Cryptosporidium Infections in Cats and Dogs

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ABSTRACT:
Cryptosporidiosis was recognized as an important zoonosis in the early 1980s. Early studies assumed that all infections in mammals, including humans, were caused by the parasite *Cryptosporidium parvum*. Recent studies using molecular biologic tools and host-specificity studies indicate that cats and dogs have their own unique species of *Cryptosporidium* (C. felis and C. canis, respectively). Surveys indicate that up to 38.5% of cats and up to 44.8% of dogs are infected with *Cryptosporidium* spp. Initial studies indicate that owning a cat or dog does not increase the risk of humans acquiring cryptosporidiosis, although human infections with *C. felis* and *C. canis* have been found in patients with AIDS, immunosuppressed patients, and children from impoverished areas. Clinical signs of cryptosporidiosis in cats and dogs vary from none to chronic or intermittent diarrhea. Fluids and other supportive measures should be used in animals with diarrhea, but there is no proven safe and effective treatment of cryptosporidiosis.

Members of the genus *Cryptosporidium* are in the protozoan phylum Apicomplexa. They are coccidia-like parasites that develop in the microvillous border of epithelial cells in the digestive, respiratory, and urinary tracts of vertebrates. Recent molecular phylogenetic studies indicate that cryptosporidia are more closely related to the gregarine parasites of invertebrates than to the true coccidial parasites of vertebrates. This may explain why cryptosporidia are not sensitive to chemotherapeutic agents normally used to treat coccidial infections. In the early 1980s, *Cryptosporidium parvum* was identified as a major cause of intestinal disease in patients with AIDS, and it was later found in immunocompetent humans who had been exposed to infected dairy calves. Several groups of researchers conducted studies in which *C. parvum* was successfully transmitted from calves to young animals, including cats and dogs. Successful cross-species transmission studies with *C. parvum* led to the proposal that the organism was responsible for all infections in mammals. Most parasitologists embraced this concept, which has been taught in most veterinary schools since the 1980s. Recent studies of *Cryptosporidium* spp from cats, dogs, and humans indicate that these organisms are biologically and genetically different from *C. parvum*; thus they are now considered separate species. *Cryptosporidium felis* is primarily found in cats and *Cryptosporidium canis* in dogs; *Cryptosporidium hominis* is the newly recognized parasite in humans.

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LIFE CYCLE

Sporulated oocysts are ingested via direct contact with the feces of an infected host or contaminated food or water (Figure 1). The oocysts excyst in the digestive tract, and the sporozoites penetrate the microvilli of a variety of epithelial cells. The location of the infected host cells depends on the species of Cryptosporidium. The elongated sporozoite rounds up and becomes a trophozoite. The trophozoite becomes a multinucleated type I schizont and produces eight type I merozoites, which penetrate other microvilli and become type II schizonts. Type II schizonts repeat this developmental cycle, resulting in four type II merozoites. Recycling of asexual stages may occur. Type II merozoites penetrate microvilli and become sexual stages. The male stage (i.e., microgamont) produces nonflagellated microgametes. In the female stage (i.e., macrogamont), fertilization occurs and oocysts are produced. Two types of oocysts are produced, both of which sporulate endogenously and contain four sporozoites, an oocyst residuum, and no sporocysts. Thin-walled oocysts are autoinfective. Thick-walled oocysts are excreted in the feces.5,11,14

Cryptosporidium spp contain approximately 5,000 members, including Plasmodium (malaria), Toxoplasma, Babesia, Neospora, Sarcocystis, and Eimeria spp. Most are obligate intracellular parasites. Apicomplexans lack appendages for locomotion and instead move by a “gliding” motion. Cell entry by this group is mechanically distinct from uptake of viruses, bacteria, and other parasites. Cryptosporidium, Eimeria, and Toxoplasma spp
form oocysts that are shed in the feces of infected hosts. Cryptosporidia oocysts are very resistant to environmental damage, chlorination, and standard cleansers. This makes Cryptosporidium spp an important food- and waterborne pathogen. Extreme temperatures and prolonged contact with ammonia destroy the oocysts.

