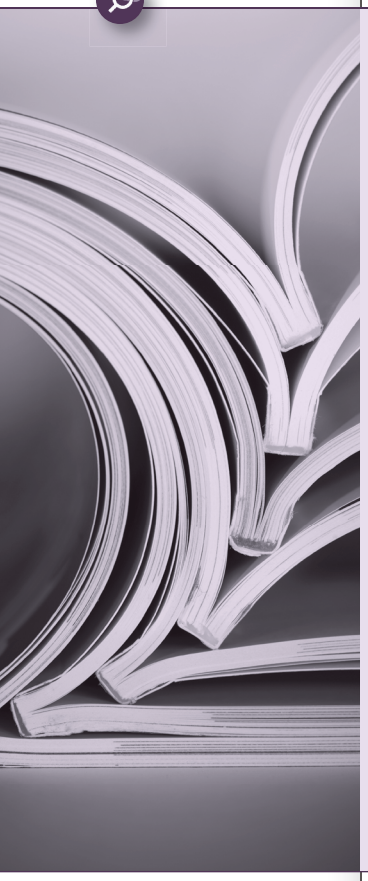
Focus on Infectious Diseases

Journal Club



It seems to be getting harder and harder for veterinarians to "keep up." Advances in technology result in ongoing discoveries every week, and the number of journals with important information appears to grow exponentially.

In this Journal Club column, some key articles about infectious diseases are highlighted. You may not have come across them in your day-to-day reading, but these articles should change the way you think about diagnosing and treating your patients.

Lee and colleagues remind us that some of the things we *know* aren't always so. The authors elegantly evaluate a large number of cases and conclude that the dogma stating that leptospirosis is a disease only of large breed dogs is just not true.

Foy and colleagues highlight the utility and limitations of a *Blastomyces* antigen assay during and after treatment. This assay was a helpful tool that is an adjunct to, but not a replacement for, the history and physical and radiographic examination for recognition of clinical remission. After achieving clinical remission, some dogs may have low concentrations of residual antigen in urine, which do not necessarily predict a relapse.

Lappin and colleagues provide insight into the management of immune and allergic disease in cats. Cyclosporine did not result in disease recrudescence or oocyst shedding in cats that were infected with *Toxoplasma gondii* prior to cyclosporine administration. However, cats treated with cyclosporine before infection with *T gondii* appeared to be at higher risk for severe disease. Therefore, screening cats for exposure to *T gondii* prior to cyclosporine treatment should be considered.

Savidge and colleagues remind us that the infectious disease landscape is constantly changing. Many of us would have never thought to test a febrile cat for anaplasmosis and, before the last decade, there was no easy way to test for this infection.

Beugnet, Reichard, and their colleagues published papers that are a testament to acaricidal agents. Not only do we live in a time with effective topical, oral, and wearable options, but we are finally generating evidence that these products can actually reduce the risk for disease transmission. This is something we have assumed (and probably marketed on) in the past. Now we have evidence that we are both reducing the "ick" factor of ectoparasites and practicing excellent preventive medicine.

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Signalment Changes in Canine Leptospirosis Between 1970 and 2009

Lee HS, Guptill L, Johnson AJ, Moore GE. *J Vet Intern Med* 2014; 28(2):294-299.

Previous large-scale epidemiologic studies of leptospirosis in dogs evaluated risk factors over a long period. Several studies reported in the 2000s indicated that changes in patient signalment and risk factors were occurring, including increased odds of disease in urban areas. This retrospective study aimed to evaluate prevalence and signalment of dogs with leptospirosis over a 40-year period.

STUDY RESULTS

- The Veterinary Medical Databases (vmdb.org) was searched; of 1,658,055 hospital visits at 26 veterinary teaching hospitals between 1970 and 2009, 1091 dogs were diagnosed with leptospirosis. Overall prevalence was calculated and then compared by age, sex, weight, or breed group in multivariate analyses.
- Canine leptospirosis prevalence peaked in 1971, decreased in the 1980s and 1990s, and has been increasing since the 2000s.
- In the 2000s, dogs aged 7 to 9.9 years had the highest prevalence of infection. Prevalence was also highest in dogs weighing less than 15 pounds and in the terrier breed group. Among small breeds in the 2000s, the Yorkshire terrier had the highest prevalence.
- These results are in contrast to those seen in the 1970s, in which prevalence did not differ widely across age groups, was highest in dogs weighing 30 to 49.9 pounds and 50 to 79.9 pounds, and was highest in mixed breed dogs.

