Toxoplasmosis and Other Intestinal Coccidial Infections in Cats and Dogs

J.P. Dubey, MVSc, PhD\textsuperscript{a,},*, David S. Lindsay, PhD\textsuperscript{b}, Michael R. Lappin, DVM, PhD\textsuperscript{c}

Toxoplasma gondii and related coccidians are intracellular protozoan parasites. Coccidia are obligate intracellular parasites normally found in the intestinal tract. Virtually all warm-blooded animals, including humans, are commonly infected with coccidia.\textsuperscript{1} Until, the discovery of the life cycle of T. gondii in 1970, coccidia were considered host-specific parasites with infection generally confined to intestines. In addition, coccidia of dogs and cats were classified in the genus Isospora, and were thought to be of little or no biologic or clinical significance.\textsuperscript{2} Since then, a lot has been learnt about public health and biological significance of canine and feline coccidia, and they are now classified into several distinct genera: Toxoplasma, Neospora, Isospora (also called Cystoisospora), Hammondia, Besnoitia, Sarcocystis, Cryptosporidium, and Cyclospora.\textsuperscript{2} Only parasites belonging to Toxoplasma, Neospora, and Isospora of cats and dogs are discussed in detail here (Tables 1 and 2).

BASIC LIFE CYCLE

All coccidians have an asexual and a sexual cycle, resulting in the production of an environmentally resistant stage, the oocyst (Figs. 1–10). In some genera, such as Sarcocystis, the asexual and sexual cycles occur in different hosts, whereas in Isospora both cycles may occur in the same host; in Toxoplasma both cycles occur in
<table>
<thead>
<tr>
<th>Species and References</th>
<th>Oocyst Size a</th>
<th>Stage Excreted</th>
<th>Main Life Cycle</th>
<th>Development Site b</th>
<th>Extraintestinal Cycle in Cat</th>
<th>Tissue Cysts</th>
<th>Pathogenicity c</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Isospora felis</em></td>
<td>40 − 30</td>
<td>Unsporulated</td>
<td>One-host</td>
<td>Villar epithelium</td>
<td>No</td>
<td>One-zoite*</td>
<td>Mild</td>
</tr>
<tr>
<td><em>Isospora rivolta</em></td>
<td>22 − 20</td>
<td>Unsporulated</td>
<td>One-host</td>
<td>Villar epithelium</td>
<td>No</td>
<td>One-zoite</td>
<td>Mild</td>
</tr>
<tr>
<td><em>Toxoplasma gondii</em></td>
<td>12 × 10</td>
<td>Unsporulated</td>
<td>Two-host</td>
<td>Villar epithelium</td>
<td>Yes</td>
<td>Many*</td>
<td>Mild</td>
</tr>
<tr>
<td><em>Hammondia hammondi</em></td>
<td>12 × 11</td>
<td>Unsporulated</td>
<td>Two-host</td>
<td>Villar epithelium</td>
<td>No</td>
<td>Many*</td>
<td>None</td>
</tr>
<tr>
<td><em>Besnoitia wallacei</em></td>
<td>10</td>
<td>Unsporulated</td>
<td>Two-host</td>
<td>Lamina propria</td>
<td>No</td>
<td>Many*</td>
<td>None</td>
</tr>
<tr>
<td><em>Darlingi</em></td>
<td>11</td>
<td>Unsporulated</td>
<td>Two-host</td>
<td>Lamina propria</td>
<td>No</td>
<td>Many*</td>
<td>None</td>
</tr>
<tr>
<td><em>Oryctofelis</em></td>
<td>11 × 11</td>
<td>Unsporulated</td>
<td>Two-host</td>
<td>Lamina propria</td>
<td>Yes</td>
<td>Many*</td>
<td>None</td>
</tr>
<tr>
<td><em>Sarcocystis spp</em></td>
<td>11 × 9d</td>
<td>Sporulated</td>
<td>Two-host</td>
<td>Lamina propria</td>
<td>No</td>
<td>Many*</td>
<td>None</td>
</tr>
</tbody>
</table>

* Average size of unsporulated oocyst in micrometers.
* Schizonts in the small intestine of the cat.
* Pathogenicity for the cat.
* Sporocyst.
* These cysts contain 1 sporozoite and have been found only in experimentally infected animals fed oocysts.
* Tissue cysts are microscopic, and contain many bradyzoites in almost all tissues of the cat.
* Tissue cysts are not found in the cat; they are found mainly in muscles of rodents fed *H. hammondi* oocysts.
* Besnoitia cysts are found only in the intermediate hosts and can be macroscopic.
* Sarcocystis cysts (sarcocysts) are often macroscopic and occur only in the intermediate.
Table 2
Summary of biology of coccidia of dogs