PATHOGENESIS

The mechanisms by which Cryptosporidium spp induce diarrhea, malabsorption, and wasting in humans and animals are not well understood. Cryptosporidial parasites can develop in a variety of epithelial cells in the body, not just in enterocytes in the intestines. This can lead to respiratory, ocular, pancreatic, and hepatic infections in humans; fortunately, these extraintestinal loci of cryptosporidial infection have not been reported in dogs or cats. Cryptosporidia develop in the microvillous border and displace it, eventually leading to loss of mature surface epithelium. This causes shortening and fusion of villi and lengthening of the crypts due to acceleration of cell division to compensate for loss of cells. This causes reduced uptake of fluids, electrolytes, and nutrients from the gut lumen.

The minimum infective dose of Cryptosporidium oocysts for cats and dogs is unknown. Experimental studies in humans using C. parvum oocysts collected from calves indicate that 10 or fewer oocysts can cause infection. Differences in infectivity among different C. parvum isolates in human volunteers have been documented.

CLINICAL SIGNS

Cats

Most cats that are excreting Cryptosporidium oocysts do not have clinical signs.7,17-20 Young17,18 or immunocompromised18,21 animals are more likely to be infected. Chronic or intermittent diarrhea, anorexia, and wasting are common clinical signs in symptomatic cats.21-25 Coinfection with Giardia spp or Tritrichomonas foetus may exacerbate clinical signs of cryptosporidiosis in cats.26,27 Administering prednisolone (10 mg/kg/day SC for 4 to 9 days7 or 2.8 to 3.8 mg/kg/day PO for 26 days27) may cause oocysts to reappear in feline feces.}

**Oocysts of C. felis and C. canis are structurally similar to the well-known and zoonotic C. parvum.**

Dogs

Most reported cases of cryptosporidiosis in dogs involve young animals.13,28-31 Cases in adult dogs are rare.34 Clinical signs can vary from none to chronic or intermittent diarrhea and wasting. Immunosuppression due to canine distemper may exacerbate infections in dogs.29,31 Concurrent canine parvovirus infection and intestinal Isospora spp infection may also enhance cryptosporidiosis in immunosuppressed dogs.13,32 Two recent reports used molecular methods to determine the Cryptosporidium spp in a fatal case involving an 8-week-old Yorkshire terrier from Georgia and a nonfatal case involving a 9-week-old bullmastiff from Australia, and both reports found that C. canis organisms were present.

**DIAGNOSIS**

The small size of Cryptosporidium oocysts makes them difficult to detect. Oocysts are often overlooked unless an examiner is specifically looking for them, and this is especially true if few oocysts are present in the sample. Fecal flotation techniques used routinely in veterinary laboratories are adequate to demonstrate Cryptosporidium oocysts if large numbers are present. The slide should be examined using the high-power objective. Sheather’s sugar solution is the best flotation medium.3 Because oocysts are small, they float in a plane higher than that of helminth ova and other protozoal cysts. They are light pink, and a central residual body is usually visible in Cryptosporidium oocysts in fecal flotations. C. felis oocysts are smaller9,17,35 than those of C. parvum, but morphology alone cannot be used to determine the species of Cryptosporidium in a sample.15 Many small animal technicians are not taught to recognize Cryptosporidium oocysts and may have difficulty identifying them when the tests are run only infrequently. In these cases, it is probably better for samples to be sent to diagnostic reference laboratories for testing.

