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6th International Conference on *Bartonella* as Medical & Veterinary Pathogens[©]

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In This Issue:

In the Fall 2009 issue of the NVL Newsletter we will discuss the scientific presentations at the 6th International Conference on *Bartonella* as Medical & Veterinary Pathogens held in conjunction with the Faculty of Veterinary Science, University of Liverpool in Chester, UK, June 21-23, 2009. Dr. Richard Birtles organized an excellent scientific meeting which was "topped off" with a wonderful Safari Evening at the Chester Zoo where the attendees had private access to the Zoo and had a delicious barbeque.

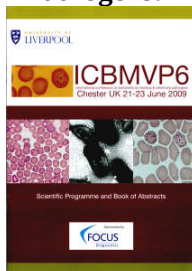


Meeting Venue- Queen Hotel, Chester, England.

The meeting venue was Chester England, a city steeped in history. Founded by the Romans in 79AD, fortified by Saxons to keep the Vikings at bay, Chester prospered ever since and is one of the best examples of a walled English medieval city, complete with a large cathedral and castle.

Abstracts

6th International Conference on *Bartonella* as Medical & Veterinary Pathogens:



The combined meeting had participants from around the world including Africa, Canada, China, Europe, Israel, Japan, South America, Russia and the United States. There were 36 abstracts at the meeting and, due to the worldwide economic decline, attendance was reduced compared to previous meetings. There were only 4 abstracts concerning *Bartonella* in cats and dogs, 7 concerning human *Bartonella*, and 5 concerning other animals, (rodents, deer, and bats). Thirteen abstracts presented molecular

subjects, 3 presented methods of detection (serology, PCR and culture), and 4 covered flea, tick, and ked vectors.



Chester Zoo barbeque

Cat *Bartonella* Abstracts

There were only 4 abstracts concerning *Bartonella* in cats or dogs, our abstract is reproduced in full below with the collaboration of Dr. Steven Petcher and Phillip Raclyn:

ATYPICAL *BARTONELLA*-ASSOCIATED DISEASES OF CATS & DOGS: PLATELET AND PANCREATIC DISORDERS

Hardy, WD¹, Jr., Zuckerman, EE¹, Petcher, SP² and Raclyn, P³. ¹National Veterinary Laboratory, Inc. Franklin Lakes, NJ, ²Citronelle Veterinary Clinic, Citronelle, AL, ³Riverside Veterinary Group, NY, NY.

Background: *Bartonella* cause inflammatory and granulomatous diseases in numerous tissues and organs in humans, cats, and dogs. Thrombocytopenia was one of the earliest reported *Bartonella* associated disorders, described in Oroya Fever in 1886. Numerous viral and bacterial infections, especially tick borne agents, induce thrombocytopenia in dogs and humans. Granulomatous inflammation of the pancreas has also been reported in *Bartonella* infected people.

Methods: We have tested 194,217 cats and 5,191 dogs by western blot for antibodies to *Bartonella*. Efficacy of *Bartonella* therapy in seropositive animals was assessed by a comparative western blot titration test of 12,768 cats and 104 dogs.

Results:

Incidence: Seropositivity for platelet disorders were: thrombocytopenia (cats 42/88 48%, dogs 33/270 12%), epistaxis (cats 20/33 61%, dogs 3/24 13%), excessive bleeding and ecchymosis (cats 16/36 44%, dogs 3/18 17%), and splenomegaly (cats 31/70 44%, dogs 9/47 19%). Seropositivity of cats and dogs for pancreatic disorders were: pancreatitis (cats 104/264 39%, dogs 4/34 12%), and insulin-dependent diabetes mellitus (cats 954/2,188 44%, dogs 3/32 9%).

Therapy: Platelet numbers returned to normal by 2-3 weeks of azithromycin therapy in 11 of 15 (73%) infected thrombocytopenic cats and 4 of 4 (100%) thrombocytopenic dogs. 4 of 4 recovered

cats had a 4 fold or greater titer decrease and 1 recovered dog had an 8 fold decrease 6 months after therapy. Follow-up data were available for 120 of the 954 infected diabetic cats. After therapy, 34 (28%) no longer required any insulin, 13 (11%) required 50-80% less insulin (39% of cats had insulin requirement reductions). 3 (2.5%) diabetic cats required more insulin after therapy.