<table>
<thead>
<tr>
<th>Species and References</th>
<th>Oocyst Size(^a)</th>
<th>Stage Excreted</th>
<th>Main Life Cycle</th>
<th>Development Site(^b)</th>
<th>Extraintestinal Cycle in Dog</th>
<th>Tissue Cysts</th>
<th>Pathogenicity(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Isospora canis</em>(^14,15)</td>
<td>38 × 30</td>
<td>Unsporulated</td>
<td>One-host</td>
<td>Villar epithelium</td>
<td>No</td>
<td>One-zoite(^a)</td>
<td>Mild</td>
</tr>
<tr>
<td><em>Isospora ohioensis</em>(^16)</td>
<td>24 × 20</td>
<td>Unsporulated</td>
<td>One-host</td>
<td>Villar epithelium</td>
<td>No</td>
<td>One-zoite</td>
<td>Mild</td>
</tr>
<tr>
<td><em>Isospora neorivolta</em>(^17)</td>
<td>×</td>
<td>Unsporulated</td>
<td>One-host</td>
<td>Villar epithelium and lamina propria</td>
<td>No</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td><em>Isospora burrowsii</em>(^18,19)</td>
<td>20 × 17</td>
<td>Unsporulated</td>
<td>One-host</td>
<td>Villar epithelium and lamina propria</td>
<td>No</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td><em>Neospora caninum</em>(^20,21)</td>
<td>12 × 10</td>
<td>Unsporulated</td>
<td>Two-host</td>
<td>Unknown</td>
<td>Yes</td>
<td>Many(^f)</td>
<td>Mild</td>
</tr>
<tr>
<td><em>Hammondia heydorni</em>(^21–23)</td>
<td>12 × 11</td>
<td>Unsporulated</td>
<td>Two-host</td>
<td>Villar epithelium</td>
<td>No</td>
<td>Rare(^g)</td>
<td>None</td>
</tr>
<tr>
<td><em>Sarcocystis</em> spp(^13)</td>
<td>11 × 9(^d)</td>
<td>Sporulated</td>
<td>Two-host</td>
<td>Lamina propria</td>
<td>No</td>
<td>Many(^h)</td>
<td>None</td>
</tr>
</tbody>
</table>

\(^a\) Average size of unsporulated oocyst in micrometers.

\(^b\) Schizonts in the small intestine of the dog.

\(^c\) Pathogenicity for the dog.

\(^d\) Sporocysts.

\(^e\) These cysts contain 1 sporozoite and have been found only in experimentally infected animals fed oocysts.

\(^f\) Tissue cysts are microscopic, contain many bradyzoites, and are found in the central nervous system and muscles.

\(^g\) Tissue cysts are not confirmed.

\(^h\) Sarcocystis cysts are often macroscopic and occur only in the intermediate hosts.

\(^i\) Oocysts are considered to be the same size as *I. ohioensis* but were not described.
Fig. 1. Life cycle of *Toxoplasma gondii*. (From Dubey JP. Toxoplasmosis – a waterborne zoonosis. Vet Parasitol 2004;126:57–72; with permission.)

Fig. 2. Life cycle of *Neospora caninum*. (From Dubey JP. Recent advances in Neospora and neosporosis. Vet Parasitol 1999;84:350; with permission.)
one host (the cat), and only the asexual cycle occurs in nonfeline hosts. The host that excretes the oocyst is called the definitive host, and those hosts wherein only the asexual cycle occurs are called intermediate hosts.

A representative coccidian life cycle is best described as follows. Oocysts are passed unsporulated in feces (Fig. 3A–C; Fig. 4; Fig. 10C). After exposure to warm (20°C) environmental temperatures and moisture, oocysts sporulate, forming 2 sporocysts. Within each sporocyst are 4 sporozoites (Fig. 3D; Fig. 10D). The sporozoites are banana-shaped and are the infective stage. The sporozoites can survive environmental exposure inside the oocysts for many months. After the ingestion of sporulated oocysts by cats or dogs, sporozoites excyst in the intestinal lumen, and the sporozoites initiate the formation of schizonts or meronts. During schizogony or merogony, the sporozoite nucleus divides into 2, 3, or more nuclei, depending on the parasite and the stage of the cycle. After nuclear division, each nucleus is surrounded by cytoplasm, forming a merozoite (Fig. 5B, D; Fig. 6A; Fig. 7B–D; Fig. 9B). The number of merozoites within a schizont varies from 2 (see Fig. 7B) to several hundred, depending on the stage of the cycle and the species of coccidia. Merozoites are released from the schizont when the infected host cell ruptures. The number of schizogonic cycles varies with the parasitic species. First-generation merozoites repeat the asexual cycle and form second-generation schizonts, or transform into male (micro) and female (macro) gamonts. The microgamont divides into many tiny microgametes (Fig. 5C; Fig. 7F; Fig. 9D). A microgamete fertilizes a macrogamete (Fig. 7E; Fig. 9C), and an oocyst wall is formed around the zygote (see Fig. 5D). The life cycle is completed when unsporulated oocysts are excreted in feces.
Members of the genus *Isospora*, the most commonly recognized coccidians infecting dogs or cats, are species specific for the definitive host. At least 4 species, *I. canis*, *I. ohioensis*, *I. burrowsi*, and *I. neorivolta*, infect dogs, and 2 species, *I. felis* and *I. rivolta*, infect cats.

The life cycle of *Isospora* infecting dogs and cats is similar to the basic coccidian intestinal cycle, except an asexual cycle can also occur in the definitive or intermediate host. On ingestion by definitive or suitable paratenic (intermediate) hosts, oocysts excyst in the presence of bile, and free sporozoites invade the intestine. Some sporozoites penetrate the intestinal wall and enter mesenteric lymph nodes or other extraintestinal tissues, where they form enlarging monozoic cysts (see Fig. 8). If no replication occurs, the term paratenic host, rather than intermediate host, is used. Monozoic cysts of *Isospora* may remain in extraintestinal tissues of paratenic hosts for the life of the host. Ingestion of monozoic cysts in paratenic hosts leads to intestinal infection in the definitive dog and cat host. The life cycle after the ingestion of paratenic host is the same as after the ingestion of sporulated oocysts from feces. The significance of the paratenic host in the life cycle of dogs and cats is unknown because the direct fecal-oral cycle is very efficient.