Fecal samples sent to diagnostic laboratories can be tested using a number of procedures.37 More than 10 different types of staining methods have been developed for use with fecal smears to aid in detecting Cryptosporidium oocysts via standard light microscopy.37 The Ziehl-Neelsen
acid-fast staining technique is most often used and produces red-stained oocysts against a blue–green background of fecal material. Fluorescently labeled monoclonal antibodies to the oocyst stage of *C. parvum* have been made and are used in a commercial direct immunofluorescent antibody (IFA) test. Most *Cryptosporidium* spp, including *C. felis* and *C. canis*, cross-react in commercial IFA-based diagnostic tests developed to detect *C. parvum*. Cross-reactivity also occurs in many ELISAs for *C. parvum*. Polymerase chain reaction (PCR) can detect *Cryptosporidium* spp in fecal samples, and PCR is more sensitive than IFA testing. Most PCR-based tests indicate only the presence of *Cryptosporidium* spp, but a recently developed set of PCR tests can differentiate between *C. felis, C. canis, C. parvum,* and *C. hominis.*

### Table 1. Transmission Studies with *C. felis* and *C. canis* Oocysts

<table>
<thead>
<tr>
<th>Source</th>
<th>Recipient</th>
<th>Results</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat</td>
<td>Guinea pigs</td>
<td>Negative</td>
<td>Iseki(^5), Arai et al(^17)</td>
</tr>
<tr>
<td>Cat</td>
<td>Mice</td>
<td>Negative</td>
<td>Iseki(^5), Arai et al(^17)</td>
</tr>
<tr>
<td>Cat</td>
<td>Newborn mice</td>
<td>Negative</td>
<td>Mtambo et al(^8), Arai et al(^17)</td>
</tr>
<tr>
<td>Cat</td>
<td>Lambs</td>
<td>Positive</td>
<td>Mtambo et al(^8)</td>
</tr>
<tr>
<td>Cat</td>
<td>Immunosuppressed mice</td>
<td>Negative</td>
<td>Mtambo et al(^8)</td>
</tr>
<tr>
<td>Cat</td>
<td>Rats</td>
<td>Negative</td>
<td>Arai et al(^17)</td>
</tr>
<tr>
<td>Cat</td>
<td>Dogs</td>
<td>Negative</td>
<td>Arai et al(^17)</td>
</tr>
<tr>
<td>Dog</td>
<td>Newborn mice</td>
<td>Negative</td>
<td>Fayer et al(^11)</td>
</tr>
<tr>
<td>Dog</td>
<td>Immunosuppressed mice</td>
<td>Negative</td>
<td>Fayer et al(^11)</td>
</tr>
<tr>
<td>Dog</td>
<td>Calves</td>
<td>Positive</td>
<td>Fayer et al(^11)</td>
</tr>
</tbody>
</table>

### Table 2. Prevalence of *Cryptosporidium* spp in Cats

<table>
<thead>
<tr>
<th>Number Examined</th>
<th>Location</th>
<th>Test</th>
<th>Prevalence (%)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>600</td>
<td>United States</td>
<td>Serology</td>
<td>8.3</td>
<td>McReynolds et al(^50)</td>
</tr>
<tr>
<td>418</td>
<td>Australia</td>
<td>Fecal</td>
<td>0</td>
<td>McGlade et al(^52)</td>
</tr>
<tr>
<td>40</td>
<td>Australia</td>
<td>PCR</td>
<td>10</td>
<td>McGlade et al(^52)</td>
</tr>
<tr>
<td>102</td>
<td>Australia</td>
<td>Fecal</td>
<td>1.2</td>
<td>Sargent et al(^9)</td>
</tr>
<tr>
<td>10</td>
<td>France</td>
<td>Fecal</td>
<td>0</td>
<td>Chermette and Blondel(^13)</td>
</tr>
<tr>
<td>300</td>
<td>Germany</td>
<td>Fecal</td>
<td>1.3</td>
<td>Augustin-Bich(^51)</td>
</tr>
<tr>
<td>13</td>
<td>Japan</td>
<td>Fecal</td>
<td>38.5</td>
<td>Iseki(^5)</td>
</tr>
<tr>
<td>507</td>
<td>Japan</td>
<td>Fecal</td>
<td>20</td>
<td>Uga et al(^54)</td>
</tr>
<tr>
<td>608</td>
<td>Japan</td>
<td>Fecal</td>
<td>3.8</td>
<td>Arai et al(^17)</td>
</tr>
<tr>
<td>57</td>
<td>Scotland</td>
<td>Fecal</td>
<td>12.3</td>
<td>Nash et al(^19)</td>
</tr>
<tr>
<td>235</td>
<td>Scotland</td>
<td>Fecal</td>
<td>8.1</td>
<td>Mtambo et al(^18)</td>
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<td>205</td>
<td>Colorado</td>
<td>Fecal</td>
<td>5.4</td>
<td>Hill et al(^31)</td>
</tr>
<tr>
<td>263</td>
<td>New York</td>
<td>Fecal</td>
<td>3.8</td>
<td>Spain et al(^30)</td>
</tr>
</tbody>
</table>
TREATMENT