Conclusion: We found an association of *Bartonella* seropositivity with platelet disorders (thrombocytopenia, epistaxis, excessive bleeding, and splenomegaly) and pancreatic disorders (pancreatitis and insulin-dependent diabetes mellitus) in both cats and dogs. Similar disorders were originally described in people infected with *Bartonella*. Appropriate antibiotic therapy caused rapid recovery of animals with platelet disorders and resolved or lowered the insulin requirement in 39% of infected cats with diabetes. *Bartonella* may inflame the pancreas in some cats leading to insulin-dependent diabetes mellitus. Our findings indicate that *Bartonella* can inflame virtually any tissue in the body and can induce varied clinical syndromes.

ASSOCIATION BETWEEN *BARTONELLA* INFECTION AND DISEASE IN PET CATS

Sykes, JE, Westropp, JL, Kasten, RW and Chomel, BB. School of Veterinary Medicine, University of California, Davis, CA.

These authors studied 299 cats by culture isolation and IFA serology. 154 (51.4%) were serologically positive whereas only 19 (6.3%) were culture positive. Using statistical methods of chi-squared analysis and the Mann-Whitney test they concluded there was no association of *Bartonella* with uveitis, neurological disease, lower urinary tract disease, or chronic kidney disease. However, they found that stomatitis was associated with *Bartonella* bacteremia (culture positive) but not seropositivity.

Editor's Note: Like these authors, for the past 15 years, we have found a strong association of *Bartonella* (seropositivity by western blot- not IFA) and feline oral inflammatory diseases but no association with lower urinary tract disease, or chronic kidney disease.¹⁻⁴ However, we have repeatedly seen a strong association of *Bartonella* with uveitis and other ocular inflammatory conditions. We feel the use of statistical methods for elucidation of the association of ubiquitous chronic persistent infectious agents with chronic diseases is problematic.

Human *Bartonella* Abstracts

NEUROLOGICAL MANIFESTATIONS OF CAT SCRATCH DISEASE: A 14-YEAR SURVEILLANCE STUDY WITH LONG-TERM FOLLOWUP. Giladi, M. *et al.* Tel Aviv Sourasky Medical Center, Tel Aviv, and Carmel Medical Center, Haifa, Israel.

This study characterized the neurological manifestations of cat scratch disease (CSD), their incidence and natural history. Between 1991 and 2005, 1,493 patients with CSD were evaluated by EEG, CT, MRI and EMG when clinically relevant. 21 (1.4%) of the 1,493 patients developed neurological complications. Eight patients (38%) had encephalitis and typically developed abrupt confusion and disorientation while 6 patients developed seizures. Four of these patients developed frontal release (signs of frontal lobe disorders) years after clinical cure. One patient developed significant memory loss. Six of 13 (46%) patients with endocarditis had neurological signs secondary to endocarditis. All 6 developed embolic strokes, 4 had hemiparesis or hemiplegia. None of the patients with endocarditis had lymphadenopathy, the most characteristic sign of CSD. One patient died and 3 remained with permanent neurological sequelae. Four patients (19%) had peripheral neuropathy with pain or numbness of the superficial cutaneous nerves of the upper limbs. Three patients recovered completely and one developed painful dysesthesia in the right forearm and palm. Of the remaining 3 patients, 1 had a cerebral infarct, 1 an epidural abscess, and 1 glossopharyngeal nerve palsy. The authors concluded that, although neurological complications of CSD are rare, significant abnormal neurological manifestations are found in half of CSD encephalitis patients.

COMPARISON BETWEEN SEROLOGY AND A REAL-TIME PCR REACTION ASSAY TARGETING THE *RPOB* GENE FOR THE DETECTION OF *BARTONELLA* SPP. IN CLINICAL PRACTICE. Senterre, JM, Brouwers, N, Carpentier, M, Minon, JM. Laboratory of Clinical Microbiology, CHR de la Citadelle, Liege, Belgium. Needle aspirates or excisional biopsies of 43 cases of regional lymphadenopathy, suspected of CSD, were studied by comparison of *Bartonella* IFA serology and PCR. 30 cases of CSD (69.8%) were identified- 29 (96.6%) were serologically positive (IgG >256) and 25 (83.3%) were PCR positive. **In this study, serology was more accurate than PCR in detecting *Bartonella* associated CSD in people.**

Other Animal Abstracts

***BARTONELLA* SPECIES IN BATS FROM EASTERN AFRICA.** Kosoy M, *et al.* Division of Vector-Borne Infectious Diseases, CDC, Ft Collins, CO and Nairobi, Kenya. This group has discovered several new *Bartonella* species in bats from Kenya, Africa. *Bartonella* was isolated from the blood of 106 of 384 (32%) bats from different locations in Kenya. The authors concluded "The finding of *Bartonella* species in a high proportion of apparently healthy bats sampled in Kenya suggests the need to investigate whether these

agents might be responsible for human illnesses in Kenya and elsewhere in Africa."



