FELINE CLINICAL PARASITOLOGY

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Dwight D. Bowman, MS, PhD, is an Associate Professor of Parasitology in the Department of Microbiology and Immunology at the College of Veterinary Medicine, Cornell University, Ithaca, New York.

Charles M. Hendrix, DVM, is a Professor of Parasitology in the Department of Pathobiology at the College of Veterinary Medicine, Auburn University, Auburn, Alabama.

David S. Lindsay, PhD, is an Associate Professor in the Department of Biomedical Sciences and Pathobiology at the Center for Molecular Medicine and Infectious Diseases, Virginia-Maryland Regional College of Veterinary Medicine, Virginia Tech, Blacksburg, Virginia.

Stephen C. Barr, BVSc MVS, PhD, is a Diplomate of the American College of Veterinary Internal Medicine and an Associate Professor of Medicine in the Department of Clinical Sciences at the College of Veterinary Medicine, Cornell University, Ithaca, New York.

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PREFACE

In 1998 the number of cats in the United States was estimated to be approximately 70.9 million; cats were found in 34 percent of the 100 million U.S. households. This figure now surpasses the number of dogs in the United States, approximately 57.6 million in 38.1 percent of households (www.petfoodinstitute.org, Pet Food Institute, Washington, D.C.). For 1985 in Canada, the number of cats was approximately 4,134,200 and also surpassed the number of dogs, 3,028,100. Nearly 23 percent of households in the United Kingdom have at least one cat, and in Australia about 35 percent of the households each have one cat or more. This love for the cat, however, is not restricted to predominantly English-speaking countries. Between 1980 and 1990, the cat populations of almost all European nations increased—in some cases dramatically—to the extent that cat populations are currently level with those of the dog. Among Europeans, the Swiss are dedicated cat lovers, preferring to own cats rather than dogs. The French and the Belgians are well-known for their love of both cats and dogs. Among nations surveyed regarding the presence of cats in households, the Japanese have the least number, with a little over 5 percent with cats in 1990. However, there are more and more households with cats all the time in Southeast Asia, especially in countries such as Taiwan and Malaysia. Regardless of national boundary, with the ever-increasing limitations of time, money, and space, the cat is rapidly becoming the cosmopolitan pet of the twenty-first century.

Awareness of cats as something other than "small dogs" has also emerged among cat owners and veterinarians as is evidenced by the increasing number of established specialized feline veterinary practices in the United States and Europe. For 1999, the number of members in the American Association of Feline Practitioners and the Academy of Medicine was 1,550, of which 33.5 percent (520) dealt exclusively with cats (Kristi Kruse Thomson, American Association of Feline Practitioners, Nashville, Tennessee). One way in which cats differ from dogs is in their parasitic infections and infestations. Although dogs and cats do share a few parasites, the vast majority of the parasites of these pets are actually specific to either dogs or cats, not to both. Also, even those parasites that are shared between cats and dogs will often cause different host responses when parasitizing the cat and often require different treatment regimens.

The purpose of this book is to offer an in-depth examination of feline parasites. Topics discussed include parasite identification, history, geographic distribution, pathogenesis, epizootiology, zoonosis if applicable, diagnosis, treatment, control, and prevention. The authors have attempted to produce a book that is international in scope due to the immense worldwide popularity of cats and due to the

amount of travel undertaken by cats and their owners. Also, it was felt that this text would prove useful to veterinarians in other countries.

It is hoped that this book will be useful to both the veterinarian and the veterinary parasitologist. It includes concise and in-depth knowledge that is useful to both groups. Overall, the ultimate goal of this book is to improve the health of cats around the world by providing a ready reference text that can be used to assist (1) in diagnosing parasitic infections or infestations and (2) in treating cats and kittens that host these parasites.

The parasites of the cats fall into four major groups: the common cosmopolitan parasites, the parasites that are important in only certain geographic areas, those that are rare and show up in rather large numbers in certain countries or certain foci, and those that tend to be rare or incidental findings where cats are serving as atypical hosts of some adult form that is usually found in the local wildlife. We have tried to include all these parasites in the text with the hope that it would help practitioners develop a better understanding of the scope of parasites around the world. Thus, there are a lot of species in the text that have appeared only once in cats or only in very limited geographical areas. Also, we are aware that we are also dealing with a number of parasites with which we do not actually have first-hand knowledge. We do believe, however, that the book will serve to stimulate individuals to consider the parasites of cats in more detail so that new information and corrections can be added to future editions.

There are many individuals that need to be thanked in the production of this text. Dr. J. Ralph Lichtenfels and Patricia A. Pilitt at the U.S. National Parasite Collection, U.S. Department of Agriculture, Agricultural Research Service, Biosystematics and National Parasite Collection Unit, require special thanks for their assistance in making the specimens of myriad trematodes from cats available for photography. There have been many individuals that have helped in the collection of the numerous references that were used to produce the text, with special thanks going to Dr. Megan Williams. Michael Porch assisted with many of the photographs of trematodes. Elizabeth A. Fogarty is thanked for her able assistance with all aspects of the book's final assembly, help with the generation of the final digitized images, and the production of the maps detailing geographic distribution. Vanessa Nicolle Bowman was a great help when the format for all the maps had to be changed for the final generation of the text. The line drawings of the life cycle of the cat flea and the life cycle of *Cuterebra* were generated by Dr. Laurie Duffield. The book has been a long time coming, and thanks go out to the original editor, Caroll C. Cann, who has since retired. The editor who helped with the actual rendition of the book that has gone to press is Lynne Bishop, and without her help this text may never have been completed. Colleagues who have been especially helpful in the generation of the text include Dr. de Lahunta, who has kept us honest relative to the neurology sections of the text, Dr. Robert Foley, who has always been helpful with practical information relative to mite infestations in cats, and Dr. William Hornbuckle for his assistance with day-to-day answers to questions.

FELINE CLINICAL PARASITOLOGY

1 THE PROTOZOA

Protozoan parasites of animals are typically single-celled organisms. Protozoa differ from bacteria in that the protozoan cell contains a discrete nucleus with a nuclear membrane. Also, undulipodia (flagella), when present on the protozoan cell, have a structure that is distinct from the flagellum of bacteria but not unlike that of the cilium of mammals and other animals. The protozoa differ from fungi in that fungal cells do not have undulipodia and typically are binucleate organisms. Protozoa differ from plants and animals by the fact that both plants and animals develop from an embryo, a developmental stage lacking from all protozoan forms.

Although the protozoal kingdom contains somewhere around 35 phyla and myriad species of organisms (Margulis et al., 1990), only 4 phyla are implicated as pathogens of the cat. Protozoa within these phyla differ markedly in their biology, which is an indication of their widely divergent relationships. Certain aspects of the biology of protozoa, the ability to form resistant stages, utilization of vectors, and genetic exchange of material through sexual union, are important in a general understanding of these parasites because they are directly related to the transmission of these pathogens between feline hosts.

