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Diagnosis & Treatment of Bartonellosis in Dogs

Of 22 known species and subspecies of *Bartonella*, 7 have been isolated from pet dogs. These organisms, which are transmitted by arthropod vectors and by the bites and scratches of wild and domestic animals, produce disease manifestations similar to those seen in humans. Unfortunately, the challenge of isolating the *Bartonella* species often complicates diagnosis and management of infection.

Currently, *Bartonella henselae* is the most frequently documented canine infection (based on cultures and polymerase chain reaction [PCR]) in diagnostic samples submitted for *Bartonella* species testing. It’s unclear whether fleas play a role in transmission of *B henselae* to dogs, whether cats can infect dogs through a bite or scratch, or whether dogs serve as accidental hosts or as chronic reservoirs for transmission. Nonetheless, efforts to decrease or eliminate flea and tick infestations are still regarded as critical to preventing transmission to dogs, and thereby decreasing the potential for human infection.

Another *Bartonella* subspecies, *B vinsonii* subsp *berkhoffii*, is also increasing in prevalence; evidence now suggests that dogs, coyotes, and gray foxes may be reservoir hosts of this organism. Even *Bartonella* species thought to be exclusively human pathogens (such as *B quintana*) are now being detected in dogs.13 *Bartonella* infection produces numerous disease manifestations in dogs, many of which are similar to those seen in humans (Table 1). Consequently, a wide variety of examination findings should prompt veterinarians to pursue testing for this pathogen.

**Findings suggest that bites from Bartonella-infected cats or dogs pose a very real occupational risk to veterinary professionals.**

The Emerging Threat of *Bartonella henselae* and *B vinsonii*

Molecular evidence has implicated *B henselae* in several canine illnesses, ranging from endocarditis to granulomatous hepatitis. In 2006, Duncan, et al reported finding this species in the blood and lymph nodes of golden retrievers with lymphoma, and even in the saliva of seemingly healthy dogs.7 In recent work in our laboratory, we have isolated both *B henselae* and *B vinsonii* in transudates or modified transudates obtained from the abdomens of dogs with cavitary effusions. In another dog that had died of advanced systemic granulomatous disease, *B vinsonii* subsp *berkhoffii* was found. Like *B henselae*, this subspecies has been linked to numerous canine illnesses. Most often associated with endocarditis and polyarthritis, *B vinsonii* subsp *berkhoffii* has also been found in the blood of dogs with lymphoma and in the saliva of otherwise healthy dogs. Bite transmission has not been confirmed, but is a potential cause for concern for the health of pets and humans in the event they are bitten.

**Diagnosis of Canine Bartonellosis**

Like other intracellular pathogens that induce chronic infection after vector-borne transmission, diagnostic confirmation of active infection with *Bartonella* can be challenging.14 Ideally, diagnosis should be confirmed by culturing the organism from biopsy specimens or blood or fluid samples that are aseptic. The potential for cross-contamination is significant in necropsy rooms and histopathology laboratories, so care must be taken when obtaining, transporting, and processing samples.
Unlike infected cats, which may easily have a bacterial load of 100,000 copies/µL, dogs are likely to have levels that are 100- to 1000-fold lower.14 Because of these low levels, a different approach to the culturing process was needed. Antibody reactivity is detected by indirect immunofluorescent antibody testing in only 50% of dogs with documented Bartonella infection4,5,14 and the presence of antibodies can only be used to infer prior exposure.

PCR amplification of Bartonella species DNA following direct extraction from patient samples is also relatively insensitive. In 2005, we introduced an insect-based liquid culture medium that, to date, has facilitated the detection of active infection in dogs with at least 4 Bartonella species (B henselae, B quintana, B vinsonii subsp berkhoffii, and B bovis) (Figure 1).15 The successful isolation of B henselae has provided the only canine-derived isolates to date, which is a significant development.11-14

**Table 1. Bartonella Infection in Dogs**

<table>
<thead>
<tr>
<th>Species/Subspecies</th>
<th>Associated Manifestations of Infection1,2,6-12</th>
</tr>
</thead>
</table>
| Bartonella vinsonii subsp berkhoffii | • Endocarditis  
• Cardiac arrhythmias  
• Myocarditis  
• Polyarthritis  
• Granulomatous rhinitis  
• Anterior uveitis  
• Chorioretinitis  
• Lymphoma |
| Bartonella henselae | • Peliosis hepatitis  
• Granulomatous hepatitis  
• Generalized pyogranulomatous lymphadenitis  
• Panniculitis  
• Endocarditis |
| Other Bartonella species  
B washoensis  
B elizabethae  
B quintana | • Endocarditis  
• Hepatic disease  
• Lymphoma |

**Diagnostic Indications that Support Testing for Bartonella Infection**

- Granulomatous inflammatory lesions
- Unexplained reactive lymphadenopathy
- Endocarditis
- Myocarditis
- Polyarthritis
- Immune-mediated hemolytic anemia
- Immune-mediated thrombocytopenia
- Eosinophilia
- Splenomegaly
- Epistaxis
- Idiopathic cavitory effusions
- Unexplained neurologic disease
- Fever of unknown origin
- Vasculitis
- Chronic hepatitis

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**Treatment of Bartonella Infection**

Most treatments for canine Bartonella infection have been derived from studies of immunocompetent and immunocompromised humans.16-18 Because of a lack of trial data, the best therapeutic strategy for canine Bartonella infections remains to be determined. Antimicrobial efficacy has not been established for any antibiotic that might eliminate B henselae bacteremia in dogs. Although untested experimentally, dogs most likely can be reinfected with heterologous strains of the same Bartonella species or with other Bartonella species following therapeutic elimination of an initial infection, and there are reports of multiple-strain coinfections.

Based on human findings, azithromycin has been recommended for treating dogs with microbiological documentation of active Bartonella infection. A standard treatment regimen using azithromycin (5 to 10 mg/kg daily for 7 days, followed by every-other-day administration for 5 weeks), has proven effective. In dogs with acute or life-threatening infection (ie, endocarditis, meningocencephalitis, systemic granulomatous disease), an aminoglycoside is recommended during the initial management period if the patient’s renal function is stable and perfusion will be maintained through administration of intravenous fluids.17-19 Doxycycline, erythromycin, and rifampin are the most frequently recommended antibiotics used for treating Bartonella species infection in people, but clinical improvement has been reported following the use of penicillin, gentamicin, ceftriaxone, ciprofloxacin, and azithromycin.16-18

In dogs with persistent bacteremia, combination therapy with azithromycin and rifampin (5 mg/kg daily) for an additional 6 weeks has been shown to be effective in small trials. Surprisingly, many dogs that experience resolution of disease manifestations will no longer have detectable antibodies at 3 to 6 months following treatment.18 Recent data show that B henselae and B vinsonii subsp berkhoffii induce sustained intravascular infections despite antibiotic therapy. Antimicrobial resistance may be responsible for treatment failures in some Bartonella-infected patients.20,21
Human Health Implications

Much remains to be learned about this highly adaptive organism’s mode of transmission and the significance of relapsing bacteremia. Since 2006, our laboratory has documented the presence of 4 Bartonella species (including 1 previously uncharacterized subspecies) in blood samples from humans with extensive arthropod and animal contact. Numerous wild and domestic animals are known to function as blood reservoirs for various species, but the potential clinical relevance of detecting Bartonella species in the blood of people with occupational animal contact has yet to be determined. Our recent detection of 4 Bartonella species in dog saliva, in conjunction with previous findings of sporadic Bartonella transmission by dogs, suggests that bites from Bartonella-infected cats or dogs pose a very real occupational risk to veterinary professionals.4,6

Our profession has a responsibility to society to gain a better understanding of this pathogen as it applies to humans with animal contact; a failure to further our knowledge and to share what we know carries the potential for serious medical and legal implications.

