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NEWSLETTER

The History of *Bartonella*: From Antiquity to the Present

Evelyn E. Zuckerman, Editor **Summer 2012** **Vol. 11 Number 3**

In This Issue:

The Summer, 2012 issue of the NVL Newsletter will review the history of *Bartonella* throughout the ages. Although the scientific literature has portrayed *Bartonella* as emerging pathogens, in fact, they have caused severe diseases for centuries. Why study history? To learn from and avoid the mistakes of the past.

Introduction:

As with all life, *Bartonella* have evolved with their animal hosts (co-evolution) for millions of years. This group of bacteria has a fascinating history in medicine and affecting civilizations. It was the first microorganism to be identified by DNA technology directly from diseased tissue without having been isolated and grown in a laboratory. There are now more than 26 known *Bartonella* species that use numerous animals, including cats and dogs as their reservoir hosts.

History:

History is replete with descriptions of outbreaks of contagious diseases that have decimated populations or have altered the efforts of warring army's. Examples are Black Death-Plague (*Yersinia pestis*), Antique Plague of Athens (*Salmonella enterica* serovar Typhi) smallpox and more recently AIDS. Using the spectacular new DNA technologies, additional diseases have been added to this list. Recently, the *Bartonella* paradigm has expanded from a "new emerging zoonotic" self-limiting mild human disease, to a group of serious chronic debilitating human and pet animal diseases.

Palaeomicrobiology:

The detection and characterization of microbial DNA is the most commonly used method for studying past pathogens. Host-associated DNA has been shown to survive for 20,000 years and bacterial DNA can be detected from permafrost specimens for 1 million years.[1,2]

Dental pulp in a canine tooth

The dental pulp is a highly vascularised tissue inside the tooth and is protected from the environment. Thus, dental pulp may be an excellent source for contemporary or ancient blood-borne microorganisms. DNA has been shown to be better conserved in dental pulp than in any other tissue, including bone.[3] The canine teeth of cats, dogs and humans are the best teeth to use since they are large, have a large pulp cavity and have only one root canal opening.

Historical Dates

2100 BC: *Bartonella* Found in a 4000-Year-Old Human Tooth.

The remains of 2 individuals were excavated from the Peyraoutes, an archaeological site in Roaix, southeastern France.

Excavation of ancient burial site

Bartonella quintana DNA was recovered from the dental pulp of a tooth from a person who died between 2100-2200BC.[4] The ancient sequences had 2 mutations that have not been found in modern *B. quintana* isolates. This shows that ancient humans were also bacteremic with *Bartonella*.

1300: *Bartonella henselae* found in teeth from 800-Year Old Cats.

135 teeth from 19 domestic cats from 7 burial sites in France were analyzed for *Bartonella* DNA. The sequencing of *Bartonella* genes from the dental pulp of the cats identified the presence of *B. henselae.* The observation of a unique mutation in the *Bartonella* species ruled out modern DNA contamination of the samples. This shows the antiquity of the relationship between *Bartonella* species and cats that act as reservoirs for the organism. Thus, domestic cats had *Bartonella henselae* bacteremia 800 years ago.[5]

1531: First Medical Description of a *Bartonella* Disease

The first medical description of a *Bartonella* disease was bartonellosis described in pre-Columbian cultures in Peru. The death of the Inca Huayna Capac, 11th Inca king (1464-1527), and many inhabitants of the Inca Empire, has been attributed to bartonellosis.

1812: Defeat of Napoleon's army in the 1812 invasion of Russia

Using modern DNA technology it was found that *Bartonella* helped to defeat Napoleon's army in the 1812 invasion of Russia.

Napoleon's retreat from Russia

This was one of the worst military defeats in history. Only about 25,000 of the 500,000 French soldiers survived. Many of these lice-infested soldiers, found in a mass grave in Vilnius, Lithuania, died of lice-borne diseases such as trench fever (*Bartonella quintana*) and typhus, not in combat.[6] Remnants of lice found

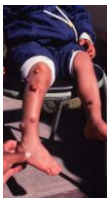
in the mass grave had *Bartonella* DNA confirming that *Bartonella*, rather than war, caused a significant percentage of the deaths of these French soldiers.

1885: Carrion's Disease, Peru

Another *Bartonella* disease is Carrion's Disease (Oroya Fever) which is the eponym in honor of the Peruvian medical student Daniel A. Carrion.

Daniel Carrion

He died in 1885 after two self-inoculations of an aspirate of the "Peruvian Wart" (papule) of a patient, in an attempt to find the cause of this disease. On autopsy, bacilli were found in Carrion's RBCs. The causative organism, *Bartonella bacilliformis*, is transmitted by the *Lutzomyia verrucarum* sandfly. *Bartonella bacilliformis* was the first named *Bartonella* species.

