Toxoplasmosis in cats and dogs

J.P. Dubey*

Animal Parasitic Diseases Laboratory, Animal and Natural Resources Institute, Agricultural Research Service, United States Department of Agricultural, Building 1001, Beltsville, MD 20705, USA

Tel: +1-301-504-8128; fax: +1-301-504-9222

E-mail address: jdubey@anri.barc.usda.gov

ETIOLOGY

Toxoplasma gondii is an obligate intracellular coccidian parasite that can infect virtually all species of warm-blooded animals, including people. Domestic cats and other Felidae are the definitive hosts. All nonfeline hosts are intermediate hosts. There are three infectious stages: sporozoites in oocysts, tachyzoites (actively multiplying stage), and bradyzoites (slowly multiplying stage) enclosed in tissue cysts. Oocysts are excreted in feces, whereas tachyzoites and bradyzoites are found in tissues.

The three major modes of transmission are congenital infection, ingestion of infected tissues, and ingestion of oocyst-contaminated food or water. Other minor modes of transmission include transfusion of fluids or transplantation of organs.

Enterop epithelial Life Cycle

This cycle is found only in the definitive feline host. Most cats are thought to become infected by ingesting intermediate hosts infected with tissue cysts. Bradyzoites are released in the stomach and intestine from the tissue cysts when the cyst wall is dissolved by digestive enzymes. Bradyzoites penetrate the epithelial cells of small intestine and give rise to schizonts. Initiate five types (ABE) of predetermined asexual stages and merozoites released from schizonts form male and female gamonts. After fertilization a wall is formed around the fertilized macrogamont to form an oocyst. Oocysts are round to oval, 10–12 μm, and are unsporulated (uninfective) when passed in feces. After exposure to air and moisture for 1 to 5 days, oocysts sporulate and contain two sporocysts, each with four sporozoites.

The entire enteroepithelial (coccidian) cycle of T. gondii can be completed within 3 to 10 days after ingestion of tissue cysts and occurs in up to 97% of naive cats. However, after ingestion of oocysts or tachyzoites, the formation of oocysts is delayed until 18 days or more, and only 20% of cats fed oocysts will develop patency.

Extraintestinal Life Cycle

The extraintestinal development of T. gondii is the same for all hosts, including dogs, cats, and...
people, and is not dependent on whether tissue cysts or oocysts are ingested. After the ingestion of oocysts, sporozoites excyst in the lumen of the small intestine and penetrate intestinal cells, including the cells in the lamina propria. Sporozoites divide into two by an asexual process known as endodyogeny and thus become tachyzoites. Tachyzoites are lunate in shape, approximately 6–2 μm and multiply in almost any cell of the body. If the cell ruptures, they infect new cells. Otherwise, tachyzoites multiply intracellularly for an undetermined period and eventually encyst. Tissue cysts vary in size from 15 to 60 μm and usually conform to the shape of the parasitized cell. Tissue cysts are formed in the CNS, muscles, and visceral organs and probably persist for the life of the host.

Parasitemia during pregnancy can cause placentitis followed by spread of tachyzoites to the fetus. In people or sheep, congenital transmission occurs usually when the woman or ewe becomes infected during pregnancy. Little is known of transplacental toxoplasmosis in dogs, although its prevalence is thought to be less common than that in sheep and goats. Many kittens born to queens infected with *T. gondii* during gestation become infected transplacentally or via suckling. Clinical illness was common, varying with the stage of gestation at the time of infection, and some newborn kittens shed oocysts.

**CLINICAL FINDINGS**

In cats clinical toxoplasmosis is most severe in transplacentally infected kittens. Affected kittens may be stillborn or may die before weaning. Kittens may continue to suckle until death. Clinical signs reflect inflammation of the liver, lungs, and CNS. Affected kittens may have an enlarged abdomen because of enlarged liver and ascites. Encephalitic kittens may sleep most of the time or cry continuously. Anorexia, lethargy, and dyspnea due to pneumonia have been commonly recognized features of postnatal toxoplasmosis (Table 80B1). Other clinical signs include persistent or intermittent fever, anorexia, weight loss, icterus due to hepatitis or cholangiohepatitis, vomiting, diarrhea, abdominal effusion, hyperesthesia on muscle palpation, stiffness of gait, shifting leg lameness, and neurologic deficits. Clinical signs may be sudden or may have a slow onset. The disease may be rapidly fatal in some cats with severe respiratory or CNS signs. Anterior or posterior uveitis involving one or both eyes is common. Iritis, iridocyclitis, or chorioretinitis can occur alone or concomitantly. Aqueous flare, keratic precipitate, lens luxation, glaucoma, and retinal detachment are common manifestations of uveitis. Chorioretinitis may occur in both tapetal and nontapetal areas. Ocular toxoplasmosis occurs in some cats without polysystemic clinical signs of disease. In experimental *T. gondii* in cats, those infected concurrently with FIV developed severe pneumonitis and hepatitis, whereas those not infected with FIV developed multifocal chorioretinitis and anterior uveitis. Neurologic and ocular manifestations that occur in the absence of other systemic signs are more common with reactivated than acute infection.