References


This summary was sponsored by an educational grant from Bayer Animal Health and includes research findings as reported in the cited references. The opinions expressed do not necessarily reflect the point of view of the publisher or the sponsor.

Insect-Based Culture Medium Method for Detecting Bartonella

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>PCR</th>
<th>Culture for 7 days at 37˚C</th>
<th>1.8 mL for storage at -80˚C</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 µl for DNA extraction</td>
<td>2 mL for BAPGM preenrichment</td>
<td>Culture for 2-4 weeks at 37˚C for bacteria colony formation</td>
<td>Resuspension in SPG buffer</td>
</tr>
<tr>
<td>PCR</td>
<td></td>
<td>Culture for 7 days at 37˚C</td>
<td>1.8 mL for storage at -80˚C</td>
</tr>
<tr>
<td>300 µl for DNA extraction</td>
<td>1 mL for blood agar plate inoculation</td>
<td>PCR</td>
<td></td>
</tr>
<tr>
<td>PCR</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

KEY: BAPGM = Bartonella-alphaproteobacteria growth medium DNA = deoxyribonucleic acid PCR = polymerase chain reaction assay SPG = sucrose-phosphate-glutamate

Figure 1. After preenrichment in the new culture medium, blood or fluid samples are subcultured on a blood agar plate. Bacterial DNA is then extracted from the plated colonies and amplified by highly sensitive PCR.

Our profession has a responsibility to society to gain a better understanding of this pathogen as it applies to humans with animal contact; a failure to further our knowledge and to share what we know carries the potential for serious medical and legal implications.
Prevention of *Bartonella* Species Infections in Cats & People

Many feline blood-borne infections are transmitted by the common cat flea (*Ctenocephalides felis*). Of the numerous organisms seen in feline practice, *Bartonella* species are most common around the world and are important as zoonotic agents and as potential causes of illness in cats. Blood culture and DNA amplification have identified several *Bartonella* species in cats.

## Etiology and Epidemiology

Based on results of seroprevalence studies, culture, or polymerase chain reaction (PCR) assay, cats are commonly exposed to or infected by *Bartonella* species. They are the main reservoir hosts for *B henselae* and *B clarridgeiae*, and are likely the reservoir for *B koehlerae*. The most common cause of cat scratch disease, *B henselae*, can manifest as far more serious conditions in immunocompromised humans; and is frequently responsible for bacillary angiomatosis and peliosis hepatis, common in humans with AIDS. Some *Bartonella* species, including *B henselae*, are believed to have intraendothelial and intraerythrocytic phases of infection, which may explain why antibiotics fail to permanently eradicate them.¹

*Bartonella* infection is most prevalent in regions where fleas are common. Recent studies comparing bacteria in cat blood with that found in the digest of fleas removed from those cats found *Bartonella*-species DNA was amplified at similar frequencies in both substances.³ *B henselae* survives for several days in flea feces, which then contaminate open wounds and the cat’s claws as it grooms itself. Consequently, when the cat scratches a human, *Bartonella* is inoculated into the human. Importantly, *Bartonella* species DNA has been amplified from the mouths of seemingly healthy cats, so care should be taken with any cat to avoid situations in which it might be prompted to bite or scratch.⁴

## Clinical Features

Although *B henselae* has been implicated in such diseases as uveitis and lymphocytic gingivostomatitis, most cats with serologic evidence of *Bartonella* infection show no signs of illness—and the presence of *Bartonella* species antibodies does not appear to correlate to most clinical syndromes in ill cats.²⁴⁵ However, feline *Bartonella* infection has been associated (directly or indirectly) with various clinical manifestations, such as fever, lethargy, lymphadenopathy, and neurologic signs. To date, we don’t know how often cats become overtly ill from *Bartonella* infection. Studies of cats with ocular disease that responded to
antibiotic therapy, combined with evidence of 
*Bartonella* DNA in the aqueous humor of cats 
previously presumed to have idiopathic uveitis, 
suggest that *Bartonella* species may cause ocular 
disease in some cats.6,7 Most likely, disease is 
associated with complex host-organism 
interactions.

**Diagnosis**

Infection with *Bartonella* species can be detected by serologic testing, blood cultures, and PCR assays. Often, a single battery of studies has limited predictive value because of misleading test results or intermittent bacteremia (which can be present both in seropositive and in seronegative cats). False-negative cultures are possible, and PCR assays carry the potential for both false-negatives and false-positives. Furthermore, positive PCR results do not necessarily indicate that the organism is living. Because of these drawbacks, testing for *Bartonella* species infection should be reserved for only those cats with suspected clinical bartonellosis. If the results of *Bartonella* testing are negative in a clinically ill cat, the organism is not likely the cause of the clinical syndrome; a single positive test result is sufficient to add bartonellosis to the list of differential diagnoses, but other causes of the clinical syndrome must also be excluded. Even therapeutic success may represent coincidence and not 
confirmation of *Bartonella* infection—the broad-spectrum antibiotics that are typically prescribed may just happen to be effective against the actual infecting organism.

**Treatment**

To date, the use of antibiotics in healthy cats has not been shown to lessen the risk of cat scratch disease—and antibiotic exposure may predispose cats to resistant strains of the organism. Treatment is generally recommended only for clinically ill cats.7 Several drugs have been studied in cats with *Bartonella* infection, and most of the agents have demonstrated some degree of effectiveness. Doxycycline (which is generally favored as first-line therapy), tetracycline, erythromycin, amoxicillin-clavulanate, and enrofloxacin have all been shown to limit bacteremia, but none has cured infection in all cats. Rifampin has recently been investigated, but adverse effects (particularly in kittens) may limit its value. Regardless of the choice of therapy, other differential diagnoses should be considered if a cat has tested positive for *Bartonella* infection but has not achieved a clinical response after trials of 2 drugs with presumed anti-*Bartonella* activity. If a clinical response is achieved, there is little use for follow-up testing because cats can become reinfected with *Bartonella* species.

**Zoonotic Aspects & Prevention**

In a recent study of imidacloprid-moxidectin (Advantage Multi®; Bayer Animal Health www.bayer-ah.com) for protection against *Bartonella* infection, we found that cats without flea control became infected with *B. henselae* after exposure to flea-infested cats 
with confirmed bacteremia. In comparison, cats that received the drug remained *B. henselae*–negative after the same exposures. We believe these results convincingly demonstrate that monthly administration of this product will block transmission of *B. henselae* among cats.

*Bartonella* infections are an occupational health risk for veterinarians.8 Contact with the organism comes not only through cat bites and scratches, but also through infected flea dirt entering breaks in the dermal barrier—such as a hangnail. For this reason, proper hand-washing is critical after handling cats with fleas.

**Contact with the Bartonella organism comes through not only cat bites and scratches, but also through infected flea dirt entering breaks in the dermal barrier.**

---

**Treatment Guidelines for Clinical Bartonellosis**

**Doxycycline, 10 mg/kg daily for 7 days**

If a beneficial response is achieved within 7 days, continue treatment for 2 weeks past clinical resolution of disease or for a minimum of 28 days.

If a poor response is achieved by day 7 (or doxycycline* is not tolerated), switch to azithromycin or a fluoroquinolone.

* To prevent esophageal strictures, administer doxycycline with water or formulate into a flavored suspension.

Consider other differential diagnoses if there is no response to trials of 2 drugs.
Recommendations to Prevent Cat-to-Human Transmission of Bartonella Infection

- Monthly flea control should be initiated and maintained year-round.
- If a family member is immunocompromised and a new cat is to be acquired, adopt a healthy cat older than 1 year and known to be free of fleas.
- Immunocompromised individuals should avoid contact with cats of unknown health status.
- Declawing is generally not required, but claws should be trimmed regularly.
- To prevent bites and scratches, rough play with cats should be avoided.
- Skin wounds should be washed promptly and thoroughly with soap and water, and medical advice should be sought.
- Although Bartonella species have not been shown to be transmitted by saliva, cats should not be allowed to lick open wounds.
- Keep cats indoors to minimize hunting and exposure to fleas and other possible vectors.