**Clinical Findings**

Enzootic infections are frequently found in catteries or kennels where animals are congregated. Clinical signs are most apparent in neonates. Diarrhea with weight
**Fig. 5.** Lesions and developmental stages of *Isospora ohioensis* in dogs. (A) The arrows bracket a necrotic area of small intestine. Hematoxylin and eosin stain. (B) Schizont in which merozoites are still attached (arrow) and a free merozoite (arrowhead). Giemsa stain. (C) Immature (arrow) and mature (arrowhead) microgamonts. Giemsa stain. (D) Schizont (orange arrow), free merozoite (arrowhead), and an oocyst (black arrow). Giemsa stain.

**Fig. 6.** Location of developmental stages of *Isospora neorivolta* from dogs. (A) Schizont with merozoites (arrow) and microgamonts (arrowheads) in epithelial cells of a villous. Hematoxylin and eosin stain. (B) Cross section of a villous demonstrating developmental stages (arrows) in the lamina propria. The epithelial (E) portion of the villous is readily observed. Hematoxylin and eosin stain.
Fig. 7. Asexual and sexual stages of *Isospora felis* from cats. (A) Asexual stages (arrows) and macrogamonts (arrows) and in a villous. Hematoxylin and eosin stain. (B) Asexual stages demonstrating an immature schizont (orange arrow), a schizont with merozoites (black arrow), and 2 large merozoites (arrowhead). Hematoxylin and eosin stain. (C) Asexual stages demonstrating a group of immature schizont (arrow) and a schizont with merozoites (arrowhead). Hematoxylin and eosin stain. (D) Schizont containing many merozoites (arrow). Hematoxylin and eosin stain. (E) Microgamont (Mi) with numerous nuclei and a macrogamont (Ma) in feline enterocytes. Iron-hematoxylin stain. (F) Microgamont containing many microgametes. Some microgametes (arrows) are at the periphery and appear fully developed, whereas others are still in groups (arrowheads). Iron-hematoxylin stain.
loss and dehydration and, rarely, hemorrhage is the primary sign attributed to coccidiosis in dogs and cats. Anorexia, vomiting, mental depression, and ultimately death may be seen in severely affected animals.

Intestinal coccidiosis may be manifest clinically when dogs or cats are shipped or weaned, or experience a change in ownership. Diarrhea might result from the extraintestinal stages of *Isospora* returning to the intestines. Pathogenesis of intestinal coccidiosis of cats and dogs is not well understood because clinical disease has not been reliably produced in experimentally infected animals, and clinical signs are not correlated with the number of oocysts found in feces. Little is known of the virulence of the different strains of these parasites.15

**Diagnosis**

Intestinal coccidial infection in dogs and cats is diagnosed by identification of the oocysts with any of the fecal flotation methods commonly used to diagnose parasitic infections. In dogs, only *I. canis* can be identified with certainty by oocyst size and shape (see Fig. 3A, B). The oocysts of the other 3 species of *Isospora*, namely *I. ohioensis*, *I. burrowsi*, and *I. neorivolta*, may overlap in size, and their distinction is not clinically important. The 2 species of *Isospora* occurring in cats can be readily distinguished by oocyst size. Although oocysts of these *Isospora* are passed unsporulated in freshly excreted feces, they sporulate partially by the time fecal examination is made. Partially sporulated oocysts contain 2 sporocysts without sporozoites. *Isospora* species may sporulate within 8 hours of excretion, and these *Isospora* are highly infectious. In cats, *I. felis* oocysts are twice the size of *I. rivolta*. In extreme cases epithelial casts may be found in feces, and schizonts, merozoites, and partially formed oocysts can be found in smears made in normal saline (not water).

**Treatment**

The primary goal of treatment of *Isospora* spp infections is to resolve diarrhea in puppies and kittens.24 Whereas controlled data are generally not available for most protocols listed in Table 3, there is anecdotal evidence that administration of drugs can lessen morbidity and mortality, and lessen oocyst shedding. Supportive care such as fluid therapy for correction of dehydration should be administered as indicated.
The majority of the drugs listed in Table 3 have only a coccidiostatic effect on the organisms and so infection may not be cleared. In addition to the potential for gastrointestinal irritation, some sulfa drugs have other significant side effects including induction of keratoconjunctivitis sicca, cholestasis, hepatocellular necrosis, and thrombocytopenia. The activity of ponazuril, diclazuril, and toltrazuril against apicomplexans has been studied recently. These drugs are currently preferred for the treatment of Isospora spp infection by many clinicians. Ponazuril is available in the United States as a treatment for Sarcocystis neurona infection in horses (Marquis Paste, Bayer Animal Health). This product can be purchased by veterinarians and diluted for use in puppies or kittens. Most compounding pharmacies alternatively will provide appropriate concentrations of ponazuril for use in small animals by prescription.
Depending on the protocol used, infection may or may not be eliminated in all puppies or kittens. In addition, repeated infection with *Isospora* spp can occur. Thus, it is unclear whether there is value in repeating diagnostic testing after successful treatment of clinical disease. Treatment of all other “in-contact” dogs or cats may lessen the likelihood of repeat infection, but also increases expense to the owner and increases the risk for drug-associated side effects. *Isospora* spp are very resistant to routine disinfectants used in small animal practice. If there is a problem with recurrent coccidiosis in a kennel or cattery, potential transport hosts should be controlled, and the treatment of all animals combined with careful environmental cleaning as well as steam cleaning of surfaces may be indicated. In shelters with recurrent problems with coccidiosis, it is recommended that ponazuril be used prophylactically by administering a dose to all puppies or kittens at 2 to 3 weeks of age (http://www.sheltermedicine.com/portal/is_parasite_control.shtml).