CONCLUSIONS

The epidemiology of canine leptospirosis has changed substantially since the 1970s, and hospital prevalence per 100,000 cases has increased since the 1980s and 1990s at veterinary teaching hospitals. Dogs with clinical signs compatible with leptospirosis, no matter the signalment, should be tested for this zoonotic disease.

Serum and Urine *Blastomyces* Antigen Concentrations as Markers of Clinical Remission in Dogs Treated for Systemic Blastomycosis

Foy DS, Trepanier LA, Kirsch EJ, Wheat LJ. *J Vet Intern Med* 2014; 28(2):305-310.

Duration of treatment for canine blastomycosis is long, and a test that could help determine when to discontinue antifungals without the need for more invasive diagnostics would be helpful. An antigen test detecting fungal cell wall galactomannan is highly sensitive and specific for the initial diagnosis of blastomycosis.

This prospective study sought to monitor urine and serum *Blastomyces dermatitidis* antigen concentrations in 21 dogs with newly diagnosed disease until remission, and in 27 dogs newly in remission, for one year after cessation of antifungals.

STUDY RESULTS

- At diagnosis, urine and serum antigen concentrations for *Blastomyces* were 100% and 90.9% sensitive, respectively.
- During treatment, the urine antigen test was more sensitive and specific than serum antigen concentrations.
- There was a slight positive correlation between baseline urine antigen concentration and time to remission.
- At drug discontinuation, 48% of dogs had measureable *Blastomyces* urine antigen concentrations. There was no statistical correlation between this finding and later clinical relapse.
- After treatment, urine and serum antigen concentrations were nearly 100% specific for clinical relapse, with sensitivities of 71% and 43%, respectively.

CONCLUSIONS

- While not recommended as the only monitoring tool, urine *Blastomyces* antigen concentrations can be helpful for monitoring dogs' clinical progression; testing was highly sensitive for disease at diagnosis and during treatment and highly specific for relapse.
- Baseline urine antigen concentration may help predict time to clinical remission, but additional studies are needed to more fully elucidate this.
- Urine antigen testing should be performed instead of serum testing for improved sensitivity and specificity.

Effect of Oral Administration of Cyclosporine on *Toxoplasma gondii* Infection Status of Cats

Lappin MR, VanLare KA, Seewald W, et al. *Am J Vet Res* 2015; 76(4):351-357.

There are several reports of cats developing toxoplasmosis while receiving immunosuppressive cyclosporine therapy. However, a definitive relationship between cyclosporine and recrudescence of toxoplasmosis or worsened initial infection has yet to be substantiated. This masked, randomized study evaluated the effect of anti-inflammatory cyclosporine (7.5 mg/kg PO Q 24 H) on cats experimentally infected with *Toxoplasma gondii*.

STUDY RESULTS

- Cats were divided into 3 groups for 126 days, and all were infected with *T gondii* on day 42: control group cats (n = 10), cats that were infected and then received cyclosporine starting on day 84 (n = 10), and cats that received cyclosporine throughout the study (n = 10).
- Clinical signs were prolonged and more severe in the cats already receiving cyclosporine when infected with *T gondii*.
- Three cats that were already receiving cyclosporine when infected with *T gondii* died or were euthanized: One died of systemic toxoplasmosis; this cat had a higher cyclosporine level than the remaining cats. A second died of pancreatitis; this cat had *T gondii* zoites identified in the pancreatic duct epithelial cells. The third cat was found dead.
- Recurrent oocyst shedding was not detected in any cat that received cyclosporine after being infected with *T gondii*.

CONCLUSIONS

At this dose, cyclosporine appears unlikely to reactivate toxoplasmosis in previously exposed cats or prolong oocyst shedding in cats infected while receiving the drug. *T gondii* naïve cats that received cyclosporine at high levels may be at higher risk for severe disease, but additional studies are needed. Efforts should be made to limit cats' exposure to *T gondii* while receiving cyclosporine, such as preventing the cat from hunting and avoiding raw diets.

Anaplasma phagocytophilum Infection of Domestic Cats: 16 Cases from the Northeastern USA

Savidge C, Ewing P, Andrews J, et al. *J Feline Med Surg* 2015; epub ahead of print.

Information on clinical disease from vector-borne infections in cats is lacking. Several studies outside the United States have described natural infection of cats with *Anaplasma phagocytophilum*, but only one small study described the disease in the U.S. The aim of this retrospective study was to describe the clinical and historical findings of cats positive for *A phagocytophilum* DNA by polymerase chain reaction (PCR) on whole blood.