*The U.S. Centers for Disease Control and Prevention does not recommend testing healthy cats owned by HIV-infected people for Bartonella species infections.*

References


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Most cases of otitis externa have a “primary” factor, which must be identified and managed to achieve long-term success and “perpetuating factors,” which are the secondary infections seen so often. Treatment should be based on appropriate diagnostic information, including cytology and culture/susceptibility results, and continued until the condition is resolved.

**Diagnostic Approach**
History should focus on previous therapy and evaluation for evidence of the underlying (primary) factor. Physical examination should include careful inspection, both visual and manual, of the ear and ear canal, including palpation of the bullae. Otoscopy should always be performed on BOTH ears; the “good” ear is often also involved.

Cytology from both ears is mandatory, at the initial examination and every recheck. Culture is often indicated (see **When to Culture**).

Computed tomography combined with a thorough otoscopic examination provides the best evaluation of the middle ear region.

**Pharmacology**
Many ear infections are caused by 2 or more organisms—bacterial and/or yeast—and require treatment with antibacterial agents and antifungal agents. In addition, glucocorticoids help reduce swelling and inflammation, allowing deeper penetration of the topical medication.

**Ototoxicity**
Ear medications can cause adverse effects on the ear canal, the middle ear, inner ear and also may cause systemic effects. Potential for ototoxicity varies according to toxicity and concentration of the active ingredient, the carrier or solvent used, dosing variables, placement of the agent (external vs middle ear), and concurrent medications.

A clinical indication of an adverse drug event involving otic agents would be an initial good response to therapy, followed by a severe relapse. In these cases cytology shows moderate to large numbers of neutrophils or eosinophils with an absence of infectious agents. Therapy should be discontinued for 48 to 72 hours to evaluate the role of the topical agent in the relapse.

**Basic Therapeutics**
Ear medications are most often in the form of an ointment (emulsions of lipids) or a solution.
Emulsions containing lipids will enhance penetration of the active ingredient into the skin of the ear; however, most of these ointment formulations are so viscous that they fail to penetrate down deep into the ear canal. Less viscous medications are more likely to allow medication to distribute deeper into the canal, especially when there is significant hair within or when the canal is hyperplastic.

At some point in the management of otitis externa, the ear canals should be completely and thoroughly cleaned. In cases when topical therapy is used, owners must be educated about application of medications. Owners should be taught to massage ears for 15 to 30 seconds after instilling medications and to use proper amounts. Treatment should be continued until there is no clinical or cytologic evidence of active disease (30 days at minimum).

A larger volume of otic medication may increase the likelihood of absorption, especially of more potent glucocorticoids. It is important to understand that larger volumes of medications may increase the likelihood of systemic side effects.

The integrity of the tympanic membrane is critical in determining the best treatment options for a patient with otitis. The best practice is to avoid topical therapy if the tympanic membrane is not intact.

**Systemic Therapy**

Systemic antibacterial therapy is indicated when inflammatory cells are seen on cytology, when a pure infection of a gram-negative bacteria is present, in recurring bacterial infections, when ulcers are present in the external ear canal, or when systemic signs accompany the otitis. Antibiotic selection is based upon the organism isolated and culture and susceptibility results. Drugs should be administered for at least 3 weeks, with regular cleaning of the ear canal.

**Dosing Ear Medications**

The volume of medication applied into the ear during treatment is critical. We recommend using dose syringes to accurately measure otic medications. Failure to apply sufficient quantities to penetrate to these areas seems to be a major cause of treatment failure.

**Dose (volume) recommendations:**
- Small dogs (< 10 kg) 0.4–0.5 mL
- Medium dogs (10–20 kg) 0.5–0.7 mL
- Large dogs (> 20 kg) 0.7–1.0 mL

**Table 1. Medical Treatment of Otitis Externa**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Suggested Medication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial treatment of mixed bacteria/yeast or mild bacterial infections</td>
<td>Animax® (nystatin, neomycin sulfate, thioestrepton, triamcinolone acetonide ointment; Dechra; <a href="http://www.dechra-us.com">www.dechra-us.com</a>) Tresaderm® (thiabendazole, dexamethasone, neomycin sulfate; <a href="http://www.merial.com">www.merial.com</a>)</td>
<td>Apply for 2–3 weeks, clean ears regularly.</td>
</tr>
<tr>
<td>Recurring infections, especially severe bacterial infections</td>
<td>Baytril Otic® (enrofloxacin, silver sulfadiazine, <a href="http://www.bayer-ah.com">www.bayer-ah.com</a>) OtoMax® (gentamicin sulfate, USP; betamethasone valerate, USP; clotrimazole, USP; <a href="http://www.intervet.com">www.intervet.com</a>) Mometamax® (gentamicin sulfate, mometasone furoate, clotrimazole; <a href="http://www.intervet.com">www.intervet.com</a>)</td>
<td>Use of these medications is best determined by cytology and culture/susceptibility testing.</td>
</tr>
<tr>
<td>Systemic fungal therapy (generally for Malassezia pachydermatis)</td>
<td>Nizoral® (ketoconazole, <a href="http://www.janssen.com">www.janssen.com</a>) Sporanox® (itraconazole, <a href="http://www.janssen.com">www.janssen.com</a>) Diflucan® (fluconazole, <a href="http://www.pfizerah.com">www.pfizerah.com</a>)</td>
<td>In cats, itraconazole or fluconazole may be as effective as ketoconazole with fewer side effects. Indicated for recurring infections or when topical therapy is unsuccessful.</td>
</tr>
</tbody>
</table>
least 3 weeks; then the patient reexamined. Systemic administration of an antifungal agent may be helpful in severe cases, in patients with severe hyperplastic changes, or when there are concurrent yeast infections of the skin.

Glucocorticoids can reduce edema or swelling of the external ear canal to facilitate topical therapy and cleaning or to control primary factors (eg, atopy). The drug of choice for systemic use is prednisone. As always, the lowest possible dose given on alternate days is preferred for longer-term therapy.

The best practice is to avoid topical therapy if the tympanic membrane is not intact.

Hyperplastic Changes
Severe hyperplastic changes of the ear canal are serious perpetuating problems in otitis (Figure 2). They cause changes in the microclimate of the ear, which allow microbial proliferation, trap debris and microorganisms in the canal, and reduce the ability to deliver topical medications to the area. Diagnostic imaging will help evaluate the canal for calcification (if not obvious) and the status of the middle ear. If the ear canal is calcified or if the fibrosis and hyperplastic changes extend into the middle ear, a total ear canal ablation may be indicated.

The goal of therapy at this stage is to determine if the canal can be salvaged. Systemic therapy should be implemented to manage the infectious component of the otitis. Prednisone is administered in high doses and potent glucocorticoids are instilled topically. If there is not significant improvement after 2 to 3 weeks, the ear canal may be injected with triamcinolone. Injections are performed through an otoscope cone placed into the canal as deeply as possible and repeated throughout the hyperplastic area circumferentially as the cone is removed. Alternatively, there is some evidence that long-term cyclosporine administration may reduce hyperplastic changes. The author has not found this therapy to be as reliable as the methods described above.

Figure 2. Severe hyperplastic changes in a 3-year-old Maltese with atopic dermatitis.
Determining parasite prevalence in pets is important when assessing the success of parasite control strategies and the risks for exposure of noninfected pets and humans to environmental stages of parasites. We may presume that newer, more effective control products will reduce the prevalence or eradicate parasites; however, in some canine populations, evidence-based assessment does not confirm declines in prevalence rates for common intestinal parasites.

**1996 National Parasite Prevalence Survey**

Blagburn and colleagues conducted the first comprehensive fecal survey of shelter dogs in the U.S. in 1996. They divided the U.S. into 4 geographic regions: Northeast, Southeast, Midwest, and West, including Alaska and Hawaii (Figure 1).