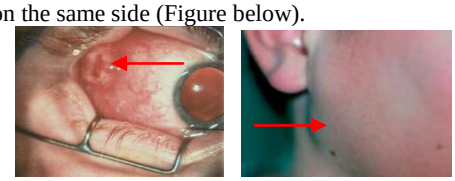


Peruvian Wart

1889: Parinaud's Oculoglandular Syndrome

The first description of a human *Bartonella henselae* disease was given by the French ophthalmologist Henri Parinaud in 1889 when he described what is now known as Parinaud's oculoglandular syndrome.[8] The syndrome is the

combination of granulomatous conjunctivitis in one eye, and lymphadenopathy in front of the ear on the same side (Figure below).



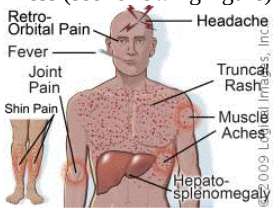
Granulomatous conjunctivitis Lymphadenopathy

1905: *Bartonella* Discovery

The discovery of *Bartonella* was made in 1905 by Alberto Barton Thompson after an outbreak in foreign workers that traveled to La Oroya, Peru. Most of the workers died of the rare disease characterized by fever and severe anemia. He discovered a bacillus in their red blood cells.[9] In 1913, Richard Strong of Harvard University confirmed Barton's discovery and named the bacteria *Bartonia* in honor of Barton; the bacterial species was subsequently named *Bartonella bacilliformis*.

1916: Trench Fever

Trench Fever was also known as 5-day fever or quintan fever and was first described in 1916 during WWI when about 1 million axis and allied soldiers were affected.[10] The disease was debilitating, though self limiting and non-lethal. They experienced spenomegaly, fever, arthropathy and arthritis, muscle pain, rash, and severe weakness (see following figure).



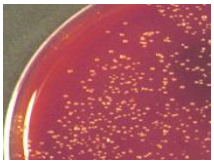
The primary vector is known to be "*Pediculus humanus*" variety *corporis*, also known as the human body louse.

1990: *Bartonella henselae* found by DNA Technology

In 1990, Relman and his collaborators used PCR-amplified DNA directly from the bacillary angiomatosis lesions of an AIDS patient and found that it was closely related to *Rochalimaea (Bartonella) quintana*, the Trench Fever agent. It was the first microorganism to be identified by DNA technology directly from diseased tissue without having been isolated and grown in a laboratory.[11]

1990: *Bartonella henselae* Isolated

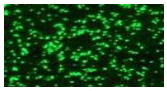
In the same year Slater and his collaborators were the first to isolate *Bartonella* from the blood of patients with fever and bacteremia.[12]



***Bartonella henselae* isolated in blood agar**

1992: *B. henselae* etiology of CSD

Bartonella henselae was recognized as the etiologic agent of CSD in 1992 by Regnery and his colleagues when they found that 88% of sera from CSD patients contained antibodies specific to this agent.[13]



IFA positive serum from a CSD patient

1994: Pet Cats Have Prolonged *Bartonella* Bacteremia in cats

Pet cats associated with human *Bartonella* zoonoses were found to have indefinite prolonged bacteremia.[14]

1995: CDC Finds High Prevalence of *Bartonella* in Pet Cats

A CDC national serological survey of pet cats found the prevalence of *Bartonella* infection was high in geographic areas in the US that were favorable for fleas. Thus, the southeast had the highest prevalence of 55% whereas the Rocky Mountain states had the lowest of 4%.[15]

1996: Experimental Infection Studies Showed *Bartonella* Induces Diseases in Cats and Demonstrated Effective Therapy.

Greene and his colleagues found 8 of 8 experimentally infected cats developed lymphadenopathy and skin papules. Antibiotic therapy was effective in clearing the infection in 6 of the 8 cats.[16]

1997: Relapsing Bacteremia

Kordick and Breitschwerdt showed that experimentally infected cats developed intermittent bacteremia.[17] This is problematic when sampling cat blood for diagnostic methods of isolation in culture and PCR. This has no effect on serologic assays for detection of antibody to *Bartonella*.

1999: Fe*Bart*® WB *Bartonella* Test Introduced for Veterinarians

The National Veterinary Laboratory introduced a practical serological *Bartonella* western blot test for cats and dogs.[18] Using this test we elucidated many feline *Bartonella* induced inflammatory diseases and developed effective therapy protocols.

2005: Insect Culture Medium

In 2005, Breitschwerdt and his colleagues introduced an insect medium culture system that has greatly improved the ability to isolate *Bartonella* in culture. Using this test system they have expanded the human *Bartonella* disease paradigm.[19]

What Have We Learned from the History of *Bartonella*?

1. All *Bartonella* do not cause self-limiting diseases. *B. bacilliformis* in Peru has one of the highest human mortalities of any bacterial disease.
2. It is imperative to prevent *B. bacilliformis* from entering the USA.
3. Many human deaths have been attributed to *B. quintana* and this species is present in the USA and is carried by pet cats.
4. Pet cats are a major reservoir for 6 *Bartonella* species and infected cats pose a zoonotic threat.
5. Veterinarians and physicians must work together to prevent infections of cats and people.

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