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NEWSLETTER

The Eyes Have It: *Bartonella* Tropism[©]

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Spring 2006

Vol. 5, Number 2

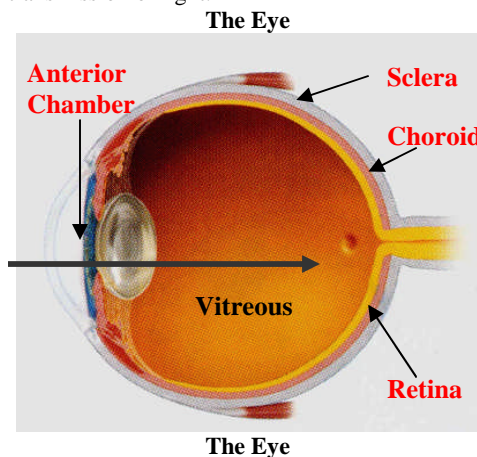
In This Issue:

In the Spring 2006 issue of the NVL Newsletter we will discuss one of the most common sites for *Bartonella* infection in cats and humans; the eyes. It appears, possibly due to the vascular architecture of the eyes, that *Bartonella* has a tropism for ocular tissues in cats and humans.

The Eye

Background:

The eye is an anatomical extension of the central nervous system (CNS) and like most cells of the CNS many cell types in the eye cannot regenerate after injury. While inflammation and immune-mediated injury can be tolerated by many tissues that are capable of regeneration, the eye cannot tolerate even mild inflammation without the potential loss of its main function, vision.¹ Thus, the eye must maintain a clear path for light from outside to traverse through the lens and reach the retina in order for sight to occur. The complex functions of the retina and the connections to the visual cortex would be meaningless if the structures from the cornea, anterior chamber, lens or vitreous were damaged by inflammation blocking the accurate transmission of light.



Anatomy:

The eye is made up of three coats: 1) Sclera: the outer fibrous protective coat, 2) Choroid: the middle vascular and pigmented coat, and 3) Retina: the inner nervous coat. The vascular nature of the choroid predisposes it to pathological damage. Bacteria and bacterial emboli often lodge in the choroid, and leukocytes can escape the vasculature to invade

the choroidal stroma and retina. The retina is often involved in inflammatory processes of the choroid and this process is called chorioretinitis. Some of the infectious agents that cause chorioretinitis are *Bartonella* spp. *Toxoplasma gondii*, *Coccidioides immitis*, *Mycobacterium tuberculosis* and various viruses.

Ocular Immune Privilege:

Nieder Korn has described this phenomenon in an excellent review entitled "Ocular Immune Privilege: Nature's Strategy for Preserving Vision."¹ The anterior chamber of the eye permits the survival of foreign tissue and tumor grafts, a phenomenon that was thought to result from sequestration of intraocular antigens from systemic lymphoid tissues of the body. It is now known that immune sequestration is not responsible for this immune privilege, but rather there are an array of local anatomic, physiologic and immunoregulatory factors responsible. The ocular fluids of the anterior chamber, the aqueous humor, possess remarkable immunomodulatory factors that suppress or dampen the immune response in order to spare collateral damage to innocent ocular bystander cells that are unable to regenerate.

Bartonella Occurrence in Cats:

As of April 1, 2006 the results of 107,606 cats tested for infection with *Bartonella* species by the western immunoblot are given in Table 1. Cats were tested from all geographic areas of the United States where exposure to fleas and ticks varies greatly. Thus, 38% of healthy cats were positive, whereas when we carefully investigated the risk factors of 860 cats in the northeast, we found only 20% were infected. Thus, we use 20% as the base line infection occurrence to analyze the occurrence of *Bartonella* in inflammatory diseases of the eye.²

Table 1 Occurrence of *Bartonella* in Cats from the United States

Status	Number Tested	Number Positive	% Positive
Healthy*	26,413	10,089	38%
1) No RFs**	5,629	1,756	31%
2) With RFs	20,784	8,333	40%
Diseased Cats	78,095	36,864	47%
Not Specified***	3,098	1,396	45%
Totals	107,606	48,349	45%

* RFs= risk factors for *Bartonella* infection- flea & tick exposure- hot & humid climates, stray or shelter origin, multi cat household.