A total of 6,458 fecal specimens were received from solicited shelters with the following results:

- Eggs of *Ancylostoma caninum* were observed with greatest frequency (19.19%).
- Eggs of *Toxocara canis* (14.54%) and *Trichuris vulpis* (14.30%) were observed with similar frequencies across the country and in 3 of the 4 geographic regions.
- Almost 36% of all dogs and 52% of dogs from the Southeast harbored at least 1 major intestinal nematode parasite.
- Dogs concurrently infected with *A caninum* and *T vulpis* (5.7%) were most common, followed by *T canis* and *A caninum* (4.55%), and *T canis* and *T vulpis* (3.21%).

Prevalence of nematodes in individual regions generally mirrored national trends.
humidity), and the nature of the pet population (ie, urban or rural; well-cared-for or not).

In fecal surveys of shelter and pet cats, feline roundworms and hookworms were the more common parasites recovered.5-7 Similar to hookworm in dogs, hookworm in cats appears more commonly in warmer regions of the U.S.4-6 Environmental stages of potentially zoonotic feline parasites may pose more risk to humans than canine pathogens because of cats’ habits to seek sheltered locations for defecation and to bury feces.

Clearly, intestinal parasites of dogs and cats have not been eliminated, despite the availability of effective products and the knowledge to use them effectively. Prevalence data reinforce the need to encourage pet owners to seek regular veterinary care and to employ practices that reduce exposure to environmental stages of potentially zoonotic parasites.

2008/2009 National Parasite Prevalence Survey

Fecal specimens were collected from 2603 dogs and 1179 cats in shelters throughout the U.S. divided into the same 4 geographic regions as in 1996.1 Shelter personnel were instructed to collect fecal, blood, and gross parasite specimens from only those dogs and cats that, to the best of their knowledge, had not been treated with internal and external parasiticides. Gross ectoparasites were collected from fresh fecal and whole blood specimens and shipped to Auburn University via overnight courier.

Approximate age, breed, sex, and reproductive status were determined when possible. Blood specimens were examined for antigens to adult Dirofilaria immitis and for antibodies to Borrelia burgdorferi, Ehrlichia canis, and Anaplasma phagocytophilum. Heartworm antigen-positive blood specimens were also examined for microfilariae of D immitis. Feline samples were sometimes tested for antibodies to developing stages of D immitis. Results of these blood tests or gross parasite identifications are not included in this interim report. Fecal specimens were examined using a centrifugal sucrose fecal flotation procedure. All fecal stages of parasites were identified to genus or genus and species using established structural and morphometric criteria. Results of the diagnostic tests were entered into a data management software program for summary and analysis.

The present study follows up the 1996 study with the addition of cats.

<table>
<thead>
<tr>
<th>Endoparasite</th>
<th>Overall Prevalence</th>
<th>Region with Highest Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascarids</td>
<td>2.23%</td>
<td>West (2.75%)</td>
</tr>
<tr>
<td>Coccidia</td>
<td>4.43%</td>
<td>Midwest (5.95%)</td>
</tr>
<tr>
<td>Giardia</td>
<td>4.03%</td>
<td>West (6.27%)</td>
</tr>
<tr>
<td>Hookworms</td>
<td>2.46%</td>
<td>Southeast (3.99%)</td>
</tr>
<tr>
<td>Whipworms</td>
<td>1.23%</td>
<td>Northeast (1.48%)</td>
</tr>
</tbody>
</table>

- A 1995 retrospective study of 8077 canine medical records representing well-cared-for dogs from the University of Pennsylvania School of Veterinary Medicine (submission years 1984–1991) resulted in a 9.7% prevalence rate for hookworms and a 5.7% rate for ascarids.2
- Little and colleagues reported the results of 1,199,293 canine fecal examinations performed by Antech Diagnostic Laboratories in 2006.3 Samples were submitted to diagnostic laboratories throughout the U.S. with the following findings:

<table>
<thead>
<tr>
<th>Endoparasite</th>
<th>Overall Prevalence</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coccidia</td>
<td>1.4%</td>
<td>&lt; 4 years; sexually intact; examination in summer, fall, and spring</td>
</tr>
<tr>
<td>Giardia</td>
<td>0.58%</td>
<td>age &lt; 4 years; mountain region</td>
</tr>
<tr>
<td>Hookworms</td>
<td>0.063%</td>
<td>age &lt; 1 year; sexually intact; mixed breed; and examination in summer; southern states</td>
</tr>
<tr>
<td>Roundworms</td>
<td>2.92%</td>
<td>&lt; 4 years; mixed breed; sexually intact; examination in summer, winter, and fall; east of Mississippi</td>
</tr>
</tbody>
</table>

- Moore and colleagues examined fecal flotation examination results for 211,105 cats from over 350 Banfield hospitals during 2003–2004.4

Related Studies

- Little and colleagues reported the results of 1,199,293 canine fecal examinations performed by Antech Diagnostic Laboratories in 2006.3 Samples were submitted to diagnostic laboratories throughout the U.S. with the following findings:

<table>
<thead>
<tr>
<th>Endoparasite</th>
<th>Overall Prevalence</th>
<th>Region with Highest Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascarids</td>
<td>2.23%</td>
<td>West (2.75%)</td>
</tr>
<tr>
<td>Coccidia</td>
<td>4.43%</td>
<td>Midwest (5.95%)</td>
</tr>
<tr>
<td>Giardia</td>
<td>4.03%</td>
<td>West (6.27%)</td>
</tr>
<tr>
<td>Hookworms</td>
<td>2.46%</td>
<td>Southeast (3.99%)</td>
</tr>
<tr>
<td>Whipworms</td>
<td>1.23%</td>
<td>Northeast (1.48%)</td>
</tr>
</tbody>
</table>

- Moore and colleagues examined fecal flotation examination results for 211,105 cats from over 350 Banfield hospitals during 2003–2004.4
Results

The study was expanded to include cats in 2008. *Toxocara canis* was the most prevalent parasite in all regions except the Southeast, where *Ancylostoma tubaeforme* was more common. Overall prevalence and prevalence by regions for common internal canine and feline parasites are displayed in Table 1.* *Ancylostoma caninum* was the most common parasite recovered nationally and in the Southeast. Eggs of *Toxocara canis* and *Trichuris vulpis* were similar to or exceeded prevalences in 1996. Regional prevalences of *T canis* and *T vulpis* were greatest in the Southeast, but were notable for the remaining regions. National prevalence of feline roundworm (*T cati*) exceeded that of all the parasites (both canine and feline) except *A caninum*; this result was unexpected, given the prevailing presumption that cats usually harbor few or no parasites. *Ancylostoma tubaeforme* was common in the Southeast but was decreased in the cooler or arid Northeast, Midwest, and West. Prevalence of *Toxascaris leonina* and *Uncinaria stenocephala* remained low and confirms the results of the 1996 study and diagnostic experiences. Canine coccidia were recovered at rates ranging from 5% (*Isospora [Cystoisospora] canis*) to 9.4% (*I ohioensis-like*) similar to those of the earlier study. Feline coccidia prevalences were 11.9% for *I felis* and 8.7% for *I rivolta*.

In cats (Figure 2), *T cati* was the most prevalent parasite in all regions except the Southeast, where *A tubaeforme* was more common.

Comparison of regional canine results from the 1996 and 2008 surveys is illustrated in Figure 3. Aside from an increase in hookworm, few demonstrable differences exist. It appears that continued introduction and use of modern internal parasiticides have had little impact on the major canine parasites in shelter animals, likely because these and other free-roaming animals are beyond the reach of the veterinarian and our excellent parasiticides.

This situation makes it vital to protect pets with year-round use of heartworm prevention medication and/or external flea control. Infected dogs and cats will continue to shed fecal stages of parasites, placing pets—and potentially owners—at increased risk for infection. The concern about zoonoses should not be underemphasized, since dogs, cats, and humans usually acquire infections by exposure to environmental stages of common parasites. Data on well-cared-for

*Results of seroprevalence of vector-borne diseases, heartworm, and prevalence of ectoparasites will be presented at a later date.