Chemotherapy for Cryptosporidium infections in animals and humans has been actively investigated over the past two decades (see box on page 871). Over 100 compounds have been tested in laboratory animal models, but none is highly effective clinically.\(^43\) Paromomycin\(^44\) and nitazoxanide (NTZ)\(^27\) are compounds that have shown some efficacy in animal models and have also been used to treat intestinal cryptosporidiosis in cats. Treatment with paromomycin (165 mg/kg PO bid for 5 days) resulted in resolution of diarrhea and disappearance of oocysts from the feces of a 6-month-old cat with persistent diarrhea.\(^44\) Paromomycin is potentially nephrotoxic, and acute renal failure was reported in four cats that received paromomycin for cryptosporidiosis or trichomoniasis.\(^45\) Treatment using NTZ (25 mg/kg PO bid for 28 days) eliminated Cryptosporidium oocysts from the feces of naturally infected laboratory cats. Use of NTZ was associated with vomiting and the presence of dark brown–black, foul-smelling diarrhea while treating these cats.\(^27\) Chlorpromazine (0.5 to 1.5 mg SC once daily) was given to alleviate vomiting in NTZ-treated cats.\(^27\) Fenbendazole administered at 50 mg/kg PO for 5 days did not affect Cryptosporidium oocyst excretion in cats.\(^26\)

Treatment of an 18-month-old cat with inflammatory bowel disease and Cryptosporidium infection was successful using a course of clindamycin (25 mg/kg/day [three-fourths of the total dose was administered in the morning and one-fourth of the total dose at night] PO for 60 days) and then tylosin (11 mg/kg PO bid with food for 28 days).\(^35\) Interpretation of these results was hampered because of the presence of Clostridium perfringens in the cat’s intestinal tract. Clindamycin administered at 15 mg/kg PO q8h for 6 days did not eliminate Cryptosporidium oocysts from a 5-year-old pointer.\(^34\)

STUDIES ON HOST SPECIFICITY OF C. FELIS AND C. CANIS

Transmission studies with C. felis and C. canis indicate that these species are relatively host-specific (Table 1). However, additional well-controlled PCR-based and PCR species–validated transmission studies need to be conducted before these earlier observations can be completely accepted. C. felis was not infectious in dogs or laboratory rodents in a limited number of studies. It is infectious in lambs\(^8\) and has been found in a naturally infected cow.\(^35\) C. canis is not infectious in laboratory rodents but is mildly infectious in calves.\(^11\) The infectivity of C. canis oocysts in cats has not been examined. C. parvum oocysts are moderately infectious in cats and dogs.\(^3,11\) Molecularly confirmed natural cases of C. parvum or C. hominis have not been reported in cats or dogs.

Several studies have suggested that humans have been infected with Cryptosporidium spp from kittens or cats.\(^36–40\) None of these studies conducted genotyping or other studies, and they should be viewed as only circumstantially incriminating cats in the transmission of Cryptosporidium spp to humans.

One study indicated that a veterinary student caring for an adult dog with cryptosporidiosis developed cryptosporidiosis.\(^34\) The parasite in the dog or the veterinary student was not genotyped or further characterized.

