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NEWSLETTER

Breathe Easier- Without *Bartonella*©

Evelyn E. Zuckerman, Editor **Summer 2014** **Vol. 13 Number 3**

In This Issue:

The Summer 2014 issue of the NVL Newsletter will discuss *Bartonella* diseases of the respiratory tract of cats, dogs and people. *Bartonella* associated respiratory diseases in cats are common, whereas they are infrequent in dogs and humans. As with most of the *Bartonella* diseases we have described in cats, respiratory *Bartonella* induced diseases were first described in humans.[1-9]

Introduction:

Bartonella Pathogenesis:

Bartonella are Gram-negative bacilli that possess pili which are hair-like structures found on the bacteria's surface. *Bartonella* have a strong tendency to stick or clump together in tissues and in culture and to stick to, and penetrate, RBCs and endothelial cells. The ability to adhere to each other, and to the membranes of RBCs and endothelial cells, leads to the wide and varied tissue pathogenesis observed in cats, dogs and people. Pili and a protein called deformin are probably responsible for the sticky properties.[10] The wide tissue tropism of *Bartonella* is due to the adhesion to endothelial cells which are the constituents of capillaries. Thus, *Bartonella* induce chronic lymphocytic plasmacytic granulomatous inflammatory reactions in tissues throughout the infected animal's body. Since capillaries are found in all tissues, all tissues are susceptible to the inflammatory effects of *Bartonella*.

Respiratory Disease:

Humans with "cat scratch disease- CSD" or bartonellosis have served as the "animal model" for veterinarians investigating *Bartonella* diseases in cats and dogs. Respiratory diseases were occasionally observed in people with CSD in publications from the 1950s to the present.[1,4-8]

Respiratory diseases are very common in cats, especially cats from multicat households, shelters, rescue groups or feral cat colonies.

Chronic URI, sinusitis and rhinitis are difficult cases for veterinarians to manage because there are many possible etiologies. The addition of *Bartonella* to the differential diagnosis has made this situation easier because there are tests for *Bartonella* infection, therapy is easy and a test to evaluate therapy is available.

Respiratory diseases (infections) are divided into upper (URI) and lower (LRI) sites:

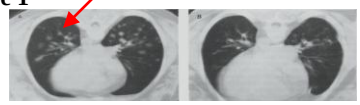
Upper Respiratory Diseases are confined to:
- Nose
- Nasal cavity- and turbinates
- Sinuses
- Nasal & oral pharynx
- Larynx

Lower Respiratory Diseases are confined to:
- Trachea
- Bronchi and lower airways
- Lung parenchyma

Human:

Bartonella respiratory diseases in humans have usually been associated with CSD and occur in both immunocompetent and immunosuppressed people. Most have occurred in the lower respiratory tract in the lungs (pulmonary nodules and pneumonia) and pleura (pleuritis).[1,3-9]

Figure 1



Pulmonary nodules- left, nodules resolved after antibiotic therapy- right. Caniza, MA et al. Ref 1

Dogs:

Bartonella induced respiratory diseases are among the most common clinical entities in *Bartonella* seropositive dogs with lameness, arthritis, epistaxis, splenomegaly, and nasal discharge found most often.[11-13] However, other studies did not find such an association.[14-15] In general, dogs are infected with *Bartonella* much less often than cats, the natural reservoir host for 6 of the most common *Bartonella* species.

Cats:

Fleas transmit *Bartonella* to the dermis where the local infection then spreads to various tissues- commonly to the mucosa of the mouth, eye and respiratory tract. *Bartonella* respiratory diseases often occur as coinfections with common feline viral or bacterial respiratory pathogens. Cats have more respiratory pathogens and diseases than dogs due to the crowding of cats in multicat households, shelters and feral cat colonies. This crowding also leads to the higher incidence of *Bartonella* infected cats.

Respiratory Pathogens in Cats:[3]

Viruses:
- Feline Herpesvirus-1 (FHV-1), cause of feline viral rhinotracheitis (FVR) **C**
- Feline Calicivirus (FCV) **C**
- Cowpox Virus
- Avian Influenza Virus A (H5N1)
- Swine Influenza A Virus (H1N1)

Bacteria:
- *Chlamydophila felis* (formerly, *Chlamydia psittaci*) **C**
- *Bordetella bronchiseptica* **C**
- *Bartonella* spp. **C**
- *Mycoplasma felis*
- *Pasteurella* spp.
- *Streptococcus* spp.
- *Escherichia coli*
- *Salmonella* spp.
- *Yesinia pestis*
- *Neisseria* spp.- Eugonic Fermenter
- *Mycobacterium* spp.
- *Rhodococcus equi*

Fungi:
- *Cryptococcus* spp.
- *Histoplasma capsulatum*
- *Aspergillus* spp.
- *Sporothrix schenkii*
- *Mucor* spp.
- *Candida* spp.
- *Coccidioides immitis*
- *Blastomyces dermatitidis*

Parasites:
- *Toxoplasma gondii*
- *Cytauxzoon felis*
- *Dirofilaria immitis*
- *Aelurostongylus abstrusus*
- *Eucoleus aerophilus*
- *Paragonimus* spp.