In dogs, toxoplasmosis is a rare primary disease of dogs. Most reports are in dogs that are immunosuppressed and not vaccinated against the distemper virus. The most dramatic clinical signs in older dogs have been associated with neural and muscular systems. Neurologic signs depend on the site of lesion in the cerebrum, cerebellum, or spinal cord. Seizures, cranial nerve deficits, tremors, ataxia, and paresis or paralysis may be seen. Dogs with myositis may initially show abnormal gait, muscle wasting, or stiffness. Paraparesis and tetraparesis may rapidly progress to lower motor neuron paralysis. Canine toxoplasmosis is clinically similar to *Neospora caninum* infection, which was previously confused with toxoplasmosis (see Neosporosis later). Although these diseases are similar, toxoplasmosis appears to be more prevalent in cats and neosporosis in dogs.

**DIAGNOSIS**

Routine hematologic and biochemical parameters may be abnormal in cats and dogs with acute systemic toxoplasmosis. Nonregenerative anemia, neutrophilic leukocytosis, lymphocytosis, monocytosis, and eosinophilia are most commonly observed. Leukopenia of severely affected cats may persist until death and is usually characterized by an absolute lymphopenia and neutropenia with an inappropriate left shift, eosinopenia, and monocytopenia.

Biochemical abnormalities during the acute phase of illness include hypoproteinemia and hypoalbuminemia. Hyperglobulinemia has been detected in some cats with chronic toxoplasmosis. Marked increases in serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) have been noted in animals with acute hepatic and muscle necrosis. Dogs generally have increased serum alkaline phosphatase (ALP) activity with hepatic necrosis, but this occurs less frequently in cats. Serum creatine kinase activity is also increased in cases of muscle necrosis. Serum bilirubin levels have been increased in animals with acute hepatic necrosis, especially cats.
that develop cholangiohepatitis or hepatic lipidosis. Cats or dogs that develop pancreatitis may show increased serum amylase and lipase activities. Cats often show proteinuria and bilirubinuria. Cats with pancreatitis may have reduced serum total calcium with normal serum albumin concentrations.

Tachyzoites may be detected in various tissues and body fluids by cytology during acute illness (see Fig. 80B3). They are rarely found in blood, CSF, fine-needle aspirates, and transtracheal or bronchoalveolar washings but are more common in the peritoneal and thoracic fluids of animals developing thoracic effusions or ascites.

Inflammatory changes are usually noted in body fluids. In suspected feline toxoplasmosis of the nervous system, CSF protein levels were within reference ranges to a maximum of 149 mg/dl, and nucleated cells were a maximum of 28 cells/ml. Lymphocytes predominate, but a mixture of cells may be found.

Thoracic radiographic findings, especially in cats with acute disease, consist of a diffuse interstitial to alveolar pattern with a mottled lobar distribution. Diffuse symmetric homogeneous increased density due to alveolar coalescence has been noted in severely affected animals. Mild pleural effusion can be present. Abdominal radiographic findings may consist of masses in the intestines or mesenteric lymph nodes or homogeneous increased density as a result of effusion. Loss of contrast in the right abdominal quadrant can indicate pancreatitis.

Multiple serologic tests for the detection of antibodies have been used in the diagnosis of toxoplasmosis. The use of these tests in cats has been reviewed. The indirect FA can be adapted to detect IgM, IgG, or IgA antibodies, using whole or immunoblotted antigen by immunoblot aids in the diagnosis of neonatal toxoplasmosis. In general, for assessing human health risk, serologic test results from healthy cats can be interpreted. 1. A seronegative cat is not likely currently shedding oocysts but will likely shed oocysts if exposed; this cat poses the greatest public health risk. 2. A seropositive cat is probably not currently shedding oocysts and is less likely to shed oocysts if re-exposed or immunosuppressed. It is still recommended that potential exposure to oocysts be minimized. Because antibodies occur in the serum of both healthy and diseased cats, results of these serologic tests do not independently prove clinical toxoplasmosis. Antibodies of the IgM class are commonly detected in the serum or aqueous humor of clinically ill or FIV-infected cats, but not healthy cats, and they may be a better marker of clinical disease than IgG or IgA. T. gondii specific IgM is occasionally detected in the serum of cats with chronic or reactivated infection and does not always correlate with recent exposure. A tentative antemortem diagnosis of clinical toxoplasmosis in dogs or cats can be based on the following combination of serology and clinical parameters: 1. Serologic evidence of recent or active infection consisting of high IgM titers, or fourfold or greater, increasing or decreasing, IgG or other antibody titers (after treatment and/or recovery) 2. Exclusion of other causes of the clinical syndrome 3. Beneficial clinical response to an anti-Toxoplasma drug.