** No risk factors reported by veterinarian.

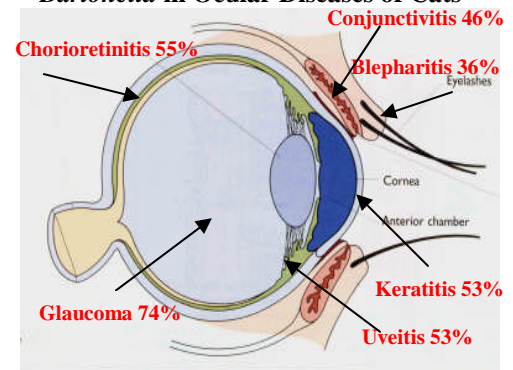
*** No diagnosis given.

Bartonella Diseases of the Eye:

Feline Ocular *Bartonella* Diseases:

Feline *Bartonella* cause inflammatory diseases of all structures of the eye due to their affinity to infect erythrocytes and vascular endothelial cells of all tissues. Since the eye is a highly vascular organ, *Bartonella* are responsible for many ocular diseases that veterinarians diagnose commonly in cats. Dr. Kerry Ketring, All Animal Eye Clinic, Cincinnati, OH, Dr. Craig Fischer and Dr. Melanie Mineo, Animal Eye Clinic of Florida, Clearwater, FL, and our laboratory have reported on the association of *Bartonella* in ocular inflammatory diseases of cats.^{3,4} Others have also reported an association of *Bartonella* in ocular disease in cats.⁵

Bartonella in Ocular Diseases of Cats



We detected *Bartonella* in 15,968 ocular inflammatory diseases of cats. Many cats had multiple simultaneous ocular inflammatory diseases such as conjunctivitis and uveitis. A summary of the *Bartonella* status of cats with ocular disease is given in Table 2.

Table 2

Bartonella Infected Cats with Ocular Inflammatory Diseases

Disease	Number Tested	Number Positive	% Positive
Conjunctivitis	12,506	5,791	46%
Uveitis	1,725	911	53%
Corneal Ulcer	687	350	51%
Keratitis	633	328	52%
Chorioretinitis	222	122	55%
Epiphora	81	41	51%
Glaucoma	72	53	74%
Blepharitis	42	15	36%
Totals	15,968	7,611	48%

There are 4 possible interpretations as to the *Bartonella* causation of the ocular inflammatory disease in a *Bartonella* antibody positive cat: 1) *Bartonella* is the sole cause of the disease, 2) *Bartonella* is a partial cause, co-etiological polymicrobial disease, 3) *Bartonella* is not the cause of the disease but is in the background only, and 4) *Bartonella* has been rejected and the positive antibody test indicates past infection. *Bartonella* are a major threat to the sight of cats and humans due to the chronic nature of the induced ocular inflammation which can eventually overcome the immune privilege of the eye and cause severe damage which the ocular tissues cannot repair by regeneration.

Conjunctivitis:

The most common feline ocular disease is conjunctivitis. Conjunctivitis is an inflammation of the conjunctiva, the mucous membrane covering the anterior surface of the eyeball and the lining of the eye lids. Conjunctivitis can be caused by bacteria, viruses, and fungi. Forty-six percent of 12,506 cats with conjunctivitis were *Bartonella* positive. The following 3 figures show the therapeutic responses of *Bartonella* infected cats with conjunctivitis.

Conjunctivitis: Before and after therapy



Dr. Rene Gandolfi, Castro Valley Companion Animal Hospital, Castro Valley, CA

Uveitis & Conjunctivitis: Before and after therapy

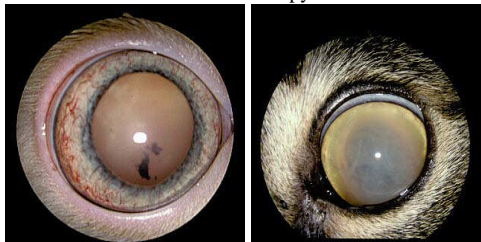


Dr. Kerry Ketring, All Animal Eye Clinic Cincinnati, OH

Uveitis:

Uveitis is inflammation of the entire uveal tract, the iris, ciliary body and the choroids. Uveitis is often a sign of systemic infection. We found 53% of cats with uveitis were *Bartonella* positive.