Protozoan parasites are typically transmitted between cats in one of four different ways (Table 1.1). First, direct contact is the means of transmission used by *Trichomonas felistomae,* a parasite of the mouth of the cat. In this form of transmission, the stage of the parasite is not resistant to environmental extremes and will die rapidly if deposited by the cat in drinking water or on skin by licking. Second, exposure to resistant stages in the environment is the means by which cats are infected with *Giardia felis, Cryptosporidium felis, Isospora* species, and on some occasions *Toxoplasma gondii.* These parasites all have a resistant stage that is protected by a thick protective wall, and once these stages enter a favorable environment, they are capable of persisting for months to years. A third means of transmission is via the ingestion of other hosts containing resistant stages; this type of transmission occurs with *Sarcocystis* species, *Hammondia hammondi, Toxoplasma gondii,* and occasionally with species of *Isospora.* In this case, the host eaten by the cat has become infected by the ingestion of a resistant stage shed into the environment in the cat's feces; with the notable exception being that there can be vertical transmission in the nonfeline host in the case of toxoplasmosis. The host protects the protozoan from environmental extremes, and the parasite is capable of persisting within the host for months to years. Fourth, there is transmission by a blood-feeding arthropod vector, which is the means by which cats typically become infected with *Leishmania* species, species of *Trypanosoma,* and the apicomplexan genera *Cytauxzoon* and *Babesia.* For the most part, the arthropod is required to increase the quantity of infectious agents ingested when the arthropod bites to a quantity sufficient for the infection of the next host. The arthropod also serves to protect the parasite from environmental extremes as it moves from host to host. Other, less frequent forms of transmission of protozoa between cats do occur, but in general, these four modes of transmission are the most typical.

Some protozoan parasites of the cat are rare or only occasionally seen, while others are very common (Table 1.2). Factors that affect the prevalence of these parasites include such things as the geographic range of the parasite or its vector, local conditions of housing or environment, and age of the cats being surveyed. For instance, *Trypanosoma cruzi* is restricted to the Americas, mainly south of Mexico. The reason for the restriction of this parasite is in part due to vectors,

TABLE 1.1—Transmission of the protozoan parasites of the cat

Phylum of parasite genus	Resistant stage	Intermediate host	Paratenic host	Vector
APICOMPLEXA				
Cryptosporidium	Oocyst	–	–	–
Isospora	Oocyst	–	Sometimes	–
Besnoitia	Oocyst	+	–	–
Hammondia	Oocyst	+	–	–
Sarcocystis	Sporocyst	+	–	–
Toxoplasma	Oocyst	–	Sometimes	–
Hepatozoon	–	–	–	Tick[1]
Cytauxzoon	–	–	–	Tick
Babesia	–	–	–	Tick
SARCOMASTIGOPHORA				
Trichomonas	–	–	–	–
Giardia	Cyst	–	–	–
Trypanosoma (Old World)	–	–	–	Fly
Trypanosoma (New World)	–	–	–	Bug
Leishmania	–	–	–	Sandfly
RHIZOPODA				
Entamoeba	Cyst	–	–	–
MICROSPORA				
Encephalitozoon	Spore	–	–	–

1. In the case of *Hepatozoon canis,* the cat is infected by eating the tick rather than by the bite of the tick.

TABLE 1.2—General prevalence and geographical distribution of the protozoan parasites of the cat

Phylum of parasite genus	General prevalence	Geographic distribution
APICOMPLEXA		
Cryptosporidium	Uncommon	Global
Isospora	Very common	Global
Besnoitia	Uncommon	Global
Hammondia	Uncommon	Global
Sarcocystis	Uncommon	Global
Toxoplasma	Very common	Global
Hepatozoon	Uncommon	Africa and Asia
Cytauxzoon	Rare	Southeast United States
Babesia	Uncommon	South Africa and Asia
SARCOMASTIGOPHORA		
Trichomonas	Common	Global
Giardia	Common	Global
Trypanosoma (Old World)	Uncommon	Africa and Asia
Trypanosoma (New World)	Sporadic	Americas
Leishmania (Old World)	Sporadic	Africa and Asia
Leishmania (New World)	Sporadic	Americas
RHIZOPODA		
Entamoeba	Potential	Tropics
MICROSPORA		
Encephalitozoon	Rare	Global

triatomid bugs, that are adapted to human dwellings in that part of the world; typically these bugs are found mainly in the wild. Local conditions can have a great effect on the prevalence of parasites in a cat population. If the cats are hunters and spend a good deal of time outdoors, they will develop parasite infections different from those of the indoor cat (e.g., the indoor cat would be free from tick bites under most circumstances). If one looks at kittens, the prevalence of protozoan parasites in this population is much different than in adult cats. Kittens are more

likely to be shedding large number of oocysts than adult cats. Of course, the truly rare parasites are probably rare because they are not typically parasites of the domestic cat.

The stages involved with the transmission of protozoan parasites are often, but not always, the same as those involved with diagnosis (Table 1.1). In those cases where the resistant stage is shed in the cat's feces, it can often be recovered using routine methodologies of flotation. However, in cases with severe diarrhea and rapid intestinal motility, the resistant stages may not form, making diagnosis more difficult. In the case of *Giardia felis,* it becomes necessary to examine the feces in a manner that will allow the diagnosis of trophozoite stages. This would also be the case in a cat with amebic dysentery and perhaps in one with severe coccidiosis. The protozoan parasites of the cat that produce stages that are found in blood or tissue samples are typically those transmitted by biting arthropods. However, it would not be uncommon for the number of circulating organisms to be at such low levels that they may not be diagnosed by a routine blood smear or biopsy specimen. Thus, other forms of diagnosis might be required.

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COCCIDIA: THE PHYLUM APICOMPLEXA

All members of the phylum Apicomplexa are obligatory parasites. The phylum contains the coccidial parasites and important blood parasites of cats. Two of the parasites, *Toxoplasma gondii* and *Cryptosporidium parvum,* are of public health importance because they are zoonotic agents. The phylum obtains its name from the assemblage of organelles that are present in the anterior end of invasive stages and collectively form the apical complex (Current et al., 1990). The apical complex is involved in the entrance of parasites in to host cells. Cats are definitive hosts for several apicomplexan parasites including the genera *Isospora, Toxoplasma, Hammondia, Besnoitia, Sarcocystis, Cryptosporidium, Babesia,* and *Cytauxzoon* (*Theileria* syn.). *Isospora* and *Cryptosporidium* are coccidial parasites that can be associated with diarrhea. *Toxoplasma, Hammondia, Besnoitia,* and *Sarcocystis* are coccidial parasites that have a two-host life cycle and use cats as definitive hosts. Intestinal infections in cats with these species are usually asymptomatic. *Babesia* and *Cytauxzoon* species are tick-transmitted blood parasites that can cause anemia and death.

Cryptosporidium felis Iseki, 1979

Etymology

Crypto (hidden) + *sporidium* (related to the spore-like oocyst stage) and *felis* for cat.

Synonyms

None.

