomegaly. Finally, 16% developed only bartonellosis or sequelae with no classic CSD prodrome signs. 77% of the cases occurred in adults. 50% of the people developed chronic myalgia and arthralgia and 30% developed mental alterations including depression, cognitive dysfunctions, "brain fog," and panic disorders.



"Brain fog" metaphor

Cats that transmitted *Bartonella* were identified in 201 of the 283 cases or 71%. 97% of the cats were serologically WB positive for *Bartonella* infection, 65% were healthy, 49% were kittens under one year of age and 83% had no fleas or flea dirt on them at the time they transmitted the bacterium to people. The routes of infection were identified in 69% of the cases. Of these, 75% by scratches, 13% by bites or scratches, 5% by administering oral medication, and 31% by unknown routes. **Thus healthy kittens, less than one year of age obtained as strays, from shelters or as feral cats, are the most likely to transmit *Bartonella* to people.** The AAFP, CDC, and many academic websites do not recommend the testing of healthy cats for *Bartonella*. Excluding the 40 veterinary professionals who had developed *Bartonella* diseases in this study 94% of the patients had **NOT** been informed of the zoonotic danger of feline *Bartonella* by their veterinarians before their illness occurred. In addition, 70% of the patients had difficulty in obtaining a diagnosis or had to urge or insist that their physician consider *Bartonella* as a possible cause of their illness. These physicians were unknowledgeable or were dismissive of *Bartonella* diseases. Veterinarians and physicians must become more aware of the correct *Bartonella* risks and diseases caused by feline derived *Bartonella*.

The Clinical Spectrum of Chronic Human Bartonellosis in Immunocompetent Patients Predominantly Originating from Lyme Disease Endemic Regions, B. Robert Mozayeni and others. Since rheumatic symptoms have sometimes been reported following CSD, this group wanted to determine if these may be associated with B*artonella*. They tested blood samples from 296 patients for evidence of *Bartonella* infection. The patients had previously been diagnosed with conditions ranging from Lyme disease, arthritis, and chronic fatigue. 62% were serologically positive for *Bartonella*, which supported prior exposure to and possible chronic infection with these bacteria. *Bartonella* DNA was found in 41% of patients allowing investigators to narrow the species of *Bartonella* present, with *B. henselae*, *B. koehlerae* and *B. vinsonii* subsp. *berkhoffii* the most prevalent.[7] Unfortunately, they did not report a response to antibiotic therapy in this group of patients. Although the evidence is suggestive, the cause and effect of *Bartonella* infection in these patients is unresolved.

Session 3: Laboratory Diagnostics In this session all four papers discussed the characterization and diagnosis of *Bartonella* infections in humans and dogs. None of these papers discussed the diagnosis of *Bartonella henselae*, the *Bartonella* species found most frequently in pet cats.

Diagnosis of Bartonellosis EB Breitschwerdt and RG Maggi, Intracellular Pathogens Research Laboratory, Center for Comparative Medicine and Translational Research NCSU-CVM, Raleigh, NC and Galaxy Diagnostics, Research Triangle Park, NC. *Bartonella* are notoriously difficult to isolate in culture from humans, dogs and cats most likely due to intermittent bacteremia and low-levels of bacteria in the blood. In dogs with active *Bartonella* infections, antibody is only detected between 25-50% by ELISA or IFA. Similarly antibody detection in humans with active *Bartonella* infection is poor. In 2005 the authors developed a novel, chemically modified, insect-based liquid culture medium (BAPGM) which greatly enhances the ability to isolate *Bartonella* in culture. In humans, this has led to the isolation of *Bartonella* from patients with many unique chronic diseases which has expanded the *Bartonella* paradigm significantly.[8,9] This method is the gold standard for the detection of *Bartonella* infection in humans. However, a shortcoming of this method is the necessity to obtain 3 sterile blood samples spaced two days apart.

Session 4- Genomics and Evolution This session contained papers discussing the genetic sequences of the various *Bartonella* species found in humans and cats. The efforts were focused on defining the *Bartonella* genes responsible for their pathogenic effects.