Uveitis: Before and after therapy

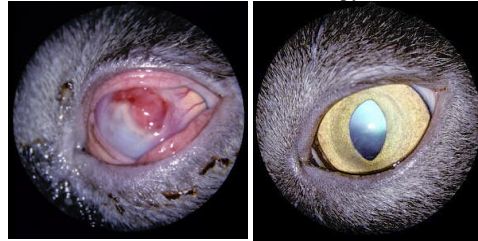


Dr. Kerry Ketring,
All Animal Eye Clinic
Cincinnati, OH

Corneal Ulcer:

The integrity of the eye is threatened by penetrating wounds or perforation by ulceration of the cornea. We found 51% of cats with corneal ulcers were infected with *Bartonella*.

Corneal Ulcer: Before and after therapy



Dr. Kerry Ketring, All Animal Eye Clinic Cincinnati, OH

Blepharitis:

Blepharitis is an inflammation of the eye lids, especially the margins of the lids.

Blepharitis: Before and after therapy



Dr. Jack Broadhurst Cat Health Clinic Pinehurst, NC

Human Ocular *Bartonella* Diseases:

Ocular inflammatory disease occurs in 5-10% of people with cat scratch disease (CSD).⁶ The eye becomes involved 1 to 4 weeks after the systemic signs of CSD appear. However, ocular *Bartonella* disease can occur without the recognition of classical CSD syndrome preceding the involvement of the eye.⁷ Human *Bartonella* ocular diseases are listed in Table 3

Table 3

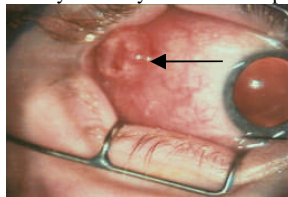
Human <i>Bartonella</i> Ocular Diseases
Parinaud's Oculoglandular Syndrome
Uveitis
Chorioretinitis
Conjunctivitis
Disciform Keratitis
Blepharitis
Orbital Granuloma

Parinaud's Oculoglandular Syndrome:

Parinaud's oculoglandular syndrome is the most common human ocular *Bartonella* syndrome. It is characterized by regional lymphadenopathy and mild swelling of the eyelid with a serous to mucopurulent discharge. Severe hyperemia and granulomatous nodules may occur on all conjunctival surfaces (Figure below).

Parinaud's Oculoglandular Syndrome

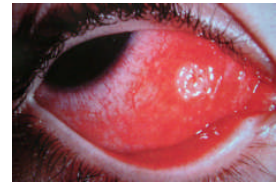
13 year old boy bitten by a cat 3 weeks prior.



Dr. Kerry Ketring, All Animal Eye Clinic Cincinnati, OH

Conjunctivitis:

Severe conjunctivitis in a 12 year old girl infected with *Bartonella henselae*.

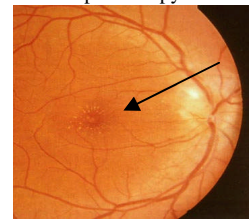


Dr. Kerry Ketring, All Animal Eye Clinic Cincinnati, OH

Chorioretinitis:

Due to its vascular nature, many infectious agents cause inflammation in the choroid layer resulting in chorioretinitis.^{8,9}

Chorioretinitis: Bilateral macular papilledema and stellate exudates (arrow) caused by *Bartonella henselae*. The boy had recently acquired 2 playful kittens. He had transient right cervical lymphadenopathy 2 weeks before blurred vision occurred. His vision returned to normal after doxycycline & rifampin therapy.



NEJM 343:1459, Nov. 16, 2000.

Conclusion:

The eye is a very specialized organ with little ability to regenerate tissue after damage by trauma or infectious processes. Thus, it is important for veterinarians and physicians to be aware of the possible involvement of *Bartonella* in inflammatory processes of the eye in order to prevent permanent damage.

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More *Bartonella* references can be obtained at:
www.nlm.nih.gov/