Gross and microscopic findings may be found in any organ but are more common in lungs, and mesenteric lymph nodes of cats. Granulomas may be present in intestines and mesenteric lymph nodes. Cholangiohepatitis, found in cats infected with Toxoplasma, has not been reported in any other host. The bile ducts are hyperplastic and plugged with desquamated bile duct epithelium and exudate. T. gondii schizonts (not tachyzoites) were seen in the biliary epithelium in both naturally occurring and experimentally induced disease.

THERAPY

Available drugs usually suppress replication of T. gondii and are not completely effective in killing the parasite. Clindamycin is the drug of choice for treating clinical toxoplasmosis in dogs and cats. Because of its good intestinal absorption, oral and parenteral dosages are similar. Clindamycin dosages for treating toxoplasmosis are greater than those for treating anaerobic infections.
infections for which the drug is marketed.

Clinical signs of systemic illness usually begin to resolve within 24 to 48 hours after institution of therapy. Appetite improves, hyperesthesia disappears, and fever usually subsides. Lower motor neuron deficits and muscle atrophy may take weeks to resolve in animals with polymyositis. Clindamycin has been effective in crossing the blood-brain and blood-vascular barriers in Toxoplasma-infected animals and people. Neurologic deficits improve, but signs may not totally resolve because of permanent damage caused by CNS inflammation. Active chorioretinitis generally subsides within 1 week. Some cases of anterior segment inflammation thought to be from toxoplasmosis have resolved with the administration of clindamycin alone. However, because intraocular inflammation commonly leads to lens luxation and glaucoma, cats with anterior segment inflammation should be treated with topical, oral, or injectable glucocorticoids. Clinical doses of glucocorticoids are not likely to exacerbate systemic disease. Cats with concurrent FIV infections do not respond as well as FIV-naïve cats to therapy. Clindamycin, given early in the course of acute experimental infection of cats, caused increased inflammatory reaction and tumor necrosis factor- levels. These effects have not been substantiated in naturally infected cats and may be related to the increased killing of actively replicating parasites, decreased IgM titer development, or decreased phagocytic activity caused by the drug.

Oral clindamycin can cause anorexia, vomiting, and diarrhea in dogs and cats, especially at higher dosages. These side effects appear to be related to local GI irritation, because parenteral therapy at similar dosages does not cause them in the same animals. The side effects stop soon after the dosage is reduced or therapy is discontinued. Clostridium difficile overgrowth has not been documented in dogs and cats as it has been in people treated with clindamycin.

Although less suitable than clindamycin, the combination of rapid-acting sulfonamides, such as sulfadiazine, sulfamethazine, sulfamerazine, and triple sulfas, and pyrimethamine is synergistic in the therapy of systemic toxoplasmosis. Pyrimethamine has greater efficacy than trimethoprim when used in combination. Because mental depression, anemia, leukopenia, and thrombocytopenia from bone marrow suppression develop rapidly in antifolate-treated cats compared with dogs, frequent hematologic monitoring is required, especially if therapy lasts longer than 2 weeks. Although trimethoprim-sulfonamide crosses the blood-brain barrier well, it has been reported to be ineffective in treating a dog with severe uveitis and optic neuritis.

Bone marrow suppression can often be corrected with the addition of folic acid (5.0 mg/day) or brewer's yeast (100 mg/kg/day) to the animal's diet. Baker's yeast, which contains folic acid, is inexpensive and as effective as folinic acid. The parasite uses preformed folic acid better than folic acid. Nevertheless, pyrimethamine and sulfonamides inhibit folicBfolinic acid metabolism in T. gondii to a greater extent than in the mammalian cell, so that supplementation with folic acid does not completely reverse therapeutic efficacy when used in combination with pyrimethamine and sulfonamides.

PREVENTION

Preventing toxoplasmosis in dogs and cats involves measures intended to reduce the incidence of feline infections and subsequent shedding of oocysts into the environment (see also Chapter 99). Kittens raised outdoors usually become infected shortly after they are weaned and begin to hunt. Cats should preferably be fed only dry or canned, commercially processed cat food. The prevalence of canine and feline toxoplasmosis has been higher in countries where raw meat products are fed to pets. Freezing or - ray irradiation can kill tissue cysts without affecting meat quality. Household pets should be restricted from hunting and eating potential intermediate hosts or mechanical vectors, such as cockroaches, earthworms, and rodents. If meat is provided, it should always be thoroughly cooked, even if frozen before feeding. Cats should be prevented from entering buildings where food-producing animals are housed or where feed storage areas are located.