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**FELINE TOXOPLASMOSIS**

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**Etiology and epidemiology.** *Toxoplasma gondii* is one of the most prevalent parasites infecting warm-blooded vertebrates. Only cats complete the coccidian life cycle and pass environmentally resistant oocysts in feces. Sporozoites develop in oocysts after 1 to 5 days of exposure to oxygen and appropriate environmental temperature and humidity. Tachyzoites disseminate in blood or lymph during active infection and replicate rapidly intracellularly until the cell is destroyed. Bradyzoites are the slowly dividing, persistent tissue stage that form in the extraintestinal tissues of infected hosts as immune responses attenuate tachyzoite replication. Tissue cysts form readily in the CNS, muscles, and visceral organs. Bradyzoites may persist in tissues for the life of the host.

Infection of warm-blooded vertebrates occurs following ingestion of any of the three life stages of the organism or transplacentally. Most cats are not coprophagic and so are infected most commonly by ingesting *T. gondii* bradyzoites during carnivorous feeding; oocysts are shed in feces from 3 to 21 days. Sporulated oocysts can survive in the environment for months to years and are resistant to most disinfectants. Results of a recent study confirm that the *T. gondii* oocyst shedding prepatent period is stage-dependent (ingestion of bradyzoites has a shorter prepatent period than ingestion of sporozoites) and is not dose-dependent. In addition, transmission of *T. gondii* is most efficient when cats consume tissue cysts (carnivorism) and when intermediate hosts consume oocysts (fecal-oral transmission). *Toxoplasma gondii* infection of rodents changes the behavior of the prey species making it less averse to cats, potentially increasing the likelihood the definitive host (felid) will become infected and potentiate the sexual phase of the organism.

Approximately 30% to 40% of cats and people in the United States are seropositive and so presumed to be infected. In a recent study of clinically ill cats, we detected *T. gondii* antibodies in 31.6% of the 12,628 cats tested.

**Clinical features.** Approximately 10% to 20% of experimentally inoculated cats develop self-limiting, small bowel diarrhea for 1 to 2 weeks following primary oral inoculation with *T. gondii* tissue cysts; this is presumed to be due to enteroparasitic replication of the organism. However, detection of *T. gondii* oocysts in feces is rarely reported in studies of naturally exposed cats with diarrhea. *T. gondii* enteroepithelial stages were found in intestinal tissues from two cats with inflammatory bowel disease. Positive response to anti-*Toxoplasma* drugs in these two cats suggests that toxoplasmosis may occasionally induce inflammatory bowel disease. Eosinophilic fibrosing gastritis was recently described in a *T. gondii*-infected cat.

Fatal extraintestinal toxoplasmosis can develop from overwhelming intracellular replication of tachyzoites following primary infection; hepatic, pulmonary, CNS, and pancreatic tissues are commonly involved. Kittens infected by the transplacental or transmammary routes develop the most severe signs of extraintestinal toxoplasmosis and generally die of pulmonary or hepatic disease. Common clinical findings in cats with disseminated toxoplasmosis include depression, anorexia, and fever followed by hypothermia, peritoneal effusion, icterus, and dyspnea. If a host with chronic toxoplasmosis is immunosuppressed, bradyzoites in tissue cysts can replicate rapidly and disseminate again as tachyzoites; this is common in people with acquired immunodeficiency syndrome (AIDS). Disseminated toxoplasmosis has been documented in cats concurrently infected with feline leukemia, feline immunodeficiency, or feline infectious peritonitis viruses, as well as following cyclosporine administration for skin disease or after renal transplantation.

Sublethal, chronic toxoplasmosis occurs in some cats. *T. gondii* infection should be on the differential diagnoses list for cats with anterior or posterior uveitis, cutaneous lesions, fever, muscle hyperesthesia, myocarditis with arrhythmias, weight loss, anorexia, seizures, ataxia, icterus, diarrhea, or pancreatitis. Based on results of *T. gondii*-specific aqueous humor antibody and PCR studies, toxoplasmosis appears to be a common infectious cause of uveitis in cats. Kittens infected transplacentally or lactationally commonly develop ocular disease. Immune complex formation and deposition in tissues and delayed hypersensitivity reactions
may be involved in chronic, sublethal clinical toxoplasmosis. Since none of the anti-Toxoplasma drugs totally clear the body of the organism, recurrence of disease is common.