<table>
<thead>
<tr>
<th>Parasite</th>
<th>SE</th>
<th>NE</th>
<th>MW</th>
<th>W</th>
<th>Nation</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>A caninum</em></td>
<td>54.0%</td>
<td>12.6%</td>
<td>19.5%</td>
<td>2.8%</td>
<td>34.0%</td>
</tr>
<tr>
<td><em>U stenocephala</em></td>
<td>3.7%</td>
<td>2.2%</td>
<td>0.6%</td>
<td>0.6%</td>
<td>2.4%</td>
</tr>
<tr>
<td><em>A tubaeforme</em></td>
<td>22.9%</td>
<td>2.9%</td>
<td>3.3%</td>
<td>8.8%</td>
<td>10.0%</td>
</tr>
<tr>
<td><em>T canis</em></td>
<td>17.4%</td>
<td>9.1%</td>
<td>14.9%</td>
<td>6.6%</td>
<td>14.2%</td>
</tr>
<tr>
<td><em>T cati</em></td>
<td>19.8%</td>
<td>28.1%</td>
<td>24.4%</td>
<td>17.9%</td>
<td>22.2%</td>
</tr>
<tr>
<td><em>T leonina</em></td>
<td>0.3%</td>
<td>1.0%</td>
<td>0.4%</td>
<td>0.3%</td>
<td>0.4%</td>
</tr>
<tr>
<td><em>T vulpis</em></td>
<td>28.1%</td>
<td>0.0%</td>
<td>14.1%</td>
<td>6.1%</td>
<td>20.5%</td>
</tr>
<tr>
<td><em>I canis</em></td>
<td>5.7%</td>
<td>6.5%</td>
<td>5.0%</td>
<td>2.3%</td>
<td>5.0%</td>
</tr>
<tr>
<td><em>I ohioensis</em></td>
<td>10.0%</td>
<td>5.2%</td>
<td>13.2%</td>
<td>5.5%</td>
<td>9.4%</td>
</tr>
<tr>
<td><em>I felis</em></td>
<td>11.9%</td>
<td>17.9%</td>
<td>9.1%</td>
<td>9.8%</td>
<td>11.9%</td>
</tr>
<tr>
<td><em>I rivolta</em></td>
<td>10.4%</td>
<td>8.1%</td>
<td>8.1%</td>
<td>6.1%</td>
<td>8.7%</td>
</tr>
</tbody>
</table>

N = 2603 canine samples; 1179 feline samples.

It is vital to protect pets with year-round use of heartworm prevention medication and/or external flea control.
pets should remind veterinarians and pet owners that both well-cared-for pets and shelter animals share the same spectrum of internal parasites.3

Our future updates will correlate signalment information with parasite prevalence. Inclusion of such data will help explain some of the numbers we report for parasites that often infect younger animals or larger, outdoor canine breeds with a higher likelihood of exposure to parasites.

References

Acknowledgments
The authors gratefully acknowledges coinvestigators Dr. Bill Kelch, and Dr. James Wright, and the assistance of Ms. Jamie Butler, Ms. Tracey Land, Dr. Jane Mount, and numerous student assistants whose tireless efforts made this study possible.

This summary was sponsored by an educational grant from Bayer Animal Health and includes research findings as reported in the cited references. The opinions expressed do not necessarily reflect the point of view of the publisher or the sponsor.
Feline chronic kidney disease (CKD) is characterized by intrarenal lesions and progressive loss of renal function. Although progression is irreversible, dietary interventions and pharmacotherapy can extend life and improve its quality. CKD management aims to reduce uremic signs, provide optimal nutrition, compensate for endocrine imbalances, and reduce progression.

Staging of CKD allows development of the best treatment strategy for the patient. Because random serum creatinine measurements can vary, the International Renal Interest Society (IRIS) recommends a staging system based on 2 sequential measurements of serum creatinine while the patient is stable and well hydrated (Table 1). CKD in cats is frequently diagnosed at an early stage, but most studies have focused on patients with overt azotemia and clinical signs.

Goals of CKD Therapy

Control Systemic Hypertension

Although unregulated arterial hypertension has not been definitively linked to feline CKD, systemic hypertension occurs in anywhere from 20% to 65% of cats with CKD. Antihypertensive therapy is recommended for patients with systolic blood pressure greater than 170 mm Hg. Therapy should also be considered for cats with CKD that have fundic lesions consistent with hypertensive retinopathy, even when blood pressure readings are normal. Amlodipine, a calcium channel blocker, is routinely successful in the correction of systemic hypertension secondary to CKD with little risk of adverse effects. Angiotensin-converting enzyme inhibitors such as enalapril and benazepril are not very effective as single agents to control systemic hypertension in cats.

Control Proteinuria

Proteinuria in cats with CKD serves as a measure of kidney function and is an ongoing mediator of further injury. As the kidney tries to compensate, altered glomerular hemodynamics and nephron hypertrophy occur. Ensuing glomerular hypertension and increased glomerular volume lead to proteinuria, glomerulosclerosis, and tubulointerstitial nephritis (Figure 1).
Even low levels of proteinuria can be problematic; in 1 study cats with urine protein:creatinine ratios greater than 0.2 were at higher risk for death or euthanasia than their counterparts with lower ratios; cats with ratios greater than 0.4 were at significantly greater risk. Although research has yielded mixed findings regarding benazepril’s effect on overall survival, the drug has been consistently shown to reduce proteinuria.

**Nutrition in CKD Management**

**Dietary Intervention**
An ideal diet has yet to be determined, but cats with CKD have been shown to benefit from phosphorus restriction and, to a lesser extent, increased intake of omega-3 fatty acids. Canned commercial foods generally contain lower levels of phosphorus than dry varieties. Restriction of phosphorus intake can control hyperparathyroidism in cats with early stages of CKD. When monitoring response to dietary changes, be aware that normal serum phosphorus concentrations do not guarantee normal levels of serum parathyroid hormone.

**When Diet Alone Isn’t Enough: Intestinal Phosphate-Binding Agents**
Renal diets may provide sufficient dietary phosphate restriction during early stages of CKD, but as many as one third of patients may also need dietary phosphate-binding agents. These agents are not licensed for veterinary use, but aluminum hydroxide, calcium carbonate, and calcium acetate are frequently prescribed. Sevelamer and lanthanum carbonate, 2 newer phosphate-binding agents approved for use in humans, have not been widely studied in cats. Preliminary research is encouraging, and lanthanum therapy seems particularly promising.

**Other Therapeutic Strategies**

**Hormone Replacement**

■ **Calcitriol.** In patients with hyperparathyroidism secondary to CKD, calcitriol has been shown to decrease serum parathyroid hormone concentrations by blocking its synthesis and inhibiting parathyroid gland proliferation. Calcitriol is effective at just 2 to 3 ng/kg daily, so a compounding pharmacy may need to reformulate the 250-ng capsules or 1000 ng/mL solution currently available.

Calcitriol should not be administered until hyperphosphatemia is controlled because of an increased risk of soft-tissue mineralization. After therapy is initiated, regular monitoring of serum ionized calcium, phosphorus, and parathyroid hormone concentrations are recommended. A recent study of dogs with CKD showed that the group receiving calcitriol survived for a median of 365 days compared with 250 days for dogs receiving placebo.