History

This species was described by Iseki in 1979, but it has taken some time for the separate designation of the species in the cat to be generally accepted. At this time, it is considered by many that this is a valid species of *Cryptosporidium.*

Geographic Distribution

Fig. 1.1.

It is believed that this species is worldwide in distribution. There have been reports specifically identifying this species taken from cats in Japan (Iseki, 1979) and Australia (Morgan et al., 1998; Sargent et al., 1998). It has also been found in a calf in Poland (Bornay-Llinares et al., 1999).

Location in Host

Mucosal cells of the small intestine. The stages are found throughout the small intestine, but the schizont and oocysts are more common in the posterior third of the intestine. The parasites tend to be found mainly at the tips of the intestinal villi and are never found in the crypts.

Parasite Identification

The oocysts of *Cryptosporidium felis* differ from those of *Cryptosporidium parvum* in that they are smaller. The oocysts of *Cryptosporidium felis* measure 4.3 μm in diameter (3.5 to 5 μm). Those of *Cryptosporidium parvum* tend to have a mean diameter of 5 μm.

Life Cycle

Cats are infected by the ingestion of an oocyst. Each oocyst contains four sporozoites. Upon stimulation by various aspects of the digestive system of the new host, the sporozoites excyst from the oocyst and penetrate cells of the mucosa. The sporozoites, like other coccidians, induce phagocytosis; however, unlike with other coccidians, the small sporozoites appear to remain on the surface of the cell; that is, the cell membrane bulges out around the small parasite. Between the host cell and the vacuole containing the parasite develops a highly convoluted membrane-like structure that is called the "feeding organelle" or "apical organelle." Within the vacuole, the parasite undergoes schizogony to produce eight daughter merozoites. These then go on to infect other cells. The next phase of the infection is the development of sexual stages, macrogametocytes and microgametocytes. The microgametes are aflagellar but are capable of movement, and they will fuse with a macrogamete. After fusion, the macrogamete deposits an oocyst wall to become an oocyst. While still within the host, the oocyst undergoes a process of sporulation to produce oocysts that contain four infective sporozoites. Iseki (1979) described that these sporozoites were sometimes seen to be undergoing spontaneous excystation within the intestinal material he examined, and he felt that autoinfection was a distinct possibility. In experimentally infected cats, the prepatent period was 5 to 6 days, and the patent period was 7 to 10 days.

Clinical Presentation and Pathogenesis

Cryptosporidium felis has not been reported to cause disease experimentally in cats, but it is very unclear as to whether cats are routinely infected with this species or with isolates of *Cryptosporidium parvum* (See the next section on cryptosporidiosis in cats.)

Asahi et al. (1991) showed that experimentally infected cats shed oocysts for an extended period, up to 3 to 5 months. They held three of these cats for a year and then initiated prednisolone inoculations. After about a week of prednisolone treatment, these cats again shed large numbers of oocysts in their feces. None of the cats developed significant diarrhea or weight loss during the infections even though they shed large numbers of oocysts.

Treatment

Cases known to be caused by *Cryptosporidium felis* have not been treated, and there have been no attempts to treat cats experimentally infected with this species.

Epizootiology

The stage shed in the feces of cats is infective when passed in the feces. Thus, cats that are infected put other animals and their handlers at risk of infection. The fact that there have been numerous cases of zoonotic infections of *Cryptosporidium parvum* amongst veterinary students who are working with neonatal calves or foals would indicate that it is highly likely that the oocysts can be spread to people who believe they are taking proper precautions.

Hazards to Other Animals

Initially, it was felt that *Cryptosporidium felis* was fairly well restricted to the cat. Iseki (1979) tried to infect mice (three) and guinea pigs (three) with this parasite and was unsuccessful. Asahi et al. (1991) gave oocysts recovered from cats to mice, hydrocortisone-treated mice, suckling mice, guinea pigs, and dogs; none of these animals developed infection. Similarly, Mtambo et al. (1996) were unable to infect suckling mice with oocysts isolated from a cat in Scotland. Recently, however, a calf in Poland was identified

that had small oocysts in its feces that were identified via molecular typing to be *Cryptosporidium felis* (Bornay-Llinares et al., 1999).

Hazards to Humans

It is unclear what the role is between *Cryptosporidium felis* and human infections. There is a report that molecular sequencing identified oocysts with the *Cryptosporidium felis* genotype in the feces of HIV-infected patients (Pieniazek et al., 1999). This would indicate that cats infected with *Cryptosporidium felis* might pose a threat to humans, perhaps only immunocompromised humans.

Control/Prevention

The oocyst is infective when passed, but it is killed by heating to over 60°C. Thus, good hygiene, the routine washing of cages, and the washing of bedding in a regular washer and drier (or drying on a line on a good sunny day) will probably destroy oocysts.

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Feline Cryptosporidiosis

No matter what species is involved, *Cryptosporidium felis* or *Cryptosporidium parvum,* cats do present with severe disease due to infection with this pathogen. A typical presentation of a cat with disease is one that has an underlying immunosuppressive disorder such as a feline leukemia virus infection (Monticello et al., 1987). However, there are cases where cats develop severe disease and persistent cryptosporidiosis where there is no apparent underlying condition (Lappin et al., 1997). Also, the recent development of serological tests that detect antibody in the blood of cats that have been infected would suggest that somewhere around 15 percent of cats throughout the United States have been or are currently infected with *Cryptosporidium* (Lappin et al., 1997; McReynolds et al., 1999).

The cat that presents with cryptosporidiosis will be having recurring bouts of diarrhea. The disease caused by *Cryptosporidium* infection is a water-losing diarrhea caused by the development of the parasites within the epithelial cells of the mucosa. Histologically, infection causes a blunting of the intestinal villus and crypt hyperplasia that is accompanied by an intense neutrophilic response (Tzipori et al., 1983). In AIDS patients with cryptosporidiosis, it has been found that net water, sodium, and chloride movement was the same as that in healthy controls (Kelly et al., 1996). From this work, these authors concluded that the diarrhea may be due to the secretion of electrolytes and water efflux distally to the site of infection or due to some yet undefined feature of the infection. Using monolayers of polarized colonic epithelial cells and the experimental infection of these cells with *Cryptosporidium parvum,* it has been shown that there is an increased macromolecular permeability of the monolayer, and it was felt that disruption of the epithelial cell barrier plays a role in the observed diarrhea (Adams et al., 1994). Additional work using the cell monolayer system has shown rather conclusively that the infection of the epithelial cells will ultimately result in significant changes in the host cell permeability and the permeability of the entire monolayer (Griffiths et al., 1994). Also, the infection will result in the death of the infected cells.

Treatment of cats that are undergoing infection is as difficult as treatment is in humans. The basic therapy is the relief of symptoms and increased fluids. Paromomycin has been used to treat cats with some success (Barr et al., 1994), but this therapy is not without potential complications that can include renal failure (Gookin et al., 1999).