**Diagnosis.** Cats with clinical toxoplasmosis can have a variety of clinicopathologic and radiographic abnormalities, but none document the disease. Nonregenerative anemia, neutrophilic leukocytosis, lymphocytosis, monocytes, neutropenia, eosinophilia, proteinuria, bilirubinuria, as well as increases in serum protein and bilirubin concentrations, and creatinine kinase, alanine aminotransferase, alkaline phosphatase, and lipase activities occur in some cats. Pulmonary toxoplasmosis most commonly causes diffuse interstitial to alveolar patterns or pleural effusion. Mass lesions may be detected on CT or MRI examinations. Cerebrospinal fluid (CSF) protein concentrations and cell counts are often higher than normal. The predominant white blood cells in CSF are small mononuclear cells, but neutrophils also are commonly found.

The antemortem definitive diagnosis of feline toxoplasmosis can be made if the organism is demonstrated; however, this is uncommon, particularly in association with sublethal disease. Bradyzoites or tachyzoites are rarely detected in tissues, effusions, bronchoalveolar lavage fluids, aqueous humor, or CSF. Detection of 10 X 12 µm oocysts in feces in cats with diarrhea suggests toxoplasmosis but is not definitive, since Besnoitia and Hammondia infections of cats produce morphologically similar oocysts.

*T. gondii*–specific antibodies (immunoglobulin [Ig]: IgM, IgG, IgA), antigens, and immune complexes can be detected in the serum of normal cats, as well as in those with clinical signs of disease, so it is impossible to make an antemortem diagnosis of clinical toxoplasmosis based on these tests alone. Of the serum tests, IgM correlates the best with clinical feline toxoplasmosis since this antibody class is rarely detected in serum of healthy cats. The antemortem diagnosis of clinical toxoplasmosis can be tentatively based on the combination of the following:

- Demonstration of antibodies in serum, which documents exposure to *T. gondii*
- Demonstration of an IgM titer above 1:64 or a fourfold or greater increase in IgG titer, which suggests recent or active infection
- Clinical signs of disease referable to toxoplasmosis
- Exclusion of other common causes for the clinical syndrome
- Positive response to appropriate treatment

Some cats with clinical toxoplasmosis will have reached their maximal IgG titer or will have undergone antibody class shift from IgM to IgG by the time they are serologically evaluated, so the failure to document an increasing IgG titer or a positive IgM titer does not exclude the diagnosis of clinical toxoplasmosis. Since some healthy cats have extremely high serum antibody titers and some clinically ill cats have low serum antibody titers, the magnitude of titer is relatively unimportant in the clinical diagnosis of toxoplasmosis. Because the organism cannot be cleared from the body, most cats will be antibody-positive for life, so there is little reason to repeat serum antibody titers after the clinical disease has resolved.

The combination of aqueous humor or CSF *T. gondii*–specific antibody detection and organism DNA detection by PCR is the most accurate way to diagnose ocular or CNS toxoplasmosis (Diagnostic Laboratory, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523). Whereas *T. gondii*–specific IgA, IgG, and organism DNA can be detected in aqueous humor and CSF of both normal and clinically ill cats, *T. gondii*–specific IgM has only been detected in the aqueous humor or CSF of clinically ill cats and so may be the best indicator of clinical disease. Since *T. gondii* DNA can be detected in blood of healthy cats, positive PCR results do not correlate to clinical disease.