■ **Erythropoietin.** Recombinant human erythropoietin (rhEPO) has been used to correct nonregenerative anemia in cats with CKD. It can correct anemia and also improve appetite and hair coat while increasing alertness and activity. Therapy may be started in a cat with a packed cell volume (PCV) of less than 20% if clinical signs of anemia are present. The starting dosage (100 U/kg) is administered subcutaneously 3 times weekly until the PCV increases to at least 30% (usually within 3 to 4 weeks). At that point, administrations are reduced to twice weekly. During therapy, the patient should be given

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**Adverse Effects of rhEPO in Cats with CKD**

■ Vomiting
■ Seizures
■ Hypertension
■ Uveitis
■ Hypersensitivity-like mucocutaneous reaction

---

**Recommmendations for Cats Receiving Aluminum- or Calcium-Based Phosphorus-Binding Agents**

■ Begin therapy with 60–90 mg/kg daily.
■ Advise owners to give binding agents with meals or within 2 hours of feeding to maximize effect.
■ Adjust dosage as needed after periodic measurements of fasting serum phosphorus levels.
■ Monitor serum calcium levels regularly to guard against hypercalcemia.
■ Consider new dosing based on PTH level.
an iron supplement (ferrous sulfate, 5–50 mg daily) and undergo regular monitoring of serum iron and iron-binding capacity levels.

A major drawback of rhEPO therapy involves the potential formation of antibodies that cross-react with native EPO within the first 3 months of treatment. The resulting anemia can be more severe than that which was present before treatment. Feline recombinant EPO, which would seem to be the solution to this problem, has yielded somewhat disappointing results: unexplained red cell aplasia developed in some cats receiving this product.

**Angiotensin-Converting Enzyme Inhibitors**

Benazepril has been the ACE-inhibitor studied in cats to date. Clinical studies have shown that benazepril consistently reduces proteinuria in cats with CKD. Studies in cats with experimental CKD treated with benazepril show that intraglomerular hypertension can be normalized without decrement in overall glomerular filtration rate. Despite the beneficial effects on glomerular hypertension and proteinuria, clinical trials using benazepril treatment have not yet shown extended survival in cats with CKD. Benazepril is licensed for treatment of CKD in cats in several countries but not in the U.S.

**References**


**Suggested Reading**


This summary was sponsored by an educational grant from Bayer Animal Health and includes research findings as reported in the cited references and suggested reading. The opinions expressed do not necessarily reflect the point of view of the publisher or the sponsor.
Uremia is the clinical syndrome that results from loss of kidney function. Impaired renal glomerular, tubular, and endocrine functions lead to retention of toxic metabolites, changes in the volume and composition of body fluids, and various hormone imbalances. The clinical signs of uremia are believed to reflect the sum effect of these derangements on organ systems throughout the body.

The pathogenesis of uremia involves 3 major mechanisms that affect virtually every organ system in the body, thereby producing the uremic syndrome:

- Disturbed excretion of electrolytes and water
- Reduced excretion of organic solutes
- Impaired renal hormone synthesis.

**Disturbed Excretion of Electrolytes and Water**
A primary kidney function is to maintain water and electrolyte balance in the body by balancing intake with excretion; glomerular filtration rate (GFR) measures the kidneys’ capacity to filter fluids. As GFR declines in the patient with chronic kidney disease (CKD), the need to excrete water and electrolytes remains the same while the excretory load of electrolytes and water per surviving nephron substantially increases. Although the kidneys have a remarkable ability to maintain water and electrolyte balance well into advanced stages of kidney disease, compensatory mechanisms ultimately fail in end-stage disease. Clinical manifestations of disturbed excretion of electrolytes and water may include edema, hypertension, hyponatremia, hyperkalemia, metabolic acidosis, and hyperphosphatemia.

**Examples of Uremic Solutes**
- Urea
- D-amino acids
- Peptides and proteins
- Guanidines
- Phenols and other aromatic compounds
- Indoles and other tryptophan metabolites
- Aliphatic amines
- 3-carboxy-4-methyl-5-propyl-2-furanpropanoic acid
- Myoinositol and other polyols
- Uric acid and its metabolites
- Oxalate

**Reduced Excretion of Organic Solutes**
Although urea and creatinine are the best known, a wide variety of organic solutes are excreted from the kidneys. Many are handled primarily by glomerular filtration, but renal tubular secretion and reabsorption may affect net renal excretion. An important difference between renal handling of organic solutes and handling of electrolytes and water is that excretion of organic solutes is generally not actively regulated. Consequently, blood concentrations of organic solutes rise with the initial decline in GFR and continue to increase as renal failure progresses.

**Criteria for Confirming a Substance as a Uremic Toxin**
- Substance’s chemical structure must be known.
- Plasma or tissue concentrations in uremic patients must be greater than those in healthy patients.
- High tissue concentrations must be related to specific uremic symptoms or signs.
- Clinical effects seen in uremic patients must be reproducible by raising the solute’s concentration in normal individuals.

*As defined by the European Uremic Toxin Work Group (EUTox).
Organic solutes can accumulate in body fluids when the kidneys fail, but not all of these substances are uremic toxins (eg, urea and creatinine). Although the plasma concentration of urea is believed to be a reasonable surrogate for the systemic concentrations of many uremic solutes, therapeutic reduction of urea concentrations is not conclusive evidence of reduced uremic toxicity. Research also suggests that some toxic uremic solutes may exert effects only when other uremic solutes are present.

Some uremic abnormalities—inhibition of sodium–potassium ATPase or platelet function, leukocyte dysfunction, loss of erythrocyte membrane, lipid asymmetry, and insulin resistance—are transferable with uremic serum or plasma, suggesting that uremic solutes may contribute to uremic syndrome.

**Impaired Renal Hormone Synthesis**

The kidneys normally produce essential hormones, including calcitriol (1,25-dihydroxycholecalciferol), erythropoietin, prostaglandins, kinins, and renin. Calcitriol and erythropoietin have particularly well established pathogenic roles in the clinical deterioration that accompanies severe kidney disease. Calcitriol, the most metabolically active form of vitamin D, is essential for calcium and skeletal metabolism. Deficiencies in its production can result in renal secondary hyperparathyroidism and renal osteodystrophy. Parathyroid hormone has been identified as a uremic toxin, although the clinical consequences of hyperparathyroidism beyond its role in renal osteodystrophy in chronic kidney disease (CKD) is poorly established. In addition, most cells have receptors for calcitriol, and inadequate activation of these receptors is believed to contribute to clinical signs of uremia. Restoring adequate levels in dogs appears to slow progression of kidney disease and prolong survival. Erythropoietin deficiency secondary to kidney failure is associated with hypoproliferative anemia that manifests as weakness, lethargy, and decreased appetite.

**Dialysis: What Is It, and What Does It Do?**

Hemodialysis and peritoneal dialysis are used to minimize fluid and electrolyte disturbances. During dialysis, blood flows over one side of a semipermeable membrane (the dialysis membrane in hemodialysis; the peritoneal membrane in peritoneal dialysis) while dialysate fluid bathes the other side of the membrane. The membrane acts as a filter to diffuse highly concentrated substances in the plasma to lower concentrations in dialysate fluid. Removal of the dialysate fluid eliminates these substances from the body (Figure 1), including uremic solutes. Some solutes are unable to pass through the dialysis membrane because of their molecular size, protein-binding capacity, or other characteristics.

Enteric dialysis (Kibow Biotech, www.kibowbiotech.com) is based on the principle of the intestinal mucosal surface functioning as a semipermeable membrane (Figure 2). The patient is given probiotics containing nonpathogenic microbes that work with the intestine’s natural...
flora to consume uremic toxins and metabolites. Other compounds, such as intestinal binders and adsorbents, have also been employed to increase gastrointestinal excretion of uremic solutes.

**Oral Adsorbents and Probiotics in Managing Uremia**

**Intestinal Electrolyte Binders**

Orally administered intestinal binders control hyperphosphatemia in dogs and cats by enhancing fecal elimination of phosphorus and potassium. Although these agents promote removal of excess phosphorus, they are only somewhat effective for lowering serum phosphorus concentrations. Phosphorus binders commonly used in dogs and cats (eg, aluminum, calcium, and lanthanum) release cations that may be retained in excess. In patients with hyperkalemia, sodium polystyrene can be used to facilitate fecal elimination of potassium.