Cats have on occasion been experimentally infected with what is thought to be *Cryptosporidium parvum* isolated from calves (Current et al., 1983; Pavlasek, 1983), but cats seem rather refractory to such infections. In a trial we performed at Cornell where two virus-free kittens were each fed 10 million oocysts, only a very few oocysts were shed in the feces of these cats, and they never developed signs of infection. Dogs have until very recently been considered to be infected with the same species, *Cryptosporidium parvum,* that occurs in calves and humans. Dogs can be experimentally infected with oocysts from calves, but the number of oocysts shed by these dogs appears to remain relatively low (Lloyd and Smith, 1997). Also, recent evidence tends to indicate that dogs may have their own phenotype as determined by DNA-sequencing methods (Pieniazek et al., 1999).

The potential transmission of *Cryptosporidium* between cats and people is currently fairly undefined. There have been reports linking feline cryptosporidiosis to human infection (Egger et al., 1990; Pieniazek et al., 1999). At the same time it would seem that many of the human isolates are neither from cats nor cattle; rather the infections are acquired from other humans. There have also been studies that have shown that pet ownership is not a risk factor for HIV-infected individuals (Glaser et al., 1998).

Fig.1.2. *Cryptosporidium parvum*

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Isospora felis Wenyon, 1923

Etymology

Isospora (*Iso* equal; *spora* spore) and *felis* for cat.

Synonyms

Diplospora bigemina of Wasielewski (1904) in part; *Isospora bigemina* of Swellengrebel (1914); *Isospora rivolta* Dobell and O'Connor, 1921; *Isospora cati* Marotel, 1921; *Lucetina felis* (Wenyon, 1923) Henry and Leblois, 1926; *Isospora felis* var. *servalis* Mackinnon and Dibb, 1938; *Levinea felis* (Wenyon, 19. 1-23) Dubey, 1977; *Cystoisospora felis* (Wenyon, 1923) Frenkel, 1977.

History

The earliest report of coccidia in cats was probably given by Finck in 1854 (Wenyon, 1923; Shah, 1970a), who described stages in the villi of cats as *corpuscles gemines.* Wenyon (1923) indicated that these stages were in the lamina propria and not in the enterocytes as were *Isospora felis* and *Isospora rivolta.* The subepithelial location would indicate that these parasites were a *Sarcocystis* spp. The oocysts of *Isospora felis* (large size) and *Isospora rivolta* (medium size) found in cats closely resemble the oocysts of *Isospora canis* (large size) and *Isospora ohioensis*-like (medium size) organisms observed in the feces of dogs (Lindsay and Blagburn, 1991). During the first half of this century dogs and cats were thought to share the same species of coccidia. Nesmeséri (1960) demonstrated that *Isospora felis* from cats was not transmissible to dogs and named the canine parasite *Isospora canis.* Shah (1970a) later confirmed these findings. Several researchers were unable to produce patent infections in dogs with *Isospora rivolta* oocysts isolated from cats (Pellérdy, 1974; Dubey et al., 1970; Dubey, 1975a) or in cats with *Isospora rivolta* oocysts isolated from dogs (Dubey, 1975a). Based on the results of these studies *Isospora rivolta* was retained for the species in cats, and the species in dogs was named *Isospora ohioensis* (Dubey, 1975a).

In the early 1970s, researchers demonstrated that oocysts of *Isospora felis* and *Isospora rivolta* would excyst in mice and the sporozoites would invade mesenteric lymph nodes and other extraintestinal sites (Frenkel and Dubey, 1972). These encysted stages are infectious when fed to cats and result in oocyst production.

Geographic Distribution

Fig. 1.3.

Isospora felis is found worldwide where cats are present.

Location in Host

Feline Definitive Hosts. Asexual and sexual multiplication occurs in enterocytes primarily in the posterior small intestine. Asexual stages are also observed in extraintestinal tissues.

Paratenic Hosts. In these hosts, sporozoites can persist within various cells in the lymphatic system of the peritoneal cavity.

Parasite Identification

Oocysts measure 38–51 by 27–39 µm (mean: 41.6 by 30.5 µm) (Shah, 1970a) (Fig. 1.4). The length to width ratio is 1.3–1.4 (mean: 1.35). The oocysts of *Isospora felis* are the largest of the coccidial oocysts observed in cats (Table 1.3). No micropyle is present. Inclusions (hazy bodies) may be observed between the sporont and oocyst wall in freshly excreted oocysts. The hazy bodies degenerate as the oocysts sporulate. No oocyst residuum is present in sporulated oocysts. Sporulated oocysts contain two sporocysts (Fig.1.5). Sporocysts measure 20–26 by 17–22 µm (mean, 22.6 by 18.4 µm) and contain a sporocyst residuum and four sporozoites but no Stieda body. The sporocyst residuum is granular and

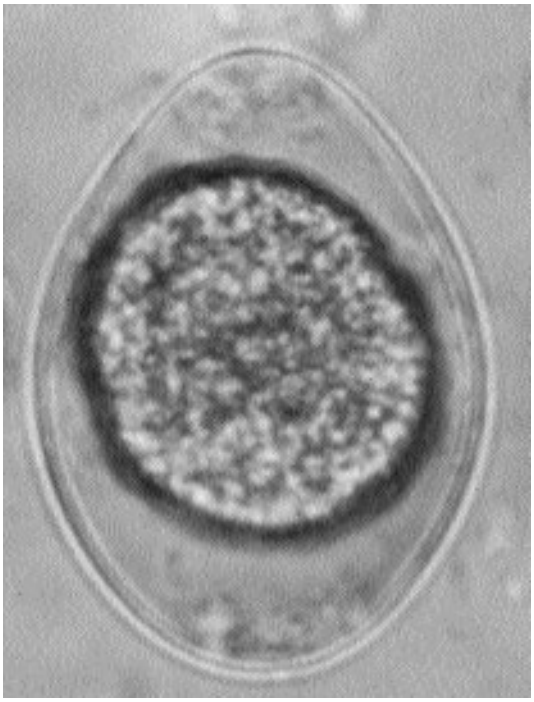

Fig. 1.4. *Isospora felis.* Oocysts passed in the feces of a naturally infected cat.

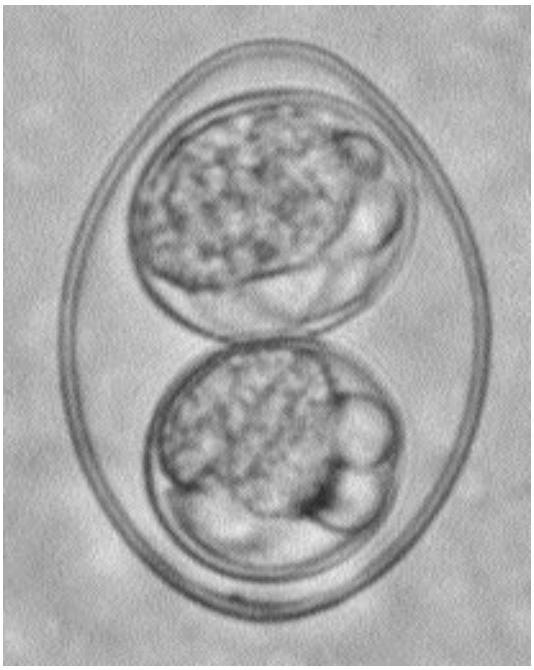

Fig. 1.5. *Isospora felis.* Sporulated oocyst.