C denotes occurring commonly

Clinically, FHV-1 and FCV have been reported as the most common infectious agents associated with feline respiratory disease.[3,16] However, our findings of the prevalence of *Bartonella* associated with almost half of the feline respiratory diseases, with and without concurrent coinfection with these viruses, suggest a more prominent etiologic role for *Bartonella*. Some bacteria found in respiratory diseases of cats appear to be opportunist rather than etiologic.

Bartonella and Feline Respiratory Disease:

We introduced the Fe*Bart*® *Bartonella* western blot serologic test, for *Bartonella* antibody, in 1999. During the first 14 years, the test has been used to detect *Bartonella* infected healthy cats and cats with inflammatory diseases. Oral inflammatory disease (gingivitis, stomatitis, etc) were the most common, followed by cats with respiratory diseases. Cats with respiratory diseases often had chronic inflammation in multiple sites such as the nose (URI) and sinuses (rhinitis/sinusitis) and were often non-responsive to routine antibiotic therapy (Table 1). 46,400 cats with respiratory diseases were tested and 22,170 (48%) were infected with *Bartonella*. Some of the cats were reported to also have FHV-1 or FCV co-infections.

Therapy Results:

2,229 of the 2,729 (82%) treated cats had a 50% or greater clinical improvement and 94% had a resultant titer decrease indicating *Bartonella* was the partial or complete cause of their disease (Table 2). *Bartonella* was not the cause of disease in the remaining 500 (18%) cats who had less than 50% clinical improvement or became worse and was "in the background." Treatment for the *Bartonella* infection, but not the disease, was successful in 62% of these clinical non-responder cats as indicated by a titer decrease. Thus, cats who clinically resolved or improved in response (Figure 2) to *Bartonella* antibiotics, azithromycin or doxycycline, and who had a resultant decrease in their *Bartonella* antibody titer (therapy titration test), were deemed to have had a *Bartonella* caused disease, even if they were co-infected with FHV-1 or FCV (Table 2).[17] However, 2 other studies, using culture and serology, but no follow-up antibiotic therapy correlations, found no association of *Bartonella* with feline respiratory diseases.[18,19]

Table 1
Bartonella-Associated Respiratory Diseases in Cats*

Disease*	# Tested	# Infected	%
URI	33,726	15,908	47%
Rhinitis	16,863	8,396	50%
Sinusitis	11,148	5,670	51%
Bronchitis	229	99	43%
Pneumonia	183	76	42%
Totals	62,149	30,149	48%

***46,400 individual cats- many cats had inflammation in multiple sites; nose, sinuses, lungs, etc. and thus the numbers in this table do not match.**

Table 2
Therapy of *Bartonella*-Associated Respiratory Diseases of Cats

% Clinical Improvement	# %	# Titer ↓	% Titer ↓
Worse	24 1%	11	46%
None <50%	476 18%	301	63%
Fair 50-59%	277 10%	235	85%
Good 60-79%	278 10%	267	96%
Excellent 80-99%	698 25%	665	95%
Cured 100%	976 36%	933	96%
Totals	2,729	2,412	88%

Figure 2
Bartonella Respiratory Disease

Chronic non-responsive rhinitis and URI before and after azithromycin therapy.

Chronic non-responsive rhinitis Pulmonary Nodules

Upper Respiratory Diseases: Upper and lower left: cases from the Oradell Animal Hospital, Paramus, NJ- URIs- Jan Corbishley CVT and Rhinitis- Dr. Larry Kantrowitz. Each of the cats was resistant to antibiotic therapy, some for more than 1 year, before beginning *Bartonella* therapy with azithromycin. Each cat clinically resolved its disease and had a decrease in antibody titer. **Lower right: Lower Respiratory Disease** *Bartonella* pulmonary nodules, pneumonia in a 2 year old DSH from **Dr. Donna Alfieri Veterinary Center of Morris County, East Hanover, NJ.** The nodules resolved slowly with azithromycin therapy and there was a 4 fold decrease in *Bartonella* antibody titer indicating elimination of *Bartonella* infection concurrently with the clinical improvement.

Conclusion:

In cooperation with practicing veterinarians, we described the various inflammatory diseases that *Bartonella* cause in cats. Many infected cats have inflammation in several tissues concurrently such as gingivitis, rhinitis, and conjunctivitis, etc. Most infected cats respond to azithromycin and the inflammatory reactions clear in all the tissues. Three cats were concurrently infected with FHV-1 and responded to azithromycin therapy with 2 cats cured and the remaining cat responding with 50% improvement. All 3 cats had *Bartonella* antibody titer decreases following the therapy. In the 2 cured cats, the FHV-1 was apparently not contributing to the respiratory disease as it is not responsive to antibiotics. The third cat (50% improved) probably had both FHV-1 and *Bartonella* contributing to the disease.

Detection of *Bartonella* in cats with respiratory diseases, a clinical response to *Bartonella* sensitive antibiotics, azithromycin or doxycycline, along with a resultant *Bartonella* antibody titer decrease after therapy, strongly indicates an etiological role for *Bartonella*. Cats with respiratory diseases should be tested for *Bartonella*.

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