**Adsorbents**

Some substances adsorb uremic toxins and contain them until they can be excreted in feces. They may remove substances that promote uremic signs, or more powerful agents can enhance survival by removing substances that facilitate progression of CKD. Charcoal use in humans has been reported to decrease levels of serum phenols, uric acid, and guanidine, but not blood urea nitrogen or creatinine. Human and rodent studies of a porous carbonaceous adsorbent have shown that it may delay the need for dialysis and slow the development of glomerular sclerosis, possibly by controlling systemic hypertension and reducing proteinuria.

**Probiotics**

Oral probiotics operate as “enteric dialyzers,” relying on the intestinal tract to eliminate wastes normally excreted by the kidneys. Live bacteria can catabolize urea and other uremic toxins, effectively trapping them within the lumen of the bowel to be excreted in the feces. Bacteria that have been used for this purpose include *Streptococcus thermophilus*, *Lactobacillus acidophilus*, and *Bifidobacteria* species. These bacteria are generally regarded as safe and are not known to have any adverse or disease-inducing effects in normal or uremic dogs or cats. Preliminary studies in rats and Gottingen mini pigs with induced CKD suggest that oral probiotic supplementation may moderate azotemia, consequently slowing the progress of disease and prolonging survival. Observational studies of cats and dogs with spontaneous CKD have also shown decreases in blood urea nitrogen and serum creatinine levels after initiation of probiotic therapy. Reductions in these surrogate markers alone, however, do not prove that probiotics remove the essential uremic toxins. Further studies are needed to determine the usefulness of “enteric dialysis” in managing CKD in domestic animals.

**Suggested Reading**

Jasmine is an 11-year-old female, spayed domestic shorthair cat that presented for her annual examination. She is 1 of 3 cats in the household, lives exclusively indoors, and has received core vaccines every 3 years as an adult. Her owners report that, since her last examination, she has been sleeping more, seems to be eating less dry food, and appears to have lost weight. She may be drinking more water than usual, but her owners have not observed urine output.

Examination
On examination, Jasmine’s weight is 7.9 lb (9.2 lb 1 year ago), and her body condition score is 2.5 of 5 (normal is 3 of 5). Skin turgor is normal. Funduscopic examination shows no hemorrhages or other abnormalities. The mucous membranes are light pink. A thyroid slip is not palpated. Her thyroxine level was 1.2 µg/dL (normal is 1.0–4.0 µg/dL). Her pulse rate is 170/min, and a grade 2/6 systolic murmur is heard best at the left base of the heart. Breath sounds are normal. Systolic blood pressure by Doppler is 170 mm Hg systolic; Jasmine seems to be relaxed during this measurement. On abdominal examination, the kidneys are small and irregular; the bladder is moderate in size.

Assessment of Data
Jasmine appears to have chronic primary kidney disease (IRIS Stage 2) based on increased serum creatinine level, submaximally concentrated urine at a time of dehydration, and renal ultrasound findings (bilaterally hyperechoic kidneys, loss of demarcation between the cortex and medulla, irregular cortical surfaces, no pylectasia). She may be dehydrated as...
her serum sodium level is increased, and this dehydration may be masking anemia. On the basis of a high-quality blood pressure measurement, her hypertension seems to be legitimate. She has borderline overt proteinuria (urine protein:creatinine ratio, 0.38 [normal, < 0.40]) and possible secondary hyperparathyroidism (serum parathyroid hormone [PTH] concentration, 4 pmol/L [normal, 0–4]). She has mild hypokalemia, and her serum phosphorus concentration is at the upper limits of normal; both findings raise concern for progression of renal disease.

**Treatments & Clinical Course**

We prescribed a gradual transition to the canned renal (phosphate-restricted) diet over the next 2 weeks. On reevaluation at the end of week 2, she is eating at a level of near-maintenance caloric needs. Her systolic blood pressure by Doppler is now 172 mm Hg. Her serum phosphorus concentration is 5.0 mg/dL. Once-daily amlodipine and lanthanum carbonate divided in meals are prescribed.

On reevaluation at the end of week 4, her body weight has increased to 8.2 lb. Blood pressure is now 140 mm Hg. Serum studies show her phosphorus level has decreased to 4.4 mg/dL, potassium is now normal, and blood urea nitrogen (BUN) and creatinine levels are unchanged. A packed cell volume of 26% suggests mild anemia but does not warrant treatment. Because her urine protein:creatinine ratio is virtually unchanged, once-daily enalapril is added to her regimen. Four weeks later, her condition appears to have stabilized.

Five months after her initial examination, Jasmine appears healthier and demonstrates increased energy levels. Her body weight and blood pressure have remained stable. Her serum creatinine level has decreased slightly to 1.9 mg/dL despite an increase in muscle mass, and BUN has decreased to 23 mg/dL from a baseline of 33 mg/dL. Her serum phosphorus level is now 4.1 mg/dL. Her packed cell volume is 25%, and her serum PTH level is unchanged from baseline despite reduction in body phosphate burden. Oral calcitriol, 9 ng/kg twice weekly, is prescribed. Two weeks later, measurements of serum calcium and phosphorus are unchanged.

On reexamination 2 weeks later, 6 months after her initial examination, Jasmine's serum PTH concentration is 1.5 pmol/L. Serum phosphorus is 4.0 mg/dL, and ionized calcium is within normal limits. Packed cell volume remains at 25%. Blood pressure and proteinuria control are nearly identical to her previous visit. Going forward, the plan is to evaluate Jasmine every 3 to 4 months if she is doing well and more frequently if problems arise.

**Future Monitoring Plans**

- Nutritional status:
  - Body weight
  - Body condition score
- Muscle condition score
- Blood pressure
- Phosphate-binding agent/calcitriol monitoring:
  - Serum phosphorus
  - Serum PTH
- BUN
- Serum creatinine
- Urine protein:creatinine ratio
- Urine culture
  (2 to 3 times yearly)
- Packed cell volume
- Chest radiograph and echocardiogram if murmur intensifies

Going forward, the plan is to evaluate Jasmine every 3 to 4 months if she is doing well and more frequently if problems arise.
Tumbleweed, a 3-year-old, spayed, female Labrador retriever was referred for evaluation of an illness that had begun approximately 9 months earlier. Initially, the dog was lethargic and intermittently inappetent and had a shifting-leg lameness suggestive of polyarthritis. When examined, the patient was mildly anemic (hematocrit, 36%) and hyperproteinemic (8.0 g/dL), but there were no obvious physical examination abnormalities. Two weeks later, the dog experienced a grand mal seizure, accompanied by spontaneous urination.

During the subsequent month, lethargy continued and the dog lost 5 kg of body weight. When examined by a second veterinarian, there were numerous intradermal hemorrhages on the neck and trunk.

The leukocyte count was 8200 cells per µL, and differential cell numbers were within normal reference ranges. There was seroreactivity to *Ehrlichia canis*, *Rickettsia rickettsii*, and nuclear (antinuclear antibodies) antigens by an indirect fluorescent-antibody assay (reciprocal titers, 50, 256, and 640, respectively). A skin biopsy identified acute necrotizing suppurative vasculitis with hemorrhage. Ehrlichiosis and systemic lupus erythematosus were diagnosed.

Treatment consisted of tetracycline hydrochloride at 750 mg 3 times a day for 14 days and prednisone at 40 mg twice a day for 3 days, after which the dosage was gradually tapered to 15 mg every other day.

**Additional Findings**

Intermittent episodes of listlessness and epistaxis resulted in referral for additional diagnostic evaluation. At admission, the dog was lethargic. Rectal temperature was normal. The heart rate was 136 beats per minute.