Session 5: Vectors and Ecology This session had five papers that explored the interactions of *Bartonella* in the mammalian hosts and arthropod vectors to ascertain if either the host or vector selected genetically different strains of *Bartonella*.

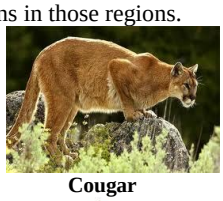
Global Distribution and Genetic Diversity of *Bartonella* in Bat Flies (Hippoboscoidae, Streblidae, Nycteribiidae). K Dittmar, and others. Department of Biological Sciences, SUNY at Buffalo, Buffalo, NY. New *Bartonella* genotypes were detected in a global sampling from 19 species of blood-feeding bat flies and from 20 host bat species. Thus, bats may be a major reservoir for *Bartonella*. Of interest is the ability of bat flies to hang onto bats while they fly at rapid speeds. As can be seen below in the figures, bat flies have unique leg hooks and mouthparts that enable them to firmly attach to bats while in flight.

Bat **Bat fly**

Bat fly attached **Leg hooks of bat fly**

Session 6: *Bartonella* in Wildlife This session had 4 papers that explored the occurrence of *Bartonella* in wildlife. Almost every species of wild animal has been shown to harbor *Bartonella* from rats, jirds, wild cats in Israel, Africa and Guatemala, to jackals and red foxes in Iraq. It is imperative to define the *Bartonella* species in wildlife in order to determine if they cause diseases in humans in those regions.

Rats



Cougar

Jackal

Jird

Session 7: *Bartonella* Taxonomy and Species Variety The final session had 4 presentations and was chaired by Dr. Russell Regnery, retired CDC researcher, who published some of the first *Bartonella* papers in the literature. Dr. Regnery posed provocative questions regarding the taxonomy and designation of *Bartonella* species names that are based on their genetic sequences and uniqueness.

Our recommendations:

1. **Discuss *Bartonella* zoonosis with your cat owners.**
2. **Recommend the *Bartonella* test.**
3. **If the owners refuse- date and note in case record.**
4. **Test all healthy & sick cats for *Bartonella.***
5. **Treat all infected cats.**

References:

1. Relman, D.A. *et al*. The agent of bacillary angiomatosis: An approach to the identification of uncultured pathogens. N. Engl. J. Med. 323: 1573, 1990.
2. Merrell, D.S. and Falkow, S. Frontal and stealth attack strategies in microbial pathogenesis. Nature 430: 250-256, 2004.
3. O'Reilly KL, Bauer RW, , *et al*. Acute clinical disease in cats following infection with a pathogenic strain of *Bartonella henselae* (LSU16). Infect Immun. 67 (6): 3066-3072, 1999.
4. Ketring, KL, Zuckerman, EE & Hardy, WD, Jr. *Bartonella*: A new etiological agent of feline ocular diseases. JAAHA, 40: 6-12, 2004.
5. Dehio, C. *Bartonella* interactions with endothelial cells and erythrocytes. Trends Microbiol 9:279, 2001.
6. Hardy, WD, Jr. & Zuckerman, EE. *Bartonella*: The Pet Cat-Human Connection. 1st International One Health Congress, Melbourne, Australia, February.14-16, 2011.
7. Maggi, RG, Mozayeni, BR, Pultorak, EL, et al. *Bartonella* spp.. Bacteremia and rheumatic symptoms in patients from Lyme disease endemic region Emerg Inf Dis 18:783-791, 2012.
8. Breitschwerdt EB & Kodick, DL. *Bartonella* infection in animals: carriership, reservoir potential, pathogenicity, and Zoonotic potential for human infection. Clin Microbiol Rev. 13:428-38, 2000.
9. Breitschwerdt EB. Feline bartonellosis and cat scratch disease. Vet. Immun & Immunopath. 123:167-171, 2008.

***Bartonella* references can be obtained at:**
www.nlm.nih.gov/ or natvetlab.com