Kenyan bats in a cave

Molecular Abstracts

TYPE IV SECRETION SYSTEM TRW OF *BARTONELLA* MEDIATE SPECIFIC RED CELLS ADHESION. Deng HK¹, Le Rhun D¹, Le Naour E¹, Biville F¹, Cescas S¹, Arnaud L¹, Dehio C², Vayssier-Taussat M¹. ¹UMR BIPAR, 23 Avenue du General de Gaulle, Maisons-Alfort, France; Institut National de la Transfusion Sanguine, Paris, France and ²Biozentrum of the University of Basel, Basel, Switzerland.

This group has studied the mechanism by which bartonellae invade red blood cells which enable them to establish long term bacteremia by avoiding the immune response due to their intra-erythrocyte location. *Bartonella* possess a Type IV secretion system (T4SS) which has 6 pathogenicity factors that enable the bacteria to adhere to and penetrate erythrocyte membranes. Once inside the erythrocytes, the bacteria are sheltered from immune attack and can persist for months if not years. Over time *Bartonella* may be released from erythrocytes to attach to endothelial cells (capillary lining cells) and thereby begin the pathogenic steps of inducing inflammation that is described in the following abstract. **This study elucidated the *Bartonella* mechanism of red blood cell penetration leading to chronic bacteremia, the beginning of the pathogenic process.**

MOLECULAR ANALYSIS OF *BARTONELLA* ADHESIN A (BAD A). Riess T¹, Kaiser PO¹, Schmidgen T¹, Linde D², Lupas D², Kempf V¹. ¹Institute fir Medical Microbiology and Infection Control, Johann Wolfgang Goethe-University, Frankfurt am Main, and Max Plank Institute for Developmental Biology, Tubingen, Germany.

This group continues to do ground-breaking molecular studies elucidating the molecular aspects by which bartonellae possess unique pathogenic mechanisms. The outer membrane protein, *Bartonella* adhesion A (BadA), is a new member of the novel family of adhesins and represents an important pathogenicity factor. Expression of BadA in *B. henselae* outer membranes allows the bacteria to adhere to endothelial cells which is the major event that stimulates inflammation and new blood vessel formation (angiogenesis). Inflammation is the hallmark disease process induced by all *Bartonella*. In this study, the authors identified the protein nature of BadA and its location in the outer membrane of *B. henselae*. *B. henselae* is the most prevalent *Bartonella* of cats, dogs and humans, which is responsible for initiating inflammation. In cats, the myriad of *Bartonella* diseases: gingivitis, stomatitis, uveitis, conjunctivitis, chorioretinitis, URI, endocarditis, and vasculitis are the result of one disease process- inflammation. **This study elucidated the protein molecules that are responsible for *Bartonella* pathogenesis.**

Vector Abstracts

DOES *IXODES RICINUS* TRANSMIT *BARTONELLA HENSELAE*? Bonnet S, Cotte V, Le Rhun D, Le Naour E, Vayssier-Taussat M. UMR BIPAR, 23 Avenue du General de Gaulle, Maisons-Alfort, France.

This group investigated the potential that *Ixodes ricinus*, the most abundant Ixodid tick that bites humans in Western Europe, can act as a vector for *B. henselae*. They found that *B. henselae* is transmitted across developmental tick stages, migration or multiplication of *B. henselae* in salivary glands after a second blood meal, and transmission of viable bacteria from ticks to blood. *Ixodes ricinus* is a competent vector for *B. henselae* and cats have been shown to be infested with these ticks in several European countries.



Ixodes ricinus- Europe

Ixodes scapularis- USA

REAL-TIME TRACKING OF *BARTONELLA HENSELAE* THROUGH *CTENOCEPHALIDES FELIS*. Robinson MT¹, Woods D², Morgan ER³, Shaw SE¹. ¹School of Clinical Veterinary Sciences, University of Bristol, Somerset, UK, ²Pfizer Animal Health, Kalamazoo, MI, and ³School of Biological Sciences, University of Bristol, Bristol, UK.

This study describes the transit time of *Bartonella henselae* through the common cat flea, *Ctenocephalides felis*. The cat flea is the most common flea present on cats and dogs in the United States and Europe. Although the gut transit time can take as long as 3 days, viable *Bartonella* are able to persist in various organs in the flea for as long as 10 days. The authors concluded that "Bacteria are retained within the flea allowing prolonged dissemination of the bacterium via faecal material. *C. felis* acts as a short-term vector for *B. henselae*. A possible site for sequestration of *B. henselae* within *C. felis* would be the malpighian tubules."



Ctenocephalides felis- the cat flea

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