Diarrhea associated with *Isospora* spp infections is generally self-limited or rapidly responsive to drug therapy. Thus, puppies and kittens with persistent diarrhea and...
Isospora spp oocyst shedding should be evaluated thoroughly for other coinfections or diseases that could potentiate Isospora spp associated disease.

**Prevention**

Coccidiosis tends to be a problem in areas of poor sanitation. The fecal shedding of large numbers of environmentally resistant oocysts makes infection likely under such conditions. Animals should be housed so as to prevent contamination of food and water bowls by oocyst-laden soil or infected feces. Feces should be removed daily and incinerated. Oocysts survive freezing temperatures. Runs, cages, food utensils, and other implements should be disinfected by steam cleaning or immersion in boiling water or by 10% ammonia solution. Animals should have limited access to intermediate hosts and should not be fed uncooked meat. Insect control is essential in animal quarters and food storage areas because cockroaches and flies may serve as mechanical vectors of oocysts. Coccidiostatic drugs can be given to infected bitches before or soon after whelping to control the spread of infection to puppies.  

**TOXOPLASMA GONDII**

Toxoplasma gondii is an intestinal coccidian of cats with all nonfeline species as intermediate hosts. Unlike other coccidian parasites, it has adapted to be transmitted
in several ways, including fecal-oral, carnivorism, and transplacental (see Fig. 1). Other minor modes of transmission include transfusion of fluids or transplantation of organs.

The coccidian phase of the (enteroepithelial) cycle is found only in the definitive feline host (Fig. 9B–D). Most cats are thought to become infected by ingesting intermediate hosts infected with tissue cysts (Fig. 9A). 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 initiate the formation of schizonts (see Fig. 9B, C). After an undetermined number of generations, merozoites released from schizonts form male or female gamonts (see Fig. 9C, D). The rest of the cycle proceeds as in other coccidians. The entire enterop epithelial cycle of *T. gondii* can be completed within 3 to 10 days after ingestion of tissue cysts, and occurs in most naive cats. However, after ingestion of sporulated oocysts, the formation of oocysts is delayed until 18 days or more, and only 20% of cats fed oocysts will develop patency. Thus, the fecal-oral cycle of *T. gondii* in cats is not very efficient.

Only cats are known to produce *T. gondii* oocysts. However, some vertebrates and invertebrates can be a transport host for *T. gondii* oocysts. Dogs can eat cat feces infected with *T. gondii* oocysts and these oocysts may pass unexcysted in dog feces. In addition, dogs can roll over in feces of infected cats and people can then become infected by petting these dogs. *T. gondii* oocysts have been identified in feces of naturally infected dogs.

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 2 by an asexual process known as endodyogeny, and thus become tachyzoites. Tachyzoites are lunate in shape, approximately 6 by 2 \( \mu \text{m} \), 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 grow intracellularly and contain numerous bradyzoites (see Fig. 9A). Bradyzoites differ biologically from tachyzoites in that they can survive the digestive process in the stomach, whereas tachyzoites are usually killed. Tissue cysts vary in size from 5 to 70 \( \mu \text{m} \) and usually conform to the shape of the parasitized cell. Tissue cysts are separated from the host cell by a thin (<0.5 \( \mu \text{m} \)) elastic wall (see Fig. 9A). Tissue cysts are formed in the central nervous system (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. Many kittens born to queens infected with *T. gondii* during gestation became infected transplacentally or via suckling. Clinical illness is common, varying with the stage of gestation at the time of infection, and some newborn kittens shed oocysts.

The type and severity of clinical illness with *T. gondii* infections are dependent on the degree and localization of tissue injury. Why some infected dogs or cats develop clinical toxoplasmosis while others remain well is not fully understood. Age, sex, host species, strain of *T. gondii*, number of organisms, and stage of the parasite ingested may account for some of the differences. Postnatally acquired toxoplasmosis is generally less serious than prenatally acquired infection. Stress may also aggravate *T. gondii* infection. Concomitant illness or immunosuppression may make a host more susceptible because *T. gondii* proliferates as an opportunistic pathogen. Clinical
Toxoplasmosis in dogs is often associated with canine distemper or other infections, such as ehrlichiosis, or with glucocorticoid therapy. In some cases, however, predisposing disorders cannot be found. The prevalence of canine toxoplasmosis historically has decreased with the routine use of distemper vaccines. Unlike dogs, clinical toxoplasmosis in cats is considered a primary disease. At present there is no conclusive evidence that concomitant infections with feline leukemia virus, feline immunodeficiency virus (FIV), and Bartonella spp infections modify the course of T. gondii infection in cats.