STUDY RESULTS
- Records of a commercial laboratory identified 40 cats with positive PCR results for *A phagocytophilum* between May 2009 and May 2011. This represented 0.92% of all samples submitted. Historical and clinical data were available for 16 cats.
- All cats had access to the outdoors and lived in the northeastern U.S. (CT, NJ, NY, MA, and VT). Most cases occurred in the spring or fall.
- The most common clinical abnormalities on the day of test submission included lethargy, fever, and anorexia; mean temperature was 104.5°F.
- Morulae were identified in neutrophils in 27% of cases, with inclusions in approximately 4% to 20% of neutrophils in those cats.
- Clinicopathologic abnormalities were nonspecific.
- Nearly all cats were treated with doxycycline (15 of 16). In all 14 cats with a known response to treatment, clinical signs resolved with doxycycline therapy.

CONCLUSIONS
This study highlights several important points:
- *A phagocytophilum* infection should be considered in ill cats with possible exposure to *Ixodes* ticks.
- Manual blood smear evaluation is needed.
- Cats with outdoor access in endemic areas may benefit from monthly insecticide–acaricide treatment.
- Additional studies to elucidate the role of these pathogens in clinical disease in cats are needed, particularly in those with hematologic abnormalities.

The Ability of an Oral Formulation of Afoxolaner to Block the Transmission of *Babesia canis* by *Dermacentor reticulatus* Ticks to Dogs

Beugnet B, Halos L, Larsen D, et al. *Parasit Vectors* 2014; 7:283.

With the exception of Lyme borreliosis, vector control is the primary means of preventing flea- and tick-borne diseases in dogs. However, insecticide–acaricide studies demonstrating prevention of disease transmission are lacking because efficacy is based on repellant ability and kill time. This randomized, blinded, and controlled study aimed to demonstrate the ability of afoxolaner (NexGard, merial.com) to block transmission of *Babesia canis* by *Dermacentor reticulatus* ticks to dogs.

STUDY RESULTS
- The 8 dogs in the treatment group received afoxolaner on day 0, and the 8 controls were untreated. Every 7 days for 4 weeks, all dogs were infested with ticks infected with *B canis*.
- Blood and serum for *B canis* serology (indirect fluorescent antibody test [IFAT] and PCR) were saved every 7 days until day 56.
- All of the untreated dogs were positive for babesiosis on blood smear and PCR; 7 of the 8 were positive on serology by day 21.
- None of the treated dogs were positive on blood smear, PCR, or serology through day 56. One treated dog was possibly IFAT positive at final testing on day 93.

CONCLUSIONS
Afoxolaner demonstrated complete efficacy in preventing transmission of *B canis* by the tick *D reticulatus* during 30 days of tick infestation.

Efficacy of an Imidacloprid 10%/Flumethrin 4.5% Collar (Seresto, Bayer) for Preventing the Transmission of *Cytauxzoon felis* to Domestic Cats by *Amblyomma americanum*

Reichard MV, Thomas JE, Arther RG, et al. *Parasitol Res* 2013; 112(Suppl 1):S11-S20.

Acaricides for cats are limited compared to those offered for dogs, and tick prevention is an important aspect of protection against vector-borne diseases. Studies have evaluated products' ability to prevent flea and tick infestation, but few have evaluated the protection of cats against transmission of disease. This randomized, controlled, prospective study evaluated the use of an imidacloprid 10%/flumethrin 4.5% collar to prevent transmission of *Cytauxzoon felis* to cats by *Amblyomma americanum*.

STUDY RESULTS
- Two groups (10 cats each) of approximately equal tick susceptibility, one of which had an imidacloprid 10%/flumethrin 4.5% collar placed 30 days earlier, were infested with *A americanum* infected with *C felis*. Tick attachment and transmission of *C felis* as determined by PCR were measured.
- No ticks were found on the collared cats. All untreated cats had ticks attached.
- None of the collared cats were positive for *C felis*, while 90% of the untreated cats were positive by PCR at 8 to 16 days after infestation.

CONCLUSIONS
An imidacloprid 10%/flumethrin 4.5% collar placed 30 days earlier completely prevented transmission of *C felis* to cats by *A americanum*. Despite the opportunity to groom, all untreated cats were infested with *A americanum*, underscoring the importance of acaricide use in all at-risk cats.

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