<table>
<thead>
<tr>
<th>Table 3. Prevalence of Cryptosporidium spp in Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Examined</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>421</td>
</tr>
<tr>
<td>493</td>
</tr>
<tr>
<td>195</td>
</tr>
<tr>
<td>25</td>
</tr>
<tr>
<td>57</td>
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<td>29</td>
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<td>200</td>
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<tr>
<td>213</td>
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<tr>
<td>140</td>
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<tr>
<td>257</td>
</tr>
<tr>
<td>81</td>
</tr>
<tr>
<td>101</td>
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<tr>
<td>100</td>
</tr>
<tr>
<td>200</td>
</tr>
<tr>
<td>130</td>
</tr>
<tr>
<td>49</td>
</tr>
<tr>
<td>100</td>
</tr>
</tbody>
</table>
One study in patients with AIDS addressed the issue of pet-to-human transmission of Cryptosporidium infection. The study found that patients with AIDS who owned cats or dogs were not at significantly higher risk of acquiring cryptosporidiosis than were patients with AIDS who did not own pets. Further critically controlled studies are needed to determine the importance of cats and dogs as sources of Cryptosporidium infection in humans.

**PREVALENCE IN CATS**

Fecal-, PCR-, and serologic-based surveys indicate that up to 38.5% of cats examined have been exposed to or are excreting Cryptosporidium oocysts (Table 2). One hundred litters of kittens from Germany were examined for Cryptosporidium infection, which was found in 4.3% of 70 litters that were kept outdoors and 3.3% of 30 litters kept indoors. One serologic study not listed in Table 1 indicated that 192 (74%) of 258 cats tested positive for IgG antibody via IFA testing. The results are questionable: Interpretation of the IFA tests may have been flawed because positive apical fluorescence was considered an indicator of a true positive reaction. Apical fluorescence is generally considered nonspecific for coccidial parasites. Prevalence studies conducted to date with cats have not used molecular methods to determine the actual species of Cryptosporidium found in cats. Therefore, the real prevalence of C. felis versus C. parvum or other Cryptosporidium spp in cats is unknown. This information is important because C. felis has a more narrow host range than C. parvum.

**PREVALENCE IN DOGS**

Fecal-, PCR-, and serologic-based surveys indicate that up to 44.8% of dogs examined have been exposed to or are excreting Cryptosporidium oocysts. One hundred litters of kittens from Germany were examined for Cryptosporidium infection, which was found in 4.3% of 70 litters that were kept outdoors and 3.3% of 30 litters kept indoors. One serologic study not listed in Table 1 indicated that 192 (74%) of 258 cats tested positive for IgG antibody via IFA testing. The results are questionable: Interpretation of the IFA tests may have been flawed because positive apical fluorescence was considered an indicator of a true positive reaction. Apical fluorescence is generally considered nonspecific for coccidial parasites. Prevalence studies conducted to date with cats have not used molecular methods to determine the actual species of Cryptosporidium found in cats. Therefore, the real prevalence of C. felis versus C. parvum or other Cryptosporidium spp in cats is unknown. This information is important because C. felis has a more narrow host range than C. parvum.

**PREVALENCE OF C. FELIS AND C. CANIS IN HUMANS**

Most studies on the prevalence of C. felis and C. canis in humans have been conducted in HIV-infected hu-
mums,72–76 children,77 or humans with cryptosporidiosis and some underlying immunosuppressive conditions78–87 (Table 4). The prevalence of *C. felis* and *C. canis* in humans is less than that of *C. hominis* and *C. parvum*. Some studies have not found *C. felis* or *C. canis* in humans.

**PREVALENCE OF CRYPTOSPORIDIUM SPECIES IN THE ENVIRONMENT**

*Cryptosporidium* oocysts are common in the environment and have been found in surveys of nondrinking surface and waste waters.88–91 However, genotyping *Cryptosporidium* isolates from nondrinking water sources indicates little contamination by *C. felis* or *C. canis*.90 One study documented *C. felis* or *C. canis* oocysts in raw waste water but found none in raw surface water.90 Although major outbreaks of human cryptosporidiosis have been linked to contaminated drinking water92–95 molecular studies indicate that *C. hominis*96–98 and *C. parvum*96,98 have been responsible for drinking water–associated outbreaks of human cryptosporidiosis. No reports indicate that *C. felis* or *C. canis* has been associated with waterborne outbreaks of human disease.