**Cardiac**

- Femoral arterial pulses were generally hyperdynamic and were accompanied by arterial pulse deficits associated with occasional premature beats. A grade 3/6 diastolic decrescendo murmur was heard best at the left base, and a 4/6 systolic regurgitant quality (plateau) murmur was heard loudest at the left apex. A resting electrocardiogram confirmed the presence of isolated, infrequent ventricular extrasystoles.
- Two-dimensional, M-mode, color flow, and spectral doppler echocardiography revealed a large vegetative lesion involving the aortic valve, associated with severe aortic valve insufficiency. A smaller vegetative lesion was also present on the anterior mitral valve leaflet, resulting in mild mitral valve insufficiency.

**Initial Laboratory Abnormalities**

- Anemia (hematocrit, 36%) with spherocytosis
- Mild thrombocytopenia (platelets, 180,000/µl)
- Hyperglobulinemia (serum globulin concentration, 4.7 g/dL)
- Proteinuria
- Hemoglobinuria (urine specific gravity, 1.034; 4+ protein, 4+ blood; 4 to 8 erythrocytes per high-power field)
The left ventricle was dilated (left ventricular and diastolic diameter, 5.9 cm), with diminished systolic functional indices (shortening fraction, 25%; elevated end systolic volume index and increased E-point–septal separation). Thoracic radiographs revealed an increase in interstitial and alveolar pulmonary infiltrates involving the accessory lung lobe.

**Hematologic**

Hematologic abnormalities included anemia (hematocrit, 33%; mild anisocytosis and macrocytosis) and thrombocytopenia (platelet count, 121,000/µL). The leukocyte count was 12,300/µL, with normal differential cell numbers. Neutrophils did not appear toxic.

**Biochemical**

Biochemical abnormalities, including hypoalbuminemia (serum albumin, 2.6 g/dL), azotemia (blood urea nitrogen, 34 mg/dL), and hypokalemia (serum potassium, 3.9 g/dL), were mild. Urinalysis again revealed proteinuria and hemoglobinuria (specific gravity, 1.011; 3+ protein, 2+ blood), hematuria (5–10 erythrocytes per high-power field), pyuria (5–10 leukocytes per high-power field), and bacteriuria.

Three aerobic and anaerobic blood cultures (Septi-Chek® blood culture bottle; Roche, www.roche.com) obtained during a 24-hour period failed to grow bacteria. Terminal subcultures and gram stains performed after 7 days of incubation were negative. Blood cultured simultaneously by the lysis centrifugation technique grew a fastidious, gram-negative organism.

Antinuclear antibodies were not detected in serum; however, seroreactivity (indirect fluorescent-antibody assay) to *E canis* and *R rickettsii* was again positive (reciprocal titers, 64 and 128, respectively). Subsequently, we confirmed a specific antibody response to *E canis* by Western immunoblot analysis.

**Conclusion**

Because of a lack of substantial clinical improvement following treatment (see **Treatment**), intractable epistaxis, and a poor long-term prognosis (the dog had vegetative valvular endocarditis), the owners elected euthanasia 17 days following discharge. Antinuclear antibodies (reciprocal titer, 2560) were again detectable.

Using a lysis centrifugation technique in our research laboratory, *Bartonella vinsonii* subsp *berkhoffii* genotype I was isolated by blood culture. Based upon serology, it is likely that the dog was infected with *E canis* and *B vinsonii* subsp *berkhoffii*. As there appears to be cross-reactivity between *Bartonella* and *Rickettsia* antigens in some *Bartonella*-infected dogs, the rickettsial antibodies were thought to be cross-reactive. Antinuclear antibodies can also occur with an increased frequency in dogs that are seroreactive to *B vinsonii* subsp *berkhoffii* antigens. Subsequent studies have shown that infection with *B vinsonii* subsp *berkhoffii* can induce polyarthritis, seizures, vasculitis, epistaxis, and endocarditis in dogs (all of which occurred in progression in this Labrador retriever).

**Treatment**

Treatment for presumed bacterial endocarditis accompanied by congestive heart failure included the following medication Q 12 H:

- Enrofloxacin, 306 mg
- Doxycycline, 400 mg
- Clavulanate-potentiated amoxicillin, 530 mg
- Furosemide, 40 mg
- Digoxin, 0.25 mg
- Enalapril, 20 mg

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**Haemobartonella felis**, one of a group of organisms responsible for hemoplasmosis in cats, was recently reclassified after it was found to be genetically related to the *Mycoplasma* species, not the rickettsiae.1 Because these parasitic bacteria are associated with red blood cells, this group of organisms is now collectively known as hemoplasmas.

There are 3 known genetically distinct species of hemoplasmas—*Mycoplasma haemofelis* (Mhf), *Candidatus Mycoplasma haemominutum* (Mhm), and *Candidatus M. turicensis* (Mtc).1-3 Mhf and Mhm are genetically similar and the most common, having been detected around the world.4 Mtc infection has been identified in cats in several countries, including the U.S.5-7

**Pathogenicity & Epidemiology**

In experimentally inoculated cats, Mhf is more likely than Mhm to produce clinical illness. Dual infection may be more severe than infection with either agent alone.8 Cats with chronic Mhm infection had more severe, persistent anemia after inoculation with Mhf. Cats infected with the Mtc strain can also develop anemia, and the organism’s pathogenicity lies between Mhf and Mhm. Coinfection with FeLV seems to potentiate Mhm infection,9 but preliminary studies show that cats coinfected with FIV and 1 of the hemoplasma strains were no more likely to be ill than cats inoculated with the hemoplasma alone. One study documented Mhm infection and clinical illness in some cats without evidence of immunodeficiency, suggesting that some strains may be primary pathogens.10

Routes of transmission remain to be fully determined, but we know that the organisms are ingested by cat fleas (*Ctenocephalides felis*) when they feed from cats.11 In one cat, my laboratory documented flea feeding to transfer Mhf,12 but no infection was documented when we fed Mhf- and Mhm-infected fleas to cats.13 Clinically ill queens can infect kittens; but the route is not known. Transmission may occur through bites—hemoplasma DNA has been amplified from the saliva of feral cats and experimentally infected cats.14,15

**Clinical Features of Hemoplasma Infection**

Clinical signs of disease depend on the degree of anemia, the stage of infection, and the immune status of infected cats.16 Anemia associated with hemoplasmosis is generally macrocytic and normochromic; chronic nonregenerative anemia is rare. Neutrophilia and monocytosis have been reported. Red blood cell destruction is due primarily to immune-mediated events; whereas direct, organism-induced injury to the cells is minimal. Fever occurs in some acutely infected cats and may be intermittent in chronically infected cats. Evidence of coexisting disease may be present. Weight loss is common in chronically
Diagnosis, Treatment, Prevention

Diagnosis

For a diagnosis of hemoplasmosis, the organism must be seen on the surface of erythrocytes on examination of a thin blood film (Figure 1) or polymerase chain reaction (PCR) assay. The organism may be difficult to find, particularly in the chronic phase, and numbers may fluctuate—so blood film examination can be falsely negative up to 60% of the time. For these reasons, PCR assays are the tests of choice. Real-time PCR can be used to monitor response to treatment but is ineffective for differentiating carriers from clinically ill cats because clinically normal cats can carry extremely high copy numbers.17

Treatment

Hemoplasmas have not been cultured and so treatment studies to date have used experimentally or naturally infected cats. Tetracyclines are generally administered to cats with suspected hemoplasmosis,6,10,17 with doxycycline being preferred because of its minimal adverse effects. Tetracyclines lessen parasitemia for at least 2 injections, may also be considered for cats with infection that does not respond to other drugs, or for those that are difficult to pill. However, this drug is inferior to tetracyclines or quinolones for most cats. Blood transfusion and other supportive care measures should be instituted as warranted.

Prevention

To prevent hemoplasma infections, advise cat owners to keep pets housed indoors to avoid potential vectors and fighting. Blood donor cats should undergo PCR assay before their blood is used.17 Until the mode of hemoplasma transmission is better understood, flea control measures should be taken consistently.

References


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