**Clinical Findings**

**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. 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, dermatitis, loss of vision, and neurologic deficits. In 100 cats with histologically confirmed toxoplasmosis, clinical syndromes were diverse but infection of pulmonary (97.7%), CNS (96.4%), hepatic (93.3%), pancreatic (84.4%), cardiac (86.4%), and ocular (81.5%) tissues were most common. 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.

**Dogs**
Clinical signs may be localized in respiratory, neuromuscular, or gastrointestinal systems, or may be caused by generalized infection. The neurologic form of toxoplasmosis may last for several weeks without involvement of other systems, whereas severe disease involving the lungs and liver may kill dogs within a week. Generalized toxoplasmosis is seen mostly in dogs younger than 1 year and is characterized by fever, tonsillitis, dyspnea, diarrhea, and vomiting. Icterus usually results from extensive hepatic necrosis. Myocardial involvement is usually subclinical, although arrhythmias and heart failure may develop as predominant findings in some older dogs.

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 seems to be more prevalent in cats and neosporosis in dogs.
There are only a few reports of ocular lesions associated with toxoplasmosis in dogs. Retinitis, anterior uveitis, iridocyclitis, ciliary epithelium hyperplasia, optic nerve neuritis, and keratoconjunctivitis have been noted. Severe keratoconjunctivitis was recently reported in a dog on prolonged topical corticosteroid therapy.\textsuperscript{57}

**Diagnosis**

Clinical signs, serum chemistry, cytology, radiology, fecal examination, and serology can aid diagnosis. Routine hematologic and biochemical parameters may be abnormal in cats and dogs with acute systemic toxoplasmosis. Nonregenerative anemia, neutrophilic leukocytosis, lymphocytosis, monocytes, 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 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. Tachyzoites are rarely found in blood, cerebrospinal fluid (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.

Despite the high prevalence of serum antibodies in cats worldwide, the prevalence of *T. gondii* oocysts (Fig. 4C) in feces is very low. In general, less than 1% of cats shed oocysts on any given day.\textsuperscript{68} Because cats usually shed *T. gondii* oocysts for only 1 to 2 weeks after their first exposure, oocysts are rarely found on routine fecal examination. Moreover, cats usually are not clinically ill and do not have diarrhea during the period of oocyst shedding. Although cats are considered immune to reshedding of oocysts, they may shed a few oocysts after rechallenge with different strains more than 6 years later. Clinical pharmacological doses of corticosteroids do not reactivate shedding of oocysts.
*T. gondii* oocysts in feline feces are morphometrically indistinguishable from oocysts of *Hammondia hammondi* and *Besnoitia* spp (see Table 1), which also occur in cats. Oocysts of these coccidians can be differentiated only by sporulation and subsequent animal inoculation. If 10- to 12-μm sized oocysts are found, they should be considered to be *T. gondii* until proved otherwise. Further inoculations should be attempted only in a diagnostic laboratory with competence in this procedure because of the infectious nature of the organism.

Because of their small size, oocysts of *T. gondii* are best demonstrated by centrifugation using Sheather sugar solution. Five to 10 g of feces are mixed with water to a liquid consistency, and the mixture is strained with gauze. Two parts Sheather sugar solution (500 g sugar, 300 mL water, and 6.5 g melted phenol crystals) are added to one part fecal suspension and centrifuged in a capped centrifuge tube. Care should be taken not to fill the tube to the top, to prevent spills or aerosols. After centrifugation at 1000 g for 10 minutes, remove 1 to 2 drops from the meniscus with a dropper, place on a microscope slide, cover with a coverslip, and examine at low-power (×100) magnification. *T. gondii* oocysts are about one-fourth the size of *I. felis* oocysts and one-eighth the size of eggs of *Toxocara cati* (the common roundworm of the cat).

Once infected, animals harbor toxoplasmic tissue cysts for life. IgG in kittens born to chronically infected queens is transferred in colostrum and persists for 8 to 12 weeks after birth. Serologic surveys indicate that *T. gondii* infections are prevalent worldwide. Approximately 30% of cats and dogs in the United States have *T. gondii* antibodies. The prevalence of seropositivity increases with age of the cat or dog because of the chance of exposure rather than susceptibility.

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.37 No single serologic assay exists that can definitively confirm toxoplasmosis. The magnitude of titer is not associated with severity of clinical signs. The measurement of serum antibodies in healthy cats cannot predict the oocyst-shedding period. In general, for assessing human health risk, serologic test results from healthy cats can be interpreted as follows. (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 reexposed 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* 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 or recovery); (2) exclusion of other causes of the clinical syndrome; (3) beneficial clinical response to an anti-*Toxoplasma* drug.

**Therapy**

Treatment of *T. gondii* infection is indicated to decrease oocyst shedding in acutely infected cats, and to control the signs of clinical toxoplasmosis in dogs and cats.
Multiple drugs have been administered to cats to shorten the oocyst shedding period. As discussed, ingestion of bradyzoites results in an enteroepithelial cycle that generally only lasts days, so duration of drug therapy can be short. The drugs most commonly available are listed in Table 4.