TABLE 1.3—Comparison of measurements in micrometers of coccidial oocysts from cats

Species	Length (mean) (μm)	Width (mean) (μm)
Isospora felis	38 to 51	27 to 39
Isospora rivolta	18 to 28	16 to 23
Toxoplasma gondii	11 to 13	11 to 13
Hammondia hammondi	10 to 13	10 to 13
Hammondia pardalis	36 to 46 (40.8)	25 to 35 (28.5)
Besnoitia darlingi	11 to 13	11 to 13
Besnoitia wallacei	16 to 19 (17)	10 to 13 (11)
Cryptosporidium parvum	4 to 5	4 to 5
Sarcocystis spp.	11 to 14	7 to 9

may contain refractile globules. Sporozoites are 10–15 μm long, lie lengthwise in the sporocyst, and contain a single nucleus and a refractile globule. Occasionally a sporulated *Isospora felis* oocyst will be observed that is *Caryospora*-like, having a single sporocyst that contains eight sporozoites (Shah, 1970a).

Life Cycle

Most members of the cat family Felidae are probably suitable definitive hosts. Levine and Ivens (1981) indicated the following were suitable definitive hosts: European wild cat (*Felis silvestris*), ocelot (*Felis pardalis*), serval (*Felis serval*), tiger (*Leo tigris*), lion (*Felis leo*), jaguar (*Leo onca*), and lynx (*Lynx lynx*). Oocysts are excreted unsporulated. Oocyst sporulate in 40 hours at 20°C, 24 hours at 25°C, 12 hours at 30°C, and 8 hours at 38°C (Shah, 1970b). Sporulation does not occur at temperatures above 45°C.

Several authors have described portions of the endogenous life cycle of *Isospora felis* in cats (Wenyon, 1923; Hitchcock, 1955; Shah, 1971; Ferguson et al., 1980a, 1980b; Daly and Markus, 1981). Sporozoites excyst from *Isospora felis* oocysts in the small intestine. Developmental stages are located in enterocytes of the distal portions of the villi in the ileum, and rarely the duodenum and jejunum. The first developmental cycle is probably by endodyogeny, and at least three structural types of meronts are produced (Shah, 1971). Mature first-generation meronts of *Isospora felis* were first observed 4 days

Table 1.4—Treatment of intestinal coccidiosis and cryptosporidiosis in cats

Antiprotozoal agent	Treatment regimen
COCCIDIOSIS	
Sulfadimethoxine (SDM)	50 mg/kg for 10 days or 55 mg/kg for 1 day and 27.5 mg/kg until signs disappear
SDM plus ormetoprim (OM)	55 mg/kg SDM plus 11 mg/kg OM for up to 23 days
Sulfaguanidine	150 to 200 mg/kg for 5 days
Sulfadiazine (SD) and trimethoprim (TRI)	25 to 50 mg/kg SD plus 5 to 10 mg/kg TRI for 6 days for cats over 4 kg 12.5 to 25 mg/kg SD plus 2.5 to 5 mg/kg TRI for 6 days for cats over 4 kg
Amprolium HCl (AMP)	300 to 400 mg/kg for 5 days 110 to 220 mg/kg for 7 to 12 days 20 to 40 mg/kg for 10 days (Blagburn)
AMP plus SDM	150 mg/kg AMP plus 25 mg/kg SDM for 14 days
Quinacrine	10 mg/kg for 5 days
Furazolidone	8 to 20 mg/kg once or twice daily Use ½ this dose if combined with sulfonamides
CRYPTOSPORIDIOSIS	
Paromomycin	165 mg/kg every 12 hours for 5 days

postinoculation (PI) and produced 16–17 merozoites. Mature second-generation meronts were first observed 5 days PI and produced about 10 merozoites. Mature third-generation meronts were first observed 6 days PI, were in the same host cell as the second-generation meronts, and produced 36 to 70 merozoites. Sexual stages were first observed 6 days PI. Oocysts were first observed 7 days PI. The prepatent period is 7–11 days, and the patent period is 10–11 days.

Mice (*Mus musculus*), Norway rats (*Rattus norvegicus*), golden hamsters (*Mesocricetus auratus*), cows (*Bos taurus*), and dogs (*Canis familiaris*) can serve as paratenic hosts (Dubey, 1975b; Dubey and Frenkel, 1972; Fayer and Frenkel, 1979; Frenkel and Dubey, 1972; Wolters et al., 1980). The sporozoites present in the tissues of these hosts are infective to cats if they are ingested.

Clinical Presentation and Pathogenesis

Experimental studies indicate that *Isospora felis* is moderately pathogenic for 6-week-old to 13-week-old kittens given 1 to 1.5 $\times$ 10^5 oocysts. Soft, mucoid, feces are observed in kittens 8 days after infection, but severe disease does not occur. Microscopic lesions in kittens examined early in infection (about 6 days after being given oocysts) are mild and consist of erosion of the superficial epithelial cells. In kittens examined later in the infection (7 to 9 days after infection) congestion, mild neutrophilic infiltration, and hypersecretion of the mucosa are observed (Shah, 1971). Additionally, epithelial hyperplasia was also noted in some kittens. *Isospora felis* is more pathogenic for younger kittens. Four-week-old kittens may develop severe disease characterized by signs of enteritis, emaciation, and death if given 1 $\times$ 10^5 oocysts (Andrews, 1926).

No signs of disease are seen in paratenic hosts.

Treatment

Coccidiosis in cats can be treated with various sulfonamides and quinacrine (Table 1.4).

Epizootiology

Cats are very commonly infected with this parasite. It is unclear whether cats are infected more commonly by oocysts or by the ingestion of paratenic hosts.

Hazards to Other Animals

None known.

Hazards to Humans

It is possible that humans could serve as paratenic hosts. No recorded cases of human infection exist.

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Isospora rivolta (Grassi, 1879) Wenyon, 1923

Etymology

Isospora (*Iso* equal; *spora* spore) and *rivolta* for Dr. Rivolta.

Synonyms

Coccidium rivolta Grassi, 1879; Diplospora bigemina of Wasielewski (1904) in part; *Isospora rivoltae* Dobell, 1919; Lucetina rivolta (Grassi, 1879) Henry and Leblois, 1926; Isospora novocati Pellerdy, 1974; *Levinea rivolta* (Grassi, 1879) Dubey, 1977; *Cystoisospora rivolta* (Grassi, 1879) Frenkel, 1977.

Geographic Distribution

Fig. 1.6.

Isospora rivolta is found worldwide where cats are present.