**CONCLUSION**

Despite extensive experimental and epidemiologic literature on *Cryptosporidium* spp, the primary species infecting dogs and cats, *C. canis* and *C. felis*, respectively, have been identified only recently, and there is little experimental work documenting their pathogenicity or zoonotic potential. The contribution of canine and feline *Cryptosporidium* spp to clinical disease in pets does not seem to be great at this time but may be underestimated because so few cats and dogs are tested for infection. In contrast, the risk of zoonotic infection has received considerably more attention. Many practicing veterinarians are unaware that, to minimize exposure to *Cryptosporidium* spp, current guidelines from the US Public Health Service and Infectious Diseases Society of America recommend that HIV-infected humans should not take into their homes stray dogs or cats, animals with diarrhea, or dogs and cats younger than 6 months of age.99 They further recommend that if a dog or cat younger than 6 months of age is acquired by an HIV-infected person, the animal should be tested for *Cryptosporidium* spp. These recommendations, dating from 1999, may be more stringent than necessary, but further molecular analysis of human and animal infections is needed to realistically assess potential transmission from pets to humans. Until more is known, practitioners should recognize that *Cryptosporidium* infection in dogs and cats is not uncommon in North America and that zoonotic transmission from pets could cause serious disease in immunocompromised humans.

**REFERENCES**

2. Carreno RA, Martin DS, Barta JR: *Cryptosporidium* is more closely related to the gregarines than to coccidia as shown by phylogenetic analysis of apicom-
plexan parasites inferred using small-subunit ribosomal RNA gene sequences. 


49. Glaser CA, Safin S, Reingold A, Newman TB: Association between Crypt-
Cryptosporidiosis infections in cats and dogs


1. Which *Cryptosporidium* spp was, until recently, believed to be responsible for all cases of cryptosporidiosis in humans and other mammals?
   a. *C. hominis*
   b. *C. felis*
   c. *C. canis*
   d. *C. parvum*

2. Waterborne outbreaks of cryptosporidiosis have been associated with
   a. *C. parvum* and *C. hominis*.
   b. *C. felis* and *C. parvum*.
   c. *C. felis* and *C. canis*.
   d. *C. felis* and *C. hominis*.

3. Paromomycin therapy for cryptosporidiosis in cats has been associated with
   a. vomiting.
   b. diarrhea.
   c. kidney failure.
   d. liver failure.

4. NTZ therapy for cryptosporidiosis in cats has been associated with
   a. vomiting.
   b. pneumonia.
   c. kidney failure.
   d. liver failure.

5. What is the best fecal flotation medium for finding *Cryptosporidium* oocysts?
   a. zinc sulfate solution
   b. Sheather’s sugar solution
   c. saturated salt solution
   d. sugar–salt solution

6. Because *Cryptosporidium* oocysts are small, they
   a. float in a plane higher than that of helminth ova and other protozoal cysts.
   b. can be seen only by using oil immersion.
   c. look like *Isospora* spp.
   d. look like *Giardia* cysts.

7. Administering ________ may cause oocysts to reappear in cat feces.
   a. NTZ
   b. paromomycin
   c. clindamycin
   d. prednisolone

8. Developmental stages of *Cryptosporidium* spp can be found in a host cell’s
   a. nucleus.
   b. microvilli.
   c. cytoplasm.
   d. neurons.

9. Immunofluorescent detection tests for *Cryptosporidium* oocysts
   a. are not reliable.
   b. cross-react with most *Cryptosporidium* spp.
   c. are highly specific for *C. canis* but not *C. felis*.
   d. are highly specific for *C. hominis* but not *C. felis*.

10. Lesions and subsequent clinical signs of cryptosporidiosis are associated with
    a. reduced uptake of fluids, electrolytes, and nutrients from the gut lumen.
    b. hemorrhagic diarrhea due to invasive stages.
    c. excretory diarrhea due to parasite toxins.
    d. fatty diarrhea due to infection of the upper small intestine.