**Treatment.** Supportive care should be instituted as needed. Clindamycin hydrochloride administered (10 to 12 mg/kg, PO, q12h) for 4 weeks or a trimethoprim-sulfonamide combination administered (15 mg/kg, PO, q12h) for 4 weeks has been used most frequently by the author for the treatment of clinical feline toxoplasmosis. Azithromycin (10.0mg/kg, PO, q24h) has been used successfully in a limited number of cats, but the optimal duration of therapy is unknown. Pyrimethamine combined with sulfa drugs is effective for the treatment of human toxoplasmosis but commonly results in toxicity in cats. Cats with systemic clinical signs of toxoplasmosis, such as fever or muscle pain combined with uveitis, should be treated with anti-Toxoplasma drugs in combination with topical, oral, or parenteral corticosteroids to avoid secondary lens luxations and glaucoma. *T. gondii*–seropositive cats with uveitis that are otherwise normal can be treated with topical glucocorticoids alone unless the uveitis is recurrent or persistent. In these situations, administration of a drug with anti-*T. gondii* activity may be beneficial.
Clinical signs not involving the eyes or the CNS usually resolve within the first 2 to 3 days of clindamycin or trimethoprim-sulfonamide administration; ocular and CNS toxoplasmosis responds more slowly to therapy. If fever or muscle hyperesthesia is not decreasing after 3 days of treatment, other causes should be considered. Recurrence of clinical signs may be more common in cats treated for less than 4 weeks. There is no evidence to suggest that any drug can totally clear the body of the organism, so recurrences are common and infected cats will always be seropositive. The prognosis is poor for cats with hepatic or pulmonary disease caused by organism replication, particularly in those that are immunocompromised.

**Zoonotic aspects and prevention.** *T. gondii* is a major zoonosis. Primary infection of mothers during gestation can lead to clinical toxoplasmosis in the fetus; stillbirth, CNS disease, and ocular disease are common clinical manifestations. Primary infection in immunocompetent individuals results in self-limiting fever, malaise, and lymphadenopathy. As T-helper cell counts decline, approximately 10% of people with AIDS develop toxoplasmic encephalitis from activation of bradyzoites in tissue cysts.

People most commonly acquire toxoplasmosis by ingesting sporulated oocysts or tissue cysts, or transplacentally. To prevent toxoplasmosis, avoid eating undercooked meats or ingesting sporulated oocysts. In a recent study of 6,282 meat samples from 698 retail meat stores, *T. gondii* was detected by bioassay in cats in none of the beef or chicken samples tested and only a small number of pork samples. Although owning a pet cat was epidemiologically associated with acquiring toxoplasmosis in one study of pregnant women, touching individual cats is probably not a common way to acquire toxoplasmosis for the following reasons:

- Cats generally only shed oocysts for days to several weeks after primary inoculation.
- Repeat oocyst shedding is rare, even in cats receiving glucocorticoids, cyclosporine, or in those infected with feline immunodeficiency virus or feline leukemia virus.
- Cats with toxoplasmosis inoculated with tissue cysts 16 months after primary inoculation did not shed oocysts.
- Cats are very fastidious and usually do not allow feces to remain on their skin for time periods long enough to lead to oocyst sporulation; the organism was not isolated from the fur of cats shedding millions of oocysts 7 days previously.
- Increased risk of acquired toxoplasmosis was not associated with cat ownership in people with AIDS or in veterinary health care providers.

However, since some cats will repeat oocyst shedding when exposed a second time, feces should always be handled carefully. If a fecal sample from a cat is shown to contain oocysts measuring 10 X 12 µm it should be assumed that the organism is *T. gondii*. The feces should be collected daily until the oocyst shedding period is complete; administration of clindamycin (25 to 50 mg/kg, divided q12h, PO) or sulfonamides (100 mg/kg, divided q12h, PO) can reduce levels of oocyst shedding.

Since humans are not commonly infected with *T. gondii* from contact with individual cats, testing healthy cats for toxoplasmosis is not recommended. Fecal examination is an adequate procedure to determine when cats are actively shedding oocysts but cannot predict when a cat has shed oocysts in the past. There is no serologic assay that accurately predicts when a cat shed *T. gondii* oocysts in the past, and most cats that are shedding oocysts are seronegative. Most seropositive cats have completed the oocyst shedding period and are unlikely to repeat shedding; most seronegative cats would shed the organism if infected. If owners are concerned that they may have toxoplasmosis, they should see their physician for testing.