Location in Host

Feline Definitive Hosts. Asexual and sexual multiplication occurs in enterocytes primarily in the posterior small intestine. Asexual stages are also observed in extraintestinal tissues.

Paratenic Hosts. In paratenic hosts, as with *Isospora felis*, sporozoites will enter and persist in cells within various lymphatic cells within the tissues of these hosts.

Parasite Identification

Sporulated oocysts measure 23–29 by 20–26 mm (mean, 25.4 by 23.4 μm). The length to width ratio is 1.08. The oocysts of *Isospora rivolta* represent the midrange of coccidial oocysts that are passed in the feces of cats (Table 1.3). No micropyle is present. Inclusions (hazy bodies) may be observed between the sporont and oocyst wall in freshly excreted oocysts. The hazy bodies degenerate as the oocysts sporulate. No oocyst residuum is present in sporulated oocysts. Sporulated oocysts contain two sporocysts. Sporocysts measure 13–21 by 10–15 μm (mean, 17.2 by 15.0 μm) and contain a sporocyst residuum and four sporozoites but no Stieda body. The sporocyst residuum is granular and may contain refractile globules. Sporozoites are 10–14 by 2.5–3 μm (mean, 12.4 by 2.8 μm) and contain a single centrally located nucleus and two refractile globules. Occasionally a sporulated *Isospora rivolta* oocyst will be observed that is *Caryospora*-like, having a single sporocyst that contains eight sporozoites.

Life Cycle

Most members of the cat family Felidae are probably suitable definitive hosts. Levine and Ivens (1981) indicated the following were suitable definitive hosts: European wild cat (*Felis silvestris*), jungle cat (*Felis chaus*), tiger (*Leo tigris*), and leopard (*Leo pardus*). Oocysts of *Isospora rivolta* are excreted unsporulated. Sporulation occurs within 24 hours at 24°C, 12 hours at 30°C, and 8 hours at 37°C.

Dubey (1979) described the endogenous development of *Isospora rivolta* in kittens. Three structural types of meronts were observed. Type 1 meronts were first observed 0.5 days PI, were divided by endodyogeny, and produced up to 8 merozoites. Type 2 meronts were first observed 2 days PI, were multinucleated and merozoite shaped, and produced an undetermined number of merozoites. Several divisional cycles probably occurred in the same parasitophorous vacuole. Type 3 meronts were first observed 3 days PI and contained 2 to 30 merozoites. Sexual stages and oocysts were first observed 5 days PI. The prepatent period is 4 to 7 days, and the patent period is greater than 2 weeks.

Mice (*Mus musculus*), Norway rats (*Rattus norvegicus*), golden hamsters (*Mesocricetus auratus*), cows (*Bos taurus*), and opossums (*Didelphis viginiana,* syn. *Didelphis marsupialis*) (Dubey and Frenkel, 1972). Rodents have been found to serve as paratenic hosts in the life cycle of *Isospora rivolta*. The developmental cycle in kittens fed mouse tissues containing *Isospora rivolta* stages was similar to that in cats given oocysts, but the appearance of the different stages was delayed 0.5 to 2 days within the cat host (Dubey and Streitel, 1976).

Clinical Presentation and Pathogenesis

Experimental studies indicate that *Isospora rivolta* is pathogenic for newborn but not weaned kittens (Dubey, 1979). Diarrhea occurs 3 to 4 days after inoculation of 1×10^5 to 1×10^6 oocysts in newborn kittens. Microscopic lesions consisting of congestion, erosion, villous atrophy, and cryptitis were seen in these kittens. No deaths occurred. No clinical signs were observed in 10- to 13-week-old kittens given 1×10^5 oocysts.

Treatment

Coccidiosis in cats can be treated with various sulfonamides and quinacrine (Table 1.4).

Epizootiology

Cats are very commonly infected with this parasite. It is unclear whether cats are infected more commonly by oocysts or by the ingestion of paratenic hosts.

Hazards to Other Animals

None known.

Hazards to Humans

It is possible that humans could serve as paratenic hosts. No recorded cases of human infection exist.

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Toxoplasma gondii (Nicolle and Manceaux, 1908)

Nicolle and Manceaux, 1909

Etymology

Toxoplasma (*Toxo* = arc shaped; *plasma* = cell) *gondii* for the type intermediate host, *Ctenodactylus gundi.*

Synonyms

Leishmania gondii Nicolle and Manceaux, 1908; several authors have described species of *Toxoplasma* from additional hosts, but they are not valid (Levine, 1977).

Type Intermediate Host

The gondi (*Ctenodactylus gundi*), a North African rodent.

Other Intermediate Hosts

Most mammals and birds are susceptible to *Toxoplasma gondii* infection. Some animal species, such as Australian marsupials, arborial monkeys, and lemurs are highly susceptible to toxoplasmosis.

Type Definitive Host

Domestic cat, *Felis catus.*

Other Definitive Hosts

Mountain lion (*Felis concolor*), ocelot (*Felis pardalis*), margay (*Felis weidii*), jaguarundi (*Felis yagouaroundi*), bobcat (*Felis rufus*), bengal tiger (*Felis bengalensis*), and Iriomote cats (*Felis iriomotensis*).

Geographic Distribution

Fig. 1.7.

Distribution is worldwide.

History

The complete life cycle of *Toxoplasma gondii* was not fully described until 1970, about 62 years after its discovery in 1908. The first case of human toxoplasmosis was reported in 1923 in an 11-month-old congenitally infected infant that had hydrocephalus and microphthalmia with coloboma (Remington et al., 1995). In the late 1930s and early 1940s it became well established that toxoplasmosis is an important disease of humans and that infections in infants are acquired prenatally. The rate of congenital toxoplasmosis in humans was too low to explain the high seroprevalence of *Toxoplasma gondii* in the populations examined. Carnivorism was suggested by several researchers and conclusively proven in 1965. Ingestion of infected meat, however, did not explain *Toxoplasma gondii* infection in vegetarians or herbivores, and other modes of transmission had to be present. Hutchison first found resistant *Toxoplasma gondii* in cat feces in 1965 and thought it was enclosed in the eggs of *Toxocara cati* (Dubey and Beattie, 1988). Several studies disproved the association of *Toxoplasma gondii* with *Toxocara cati,* and in 1969–1970 several groups of researchers reported the presence of a coccidial oocyst in cat feces that was *Toxoplasma gondii* (Figs. 1.8 and 1.9). *Toxoplasma gondii* oocyst excretion has been observed in several species of felids in addition to the domestic cat (Miller et al., 1972; Jewell

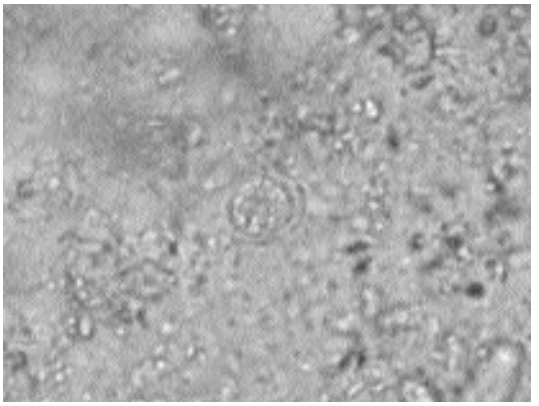

Fig. 1.8. *Toxoplasma gondii.* Oocyst passed in the feces of a cat.

