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NEWSLETTER

The Fe*Bart* (*Bartonella*) Test is Sweet 16©

Evelyn E. Zuckerman, Editor **Fall 2015** **Vol. 14, Number 4**

In This Issue:

On November 4, 2015 I was again trying to decide on a subject for our 56th quarterly NVL Newsletter when it finally dawned on me that this very date was the 16th anniversary of our introduction of the Fe*Bart* Test, a western blot (WB) serological test, for detection of *Bartonella*. Yes, 16 years ago the National Veterinary Laboratory was the first diagnostic laboratory to offer a routine *Bartonella* screening test. During these stimulating 16 years we have tested 338,393 cats and 9,381 dogs for *Bartonella*. In this Newsletter I will recall our experiences, both good and bad, during these years. The most rewarding aspect has been the interactions with the thousands of veterinarians who utilized our services and taught us about the clinical aspects of *Bartonella*.

William D. Hardy, Jr. V.M.D.
Director and Owner
National Veterinary Laboratory, Inc.

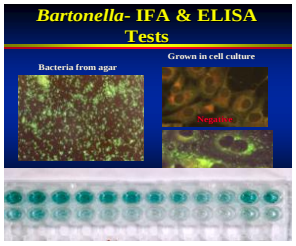
Introduction:

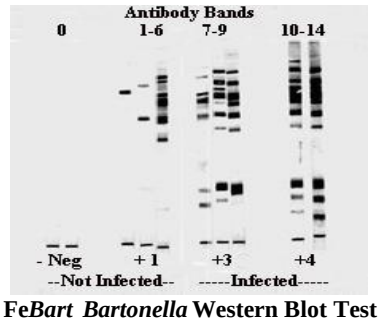
We began to study the zoonotic pathogen *Bartonella* shortly after its discovery in 1990.[1] In 1995, after 5 years of research of comparison of culture isolation with serology, our data showed that the most accurate and reproducible test for detection of *Bartonella* infection in cats was the serologic detection of antibodies to the bacteria using the western blot (WB). The WB is the most specific (accurate) and sensitive serologic assay for the detection of many microorganisms. It is used in human medicine to confirm ELISA positive HIV screening tests, Lyme positive serology and several others. In veterinary medicine it is also used to confirm FIV ELISA positive serology. Detection of antibodies to an etiological agent is an amplification system when antibodies coexist with etiological agents as they do in FIV and *Bartonella* infections in cats.

The National Veterinary Laboratory Inc. (NVL) is the oldest private veterinary diagnostic laboratory in the country. Dr. Hardy developed the first diagnostic test for FeLV infection in 1972 while at the Memorial Sloan Kettering Cancer Center, the IFA test for detection of FeLV antigens in cat leukocytes and platelets (FeLeuk Test). He and his colleagues used the test to discover that FeLV is spread contagiously between cats.

This discovery changed the paradigm that retroviruses were no longer thought to only be transmitted genetically (vertically). NVL was then established in 1973 to provide this practical and accurate test for screening cats for this virus and led to programs that lowered the transmission among cats. The FeLeuk Test remains the "Gold Standard" confirmatory screening test for detection of FeLV infection.

***Bartonella*:** During the early HIV retrovirus epidemic in the early 1990s, physicians in the many medical centers began to observe life-threatening cases of *Bartonella* infections in HIV infected patients. Since we had worked with feline retroviruses, and since *Bartonella* was known to be transmitted by cats, we began to study the occurrence of *Bartonella* in cats and developed IFA, ELISA and WB tests for *Bartonella*. It took more than 5 years, and tests of more than 5,000 cats, to develop and verify the accuracy of our diagnostic *Bartonella* tests. After thousands of comparative IFA, ELISA and western blot tests we chose the much more specific western blot (WB) as a screening test because, in our laboratory, it is more sensitive and more reproducible than the other *Bartonella* serological methods.[2]





Fe*Bart* *Bartonella* Western Blot Test
Happy Sweet 16th Birthday!

The WB test can differentiate *Bartonella*-infected cats from cats that may react non-specifically, or have cross-reactive antibodies, in IFA or ELISA tests, to *Chlamydia* or other microorganisms. The Fe*Bart* test detects antibodies to as many as 14 *Bartonella* proteins and the test correlates well with infection or lack of infection in cats.

The Early Days

As our early *Bartonella* testing days evolved, there appeared a great deal of online chat, especially from a practitioner on VIN where I was referred to as a money grubbing reptile for introducing the *Bartonella* test.[3] Of course I could not resist a little fun when I was invited to speak at the Fall AAFP conference in San Francisco in 2004. I presented the slide below and, in the front row, was that very practitioner who was suddenly not so outspoken.