It is difficult to induce clinical toxoplasmosis in dogs or cats without concurrent immune suppression, so controlled studies on the effect of treatments are lacking. Based on studies in vitro or in other research species, clindamycin, potentiated sulfas, azithromycin, and ponazuril have activity against *T. gondii* and are relatively safe to use in dogs and cats (see Table 4). Clindamycin hydrochloride or a trimethoprim-sulfonamide combination has been used most frequently by one of the authors (M.L.) for the treatment of clinical toxoplasmosis in dogs and cats. Clindamycin has been used successfully for the treatment of a variety of clinical signs including fever, myositis, uveitis, and CNS disease. The primary problems associated with clindamycin include gastrointestinal irritation in some animals and induction of small bowel diarrhea, possibly from changing the normal anaerobic flora of the gastrointestinal tract. However, coagulation abnormalities or *Clostridium difficile* toxins were not detected in experimentally treated cats.

Azithromycin has been used successfully in a limited number of cats, but the optimal protocol is unknown (Lappin MR, unpublished data, 2009). Pyrimethamine combined with sulfa drugs or azithromycin is effective for the treatment of human toxoplasmosis, but commonly results in toxicity in cats.

Ponazuril has been shown to inhibit *T. gondii* in vitro and to be useful for the treatment of toxoplasmosis in rodent models. In addition, the drug was administered to a dog with a *T. gondii* associated conjunctival mass that recurred after clindamycin therapy, with no known further recurrence.

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. Some dogs and cats with CNS disease will require supportive care such as anticonvulsants.

### Table 4

<table>
<thead>
<tr>
<th>Drug</th>
<th>Protocol</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhibition of oocyst shedding</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>50 mg/kg, PO or IM, every 24 h for 1–12 d</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>12.5–25 mg/kg, PO or IM, every 12 h for 1–2 d</td>
<td></td>
</tr>
<tr>
<td>Toltrazuril</td>
<td>5–10 mg/kg, PO, every 24 h for 2 d</td>
<td>C</td>
</tr>
<tr>
<td><strong>Systemic infections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>3–13 mg/kg, PO or IM, every 8 h for a minimum of 4 wk</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>10–20 mg/kg, PO or IM, every 12 h for a minimum of 4 wk</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>8–17 mg/kg, PO or IM, every 8 h for a minimum of 4 wk</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>10–12.5 mg/kg, PO or IM, every 12 h for a minimum of 4 wk</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim-sulfonamide</td>
<td>15 mg/kg, PO, every 12 h for a minimum of 4 wk</td>
<td>D, C</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>10 mg/kg, PO, every 24 h for a minimum of 4 wk</td>
<td>C</td>
</tr>
</tbody>
</table>

PO, by mouth; IM, intramuscularly.
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 respond 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 *T. gondii*, so recurrence of clinical illness can occur in infected dogs or cats. In addition, infected dogs and cats will generally always be seropositive and so there is little clinical use in repeating serum antibody titers after the initial diagnostic workup. Administration of immunosuppressive doses of cyclosporine A (CsA) or glucocorticoids has been associated with activated toxoplasmosis in some cats. Because administration of drugs does not eliminate the organism from canine or feline tissues, whether to test patients and treat positive animals with a drug with anti-*T. gondii* activity before administering CsA or glucocorticoids is of unknown benefit. Cats experimentally infected with *T. gondii* and treated with clindamycin at 20 mg/kg by mouth for 21 days did not repeat *T. gondii* oocyst shedding when immune-suppressed with dexamethasone. In contrast, some cats in the control group repeated oocyst shedding, which suggested a clindamycin effect. In another unpublished research study (Lappin MR, unpublished data, 2009), cats with activation of chronic toxoplasmosis resulting in systemic illness after administration of CsA had extremely high blood levels, reflecting the wide range of bioavailability sometimes detected in cats. These findings led to the recommendation that *T. gondii*-seropositive cats to be administered CsA should have trough levels of CsA determined approximately 2 weeks after initiating CsA. If the levels are high, the dose of CsA should be decreased immediately.

The prognosis is poor for cats and dogs with disseminated toxoplasmosis, particularly in those that are immunocompromised. In some research cats with experimental intravenous *T. gondii* inoculation, administration of clindamycin had a potential paradoxic effect.

**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. 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 g-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. At present there is no vaccine to prevent oocyst shedding or clinical disease.

**Public Health Considerations**

Although oocysts are key in the epidemiology of toxoplasmosis, there is no correlation between toxoplasmosis in adults and cat ownership. Most cats become infected from carnivorousness soon after weaning, and shed oocysts for only short periods (<3 weeks) thereafter. Cats found to be shedding *T. gondii* oocysts should be hospitalized for this period and treated to eliminate shedding, particularly when a pregnant woman is present in the household. To prevent inadvertent environmental
contamination, cat owners should practice proper hygienic measures on a routine basis. Because infected cats rarely have diarrhea and they groom themselves regularly, direct fecal exposure from handling infected cats is unlikely. Oocysts were not detected in fur of cats that had shed large numbers of *T. gondii* oocysts.

Litter boxes should be changed daily, because usually at least 24 hours are necessary for oocysts to reach the infective stage. Oocyst sporulation depends on environmental temperature. Unsporulated oocysts are more susceptible to disinfection and environmental destruction; therefore, control efforts should be directed at this stage. Litter pans should be disinfected with scalding water. Cat feces should be disposed of in the septic system, incinerated, or sealed tightly in a plastic bag before placing in a sanitary landfill. Only organic litters that are biodegradable should be placed in the septic system. High-temperature composting to kill oocysts remains to be proved. Under no circumstances should litter boxes be dumped into the environment.