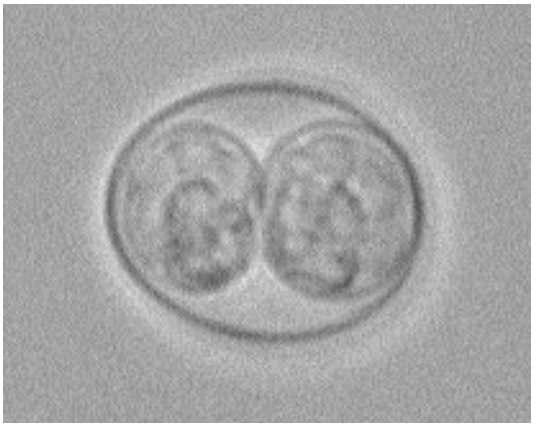

Fig. 1.9. *Toxoplasma gondii.* Sporulated oocyst.

et al., 1972). The first case of fatal toxoplasmosis in a cat was reported in 1942 (Dubey and Beattie, 1988). Fatal toxoplasmosis has been reported in wild felids in zoos and from pelt farms (Dubey et al., 1987).

Life Cycle of *Toxoplasma gondii* in Cats. The life cycle of *Toxoplasma gondii* is complex. Cats serve as both definitive and intermediate hosts for the parasite. There are two distinct types of asexual stages that are present in extraintestinal tissues of cats and other intermediate hosts (Dubey and Frenkel, 1972, 1976) These stages are intracellular except for brief periods of time when they have ruptured host cells and are

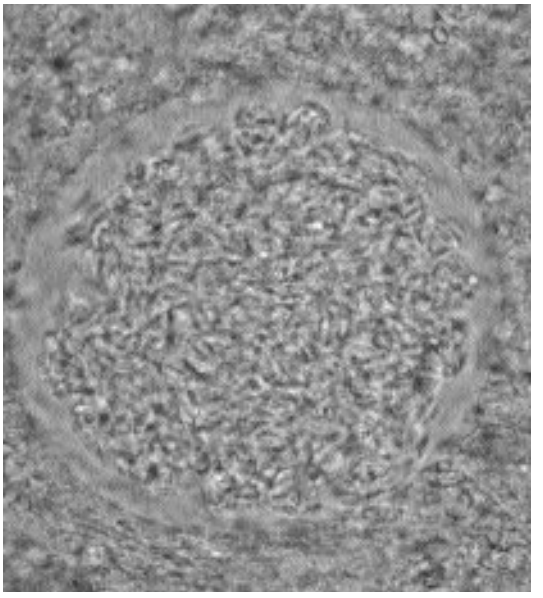

Fig. 1.10. *Toxoplasma gondii.* Cyst of strain T264 in the brain of experimentally infected mouse.

actively seeking new host cells. Tachyzoites are rapidly dividing stages that cause tissue damage and disseminate the infection in host tissues. After a period of multiplication (about 3 days) some tachyzoites will begin to produce the latent tissue cyst stages that contain bradyzoites. Bradyzoites are slowly dividing stages that are found in tissue cysts. Both tachyzoites and bradyzoites divide into two by endodyogeny. Bradyzoites can transform into tachyzoites (Fig. 1.10). Bradyzoites are the only life cycle stage that can give rise to the enteroepithelial developmental cycle (oocyst-producing cycle) in the cat's intestine. Tissue cysts are present for up to 1.3 years (probably until host death) after inoculation in cats, and most tissue cysts are located in the heart (Dubey, 1977).

The life cycle of *Toxoplasma gondii* in the cat varies based on the developmental stage that the cat ingests (Dubey and Frenkel, 1972, 1976; Dubey, 1979; Freyre et al., 1989). When cats ingest tissue cysts, the bradyzoites are released after passage through the stomach. Some bradyzoites will penetrate enterocytes and begin the enteroepithelial cycle that will terminate in oocyst production (Dubey, 1979) (Fig. 1.11). However,

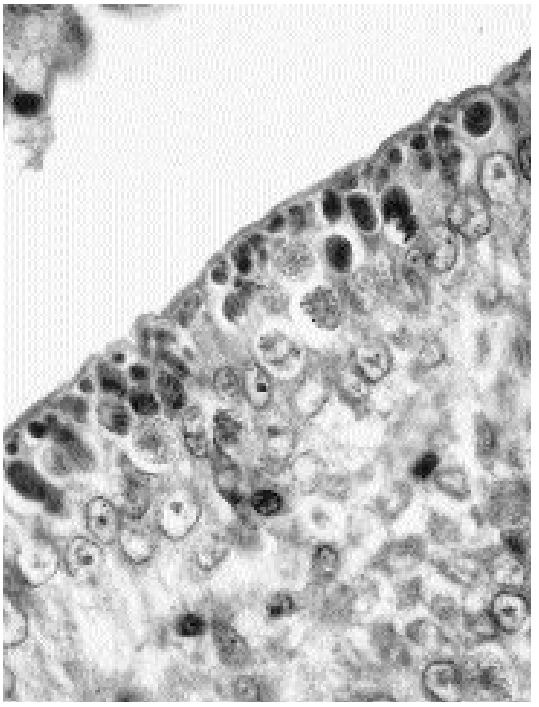

Fig. 1.11. *Toxoplasma gondii.* Gametocytes and schizonts in the epithelial cells of an experimentally infected cat. (Photo courtesy of JP Dubey)

some bradyzoites will penetrate into the intestinal lamina propria and begin development as tachyzoites. Infectious stages of *Toxoplasma gondii* are present in the liver and mesenteric lymph nodes as early as 8 hours after tissue cysts are ingested and chronic infections are produced by these stages. Five structurally distinct types of schizonts are produced in the enterocytes of the small and large intestine prior to the formation of sexual stages at 3–4 days (Dubey and Frenkel, 1972; Dubey, 1979). The prepatent period is 3 to 10 days for tissue cyst–induced infections. Oocysts are excreted in the feces for 7 to >20 days, with most being excreted between days 5 and 8.

Ingestion of sporulated *Toxoplasma gondii* oocysts or tachyzoites results in oocyst-excreting infections in only 16 to 20 percent of cats as compared with 97 percent of cats that are fed tissue cysts (Dubey and Frenkel, 1976; Freyre et al., 1989; Dubey, 1996). The prepatent period is at least 18 days in cats fed oocysts as compared with 3 to 10 days in cats that are fed tissue cysts (Dubey, 1996). The reason for the extended prepatent period is that the sporozoites or tachyzoites must first produce tissue cysts that contain bradyzoites. These bradyzoites will then find their way back to the intestine to produce the enteroepithelial cycle that results in oocyst production.