There was ongoing discussions on VIN, in early publications, and in meeting presentations, to the effect (see the original paradigm below) that *Bartonella* was not important, that there was no test for *Bartonella*, that no therapy was effective at eliminating *Bartonella* from cats, that cat scratch disease (CSD) was mostly a mild self-limiting disease of children that need not be treated, that *Bartonella* did not cause any disease in infected carrier (reservoir) cats, that fleas had to be present on cats at the time they transmitted the infection to people, and that the CDC and AAFP both said there was no rational to test healthy cats for *Bartonella* infection, even though any cat, healthy or sick, is capable of zoonotic transmission.[3,4]

Original *Bartonella* Paradigm:

Cats:

1. *Bartonella* cause no disease in cats.
2. There is no test for *Bartonella*.
3. There is no therapy for *Bartonella*.
4. Serology only shows past exposure.

Humans:

1. *Bartonella* causes mostly CSD.
2. CSD occurs mostly in children.
3. CSD is self-limiting- no need to treat.
4. Fleas or flea feces have to be present on cats for zoonotic transmission to occur.
5. CDC & AAFP did not recommend testing cats.

Of course with time, and with the collaboration of many practitioners, we and others have changed these statements causing a paradigm shift. With more that 4,000 *Bartonella* publications at present, there is ample evidence that *Bartonella* infection

(updated paradigm) is not always self-limiting in people, that there are *Bartonella* tests available, and that *Bartonella* do cause inflammatory diseases in cats.[6-15] In fact, two of the academics who made many of the early negative statements regarding testing cats later developed their own commercial *Bartonella* tests.

Veterinarians and Physicians Must Consider *Bartonella* as Important Pathogens- Updated Paradigm:

After interacting with thousands of veterinarians during the past 16 years I still feel that many in our profession do not fully appreciate the importance of *Bartonella* in cats or in people. Likewise, after interviewing more that 500 people infected with *Bartonella*, it is clear that a substantial proportion of physicians do not know much about *Bartonella* or are dismissive of their clinical importance. Our findings, presented at the 7th International Conference on *Bartonella* in 2012, support these conclusions (see abstract below).

All *Bartonella* Diseases are not "Cat Scratch Disease:" Misconceptions about Bartonellosis. WD Hardy and EE Zuckerman, 7th International Conference on *Bartonella* as Animal and Human Pathogens, Raleigh, NC, April 25-28, 2012.

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. 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.

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*.

Updated *Bartonella* Paradigm: (The Paradigm Shift)

Cats:

1. *Bartonella* cause inflammatory disease in cats.
2. There are tests available for *Bartonella.*
3. There is therapy for *Bartonella.*
4. Serology can show current or past infection.

Humans:

1. *Bartonella* cause CSD and severe diseases.
2. CSD occurs equally in children and adults.
3. CSD is not always self-limiting- treatment may be necessary.
4. Fleas do NOT have to be present on cats for zoonotic transmission to occur.
5. CDC still does not recommend testing cats.

CDC Healthy Pets Healthy People Website: www.cdc.gov/healthypets/

The CDC has redesigned this website on October 2, 2015 with information about "diseases that can be spread from pets to people." The director of the One Health Office in the CDC National Center for Emerging and Zoonotic Infectious Diseases said it is an excellent resource for practitioners and their clients. In the alphabetical list of diseases, *Bartonella henselae* and Cat Scratch Disease are listed with identical information given for both subjects. The information is outdated and inadequate considering there are more than 4,000 published articles on these subjects. Incorrectly, the website uses the term "CSD" as if it is the etiologic agent "*Bartonella."* "Although rare, CSD can cause people to have serious complications. CSD can affect the brain, eyes, heart, or other internal organs." In another sentence concerning *Bartonella* in cats they state "*Bartonella henselae* infection may also develop in the mouth, urinary system, or eyes." They probably mean that "inflammation or disease" may also develop. We know of no association of *Bartonella* with urinary system diseases. Under "Prevention," there is no mention of testing cats for *Bartonella* infection and therapy. Under "Available Tests & Treatments" "People: Talk to your doctor about testing and treatments for CSD. CSD is typically not treated in otherwise healthy people." Of course CSD is only the tip of the iceberg of *Bartonella* inflammatory disease in people (see our Newsletters on www.natvetlab.com). Under "Cats: Talk to your veterinarian about testing and treatments for your cat. Your veterinarian can tell you whether your cat requires testing or treatment." Thus, the US national health site, the CDC, still does not give any concrete recommendation to assist cat owners and veterinarians to understand this dangerous zoonotic pathogen. In addition, the site leaves the reader with the impression that CSD is the most important *Bartonella* disease. We hope the CDC will quickly modify this part of their website.

****We thank all of our clients for making these 16 years so productive****

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www.nlm.nih.gov/ or natvetlab.com