Oocysts survive best in warm, moist soil, a factor that helps to explain the high prevalence of disease in temperate and tropical climates. Oocysts also withstand exposure to constant freezing temperature, drying, and high environmental temperature for up to 18 months or more, especially if they are covered and out of direct sunlight. A cat’s natural instinct to bury or hide its feces provides the protected environment for oocyst survival. Children’s sandboxes should be covered to prevent cats from defecating in them. Mechanical vectors, such as sow bugs, earthworms, and houseflies, have been shown to contain oocysts, and cockroaches and snails are additional mechanical vectors. Control of these invertebrates will help reduce the spread of infection. Dogs that commonly roll in cat feces can be examined for their potential to act as mechanical vectors for oocysts.

Sporulated oocysts resist most disinfectants, and only 10% ammonia is effective when it is in contact with contaminated surfaces for 10 minutes. Because of the time required for chemical disinfection and the fumes produced by ammonia, immersing litter pans in boiling or scalding water usually is the easiest means of disinfection. Steam cleaning can decontaminate hard impervious surfaces.

Outbreaks of human infections have been reported when oocyst-contaminated dust particles were inhaled or ingested. Dispersion of oocysts can also occur by earth-moving or cultivating equipment, shoes, animal feet, wind, rain, and fomites. Streams can become contaminated via water runoff. Stray and wild cats have been known to contaminate streams. A report of military recruits infected by drinking oocyst-contaminated stream water in a jungle has been made. Water from streams or ponds should always be boiled before drinking. Heating utensils to 70°C for at least 10 minutes will kill oocysts.

**NEOSPORA CANINUM**

*Neospora caninum* is morphologically similar to *T. gondii*. The tachyzoites and tissue cysts of *N. caninum* resemble those of *T. gondii* under the light microscope (see Fig. 10A, B). The domestic dog and the coyote (*Canis latrans*) are the definitive host. As with other coccidia, herbivores likely become infected from ingesting oocysts shed by the definitive host and by subclinical congenital infection from transplacental transmission. Tachyzoites are 5 to 7 by 1 to 5 μm, depending on the stage of division (see Fig. 10A). The tachyzoites divide into 2 zoites by endodyogeny. In infected carnivores, tachyzoites are found within macrophages, polymorphonuclear cells, spinal fluid, and neural and other cells of the body. Individual organisms are ovoid, lunate, or globular; they contain 1 or 2 nuclei and are arranged singly, in pairs, or in groups of 4 or more. Cell necrosis occurs after rapid intracellular replication of
tachyzoites. Widespread dissemination of tachyzoites to many organs may occur in the acute phases, with subsequent restriction to neural and muscular tissues in more chronically affected dogs.

Tissue cysts (up to 100 μm in diameter) are found mainly in neural cells (brain, spinal cord, peripheral nerves, and retina). Tissue cysts may be round or elongated. The cyst wall is up to 4 μm thick (see Fig. 10B) and encloses slender periodic acid Schiff positive bradyzoites. Rupture of tissue cysts is associated with a granulomatous inflammatory reaction in the involved tissue. Oocysts are shed unsporulated in dog feces 5 days or later after ingesting tissue cysts, and are 10 to 14 μm in diameter (see Fig. 10C). Sporulation occurs outside the body. Sporulated oocysts contain 2 sporocysts, each with 4 sporozoites (see Fig. 3D; Fig. 10D).

Naturally occurring infections in dogs have been found throughout the world. Seroprevalence of clinically healthy dogs is usually much less than 20% but much greater than the prevalence of clinical illness, suggesting subclinical infections. Purebred dogs, especially German shorthaired pointers, Labrador retrievers, boxers, golden retrievers, basset hounds, and greyhounds, have been noticeably prevalent in published case reports. Experimental transmission in dogs can occur after oral (carnivorousness) and parenteral (experimental) administration, but transplacental transmission may be the predominant route in natural infections. Suppositions are that the chronically infected bitch develops parasitemia during gestation, which spreads transplacentally to the fetus. Successive litters from the same subclinically infected dam may be born infected. However, transplacental transmission alone will not be able to propagate *N. caninum* infection in nature. Most, but not all, puppies in a litter have clinical manifestations. Other pups may carry the infection subclinically, with reactivation in later life with immunosuppressive illnesses or administration of modified live virus vaccines or glucocorticoids. In contrast to toxoplasmosis, underlying immunodeficiencies or concurrent illnesses are not consistently detected in canine neosporosis. Postnatal infections may be more frequent than initially recognized.

**Dogs**

It is likely that many dogs diagnosed with toxoplasmosis before 1988 actually had neosporosis. In general, clinical findings in dogs are similar to those of toxoplasmosis, but neurologic deficits and muscular abnormalities predominate. Clinical signs may also include those of hepatic, pulmonary, and myocardial involvement, but any tissue can become involved. Both pups and older dogs are clinically affected, and the infections can be transmitted congenitally. The most severe and frequent infections have been in young (<6 months) dogs that presented with ascending paralysis of the limbs. In the youngest pups, signs are often noticed beginning at 3 to 9 weeks of age. Features that distinguish neosporosis from other forms of paralysis are gradual muscle atrophy and stiffness, usually as an ascending paralysis; the pelvic limbs are more severely affected than the thoracic limbs. Paralysis progresses to rigid contracture of the muscles of the affected limb. This arthrogryposis is a result of the scar formation in the muscles from lower motor neuron damage and myositis. In some pups, joint deformation and genu recurvatum may develop. Cervical weakness, dysphagia, megaeosophagus, and ultimately death occur. In some dogs, the progression may become static. Dogs do not develop severe intracranial manifestations and maintain alert attitudes. Dogs can survive for months with hand feeding and care, but remain paralyzed with associated complications. Older dogs, which are less commonly affected, often have signs of multifocal CNS involvement or polymyositis; less common manifestations result from myocarditis, dermatitis, pneumonia, or multifocal dissemination. Death can occur in dogs of any age.
Experimental studies suggest that *N. caninum* can cause early fetal death, mumification, resorption, and birth of weak pups. Although abortion is a major feature of the disease in cattle, there are no reports of abortion in dogs.

**Cats**

Natural clinical infections have not been documented, although antibodies to *N. caninum* have been reported in domestic and wild felids.77

**Diagnosis**

Hematologic and biochemical findings have been variable, depending on the organ system of involvement. With muscle disease, creatine kinase and AST activities have been increased. Serum ALT and alkaline phosphatase activities are increased in dogs that develop hepatic inflammation. CSF abnormalities have included mild increases in protein (>20 but <150 mg/dL) and nucleated cell (>10 but <100 cells/dL) concentrations. Differential leukocyte counts included lymphocytes, monocytes and macrophages, neutrophils, and eosinophils in decreasing numbers. CSF results can be within reference limits in some dogs. Electromyographic abnormalities have consisted of spontaneous activity of fibrillation potentials, positive sharp waves, and occasional repetitive discharges. Nerve conduction velocities may be reduced in the most severely affected limbs, especially proximally, but they are often within reference range. Low evoked action potentials may be found with myositis.

Demonstrating serum antibodies to *N. caninum* can help confirm the diagnosis of neosporosis. Serum is reacted with cell-cultured *N. caninum*. Serum indirect fluorescent antibody (FA) titers can vary between laboratories; however, in one reference laboratory, values of 50 or greater are considered positive and values are often greater than 800. CSF can be tested, but titers are of lesser magnitude. Some false-positive titers exist in previously exposed dogs that may be infected, but they remain nonsymptomatic, with values of 800 or greater. Indirect FA IgG titers in most species increase 1 to 2 weeks after infection. Higher indirect FA titer values have been found in clinically versus subclinically affected dogs and in those with the longest duration of illness. However, there is no correlation between the magnitude of titer and clinical signs. There are several enzyme-linked immunosorbent assay methods to detect *N. caninum* antibodies. A direct agglutination test measuring IgG was as sensitive and specific as an indirect FA test, with the advantage of being useful in a variety of host species.

*N. caninum* may be found in CSF or tissue aspirates and biopsies of some dogs, and may be detected with any material used to stain blood films. Biopsy of affected muscle may yield a definitive diagnosis when organisms are detected. *N. caninum* tachyzoites are similar to *T. gondii* tachyzoites under light microscopy. Tissue cysts of *N. caninum* have thicker walls than those of *T. gondii*. *N. caninum* can be grown in cell culture and in mice. *N. caninum* must be distinguished from *T. gondii* in sections by immunochromical stains. Structural differences can also be detected with transmission electron microscopy. *T. gondii* has a thinner cyst wall, and fewer micronemes and rhoptries. The use of molecular genetics and the polymerase chain reaction to distinguish *Neospora* from other related parasites has been reviewed.

*N. caninum* oocysts in canine feces are rare. These oocysts are few in number and morphologically resemble oocysts of *T. gondii*, *Hammondia hammondi*, and *H. heydorni*, all of which can be present in feces of dogs.21–23,75,85,86 Differentiation of these 4 species of coccidia in canine feces is technically difficult and needs the assistance of specialized laboratories.
Therapy

Information on effective therapy for this disease is limited. However, drugs used as therapy for toxoplasmosis should be tried early in the course of illness. Clindamycin, sulfadiazine, and pyrimethamine alone or in combination have been administered to treat canine neosporosis. However, clinical improvement is not likely in the presence of muscle contracture or rapidly advancing paralysis. To reduce the chance of illness, all dogs in an affected litter should be treated as soon as the diagnosis is made in one littermate. Older (>16 weeks) puppies and adult dogs respond better to treatment. In adult dogs with acute lower motor neuron paralysis from myositis, dysfunction is often more amenable to early treatment because scar contracture is less common. There is no known therapy to prevent a bitch from transmitting infection to her pups.

In dogs, *N. caninum* can be transmitted repeatedly through successive litters and litters of their progeny. This fact should be considered when planning the breeding of *Neospora*-infected bitches. Dogs should not be fed uncooked meat, especially beef. There is no vaccine to combat neosporosis. No drugs are known to prevent transplacental transmission. At present there is no evidence that *N. caninum* infection is zoonotic.

SUMMARY

In conclusion, much needs to be learned concerning the pathogenesis of clinical coccidiosis in dogs. Why coccidiosis occurs after shipping is unknown, and nothing is known of biologic differences among isolates of *Isospora* species of dogs and cats. Transmission of *Isospora felis* in cats in breeding colonies despite very strict hygiene remains an enigma. Prevention of transmission of *T. gondii* oocysts from cat feces to pregnant women, marine mammals, and other endangered animals is a problem. Transmission of *N. caninum* in nature is still not fully known because dogs shed only a few oocysts.

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