Oocyst Biology. Unsporulated *Toxoplasma gondii* oocysts are spherical to subspherical, and contain a single mass (sporont) (Fig. 1.8). Sporulation occurs in the environment and is dependent on temperature and moisture (Dubey et al., 1970a). Sporulation is asynchronous, and some oocysts will be sporulated before others. Completely infectious oocysts are present by 24 hours at 25°C (room temperature); by 5 days at 15°C, and by 21 days at 11°C (Dubey et al., 1970b). Unsporulated oocysts do not survive freezing but can remain viable at 4°C for several months and become infectious if placed under the appropriate conditions. Unsporulated oocysts die if kept at 37°C for 24 hours and are killed by 10-minute exposure to 50°C.

A small population of unsporulated oocysts can survive anaerobic conditions for 30 days and remain capable of developing. Oocysts do not sporulate in 0.3 percent formalin, 1 percent ammonium hydroxide solution, or 1 percent iodine in 20 percent ethanol but can sporulate in 5 percent sulfuric acid, 20 percent ethanol, 10 percent ethanol plus 10 percent ether, 1 percent hydrochloric acid, 1 percent phenol, and tap water (Dubey et al., 1970a, 1970b). Drying kills *Toxoplasma gondii* oocysts. Cockroaches, flies, earthworms, and other phoretic hosts can serve to distribute *Toxoplasma gondii* oocysts from the site of defecation in the soil (Dubey and Beattie, 1988).

Sporulated *Toxoplasma gondii* oocysts are subspherical to ellipsoidal, and each contains two ellipsoidal sporocysts, which enclose four sporozoites (Fig. 1.9). Sporulated oocysts are more resistant to environmental and chemical stresses than are unsporulated oocysts. Viable oocysts of *Toxoplasma gondii* have been isolated from soil samples (Ruiz et al., 1973; Coutinho et al., 1982; Frenkel et al., 1995), and experimentally they can survive for over 18 months in the soil (Frenkel et al., 1975). Sporulated oocysts cannot survive freezing or temperatures of 55°C or greater (Ito et al., 1975; Dubey, 1998). Sporulated oocysts survive for several years at 4°C in liquid medium (Dubey, 1998).

***Toxoplasma gondii* Oocyst Excretion.** All ages, sexes, and breeds of domestic cats are susceptible to *Toxoplasma gondii* infection (Dubey et al., 1977). Transplacentally or lactogenically infected kittens will excrete oocysts, but the prepatent period is usually 3 weeks or more because the kittens are infected with tachyzoites (Dubey et al., 1995b). Domestic cats under 1 year of age produce the most numbers of *Toxoplasma gondii* oocysts. Cats that are born and raised outdoors usually become infected with *Toxoplasma gondii* shortly after they are weaned and begin to hunt. *Toxoplasma gondii* naive adult domestic cats will excrete oocysts if fed tissue cysts, but they usually will excrete fewer numbers of oocysts and excrete oocysts for a shorter period of time than recently weaned kittens.

Immunity to Oocyst Excretion. Intestinal immunity to *Toxoplasma gondii* is strong in cats that have excreted oocysts (Frenkel and Smith, 1982a, 1982b, Dubey 1995). Primary *Toxoplasma gondii* infection in cats does not cause immunosuppression (Lappin et al., 1992a; Davis and Dubey, 1995). Serum antibody does not play a significant role in resistance to intestinal infection, and intestinal immunity is most likely cell mediated. Oocysts begin to be excreted in the feces before IgM, IgG, or IgA antibodies are present in the serum (Lappin et al., 1989a; Lin and Bowman, 1991; Burney et al., 1995). Partial development of the enteroepithelial stages occurs in the intestines of immune cats, but oocyst production is prevented (Davis and Dubey, 1995). Most cats that have excreted oocysts once do not re-excrete oocysts if challenged within 6 months to 1 year. Intestinal immunity will last up to 6 years in about 55 percent of cats (Dubey, 1995).

Immunosuppression with high doses of corticosteroid (10 to 80 mg/kg methylprednisolone acetate intramuscularly [IM] weekly or 10 to 80 mg/kg prednisone orally daily) will cause some chronically infected cats to re-excrete *Toxoplasma gondii* oocysts (Dubey and Frenkel, 1974). However, clinically relevant doses of 5 to 20 mg/kg corticosteroid given weekly for 4 weeks do not cause recently or chronically infected cats to re-excrete *Toxoplasma gondii* oocysts (Lappin et al., 1991). Doses of 5 mg/kg cortisone acetate for 7 days will not cause oocyst excretion in chronically infected cats (Hagiwara et al., 1981).

Cats that are chronically infected with *Toxoplasma gondii* and then undergo a primary feline immunodeficiency virus infection demonstrate an increase in *Toxoplasma gondii* antibody titers, suggesting some reactivation of encysted stages. However, experimental studies indicate that there is no reactivation of *Toxoplasma gondii* oocyst excretion or development of clinical toxoplasmosis (Lappin et al., 1992b; 1993; 1996b; Lin and Bowman, 1992; Lin et al., 1992a). Rarely has clinical disease been associated with reactivated toxoplasmosis in feline immunodeficiency virus (FIV) positive cats. Experimental feline leukemia virus infection prior to *Toxoplasma gondii* challenge does not appear to predispose cats to acute toxoplasmosis and has no effect on oocyst excretion (Patton et al., 1991).

There is an interesting relationship that exists between the intestinal coccidium *Isospora felis* and *Toxoplasma gondii* in cats (Chessum, 1972; Dubey, 1976). Cats that have previously recovered from a *Toxoplasma gondii* infection will re-excrete *Toxoplasma gondii* oocysts if they obtain a primary *Isospora felis* infection afterwards. Cats that have a primary *Isospora felis* infection followed by a primary *Toxoplasma gondii* infection develop strong immunity to *Toxoplasma gondii* and will not re-excrete *Toxoplasma gondii* oocysts if challenged with *Isospora felis* (Dubey, 1978a). The mechanism for this unusual relationship is not known.

Toxoplasmosis in Cats

Dubey and Carpenter (1993a) examined 100 cases of histologically confirmed toxoplasmosis in domestic cats and provided the definitive report on clinical toxoplasmosis in cats. Eleven of 100 cats were purebred, cats ranged in age from 2 weeks to 16 years, and 65 were male, 34 were female, and the sex of 1 was not determined. Of the 100 cats 36 had generalized, 26 had pneumonic, 16 had abdominal, 7 had neurologic, 9 had neonatal, 2 had hepatic, 2 had cutaneous, 1 had pancreatic, and 1 had cardiac toxoplasmosis (Figs. 1.12–1.16).

Fever (40 to 41.7°C) is present in many cats with toxoplasmosis. Clinical signs of dyspnea, polypnea, and icterus and signs of abdominal discomfort are frequent findings. Gross and microscopic lesions are found in many organs but are

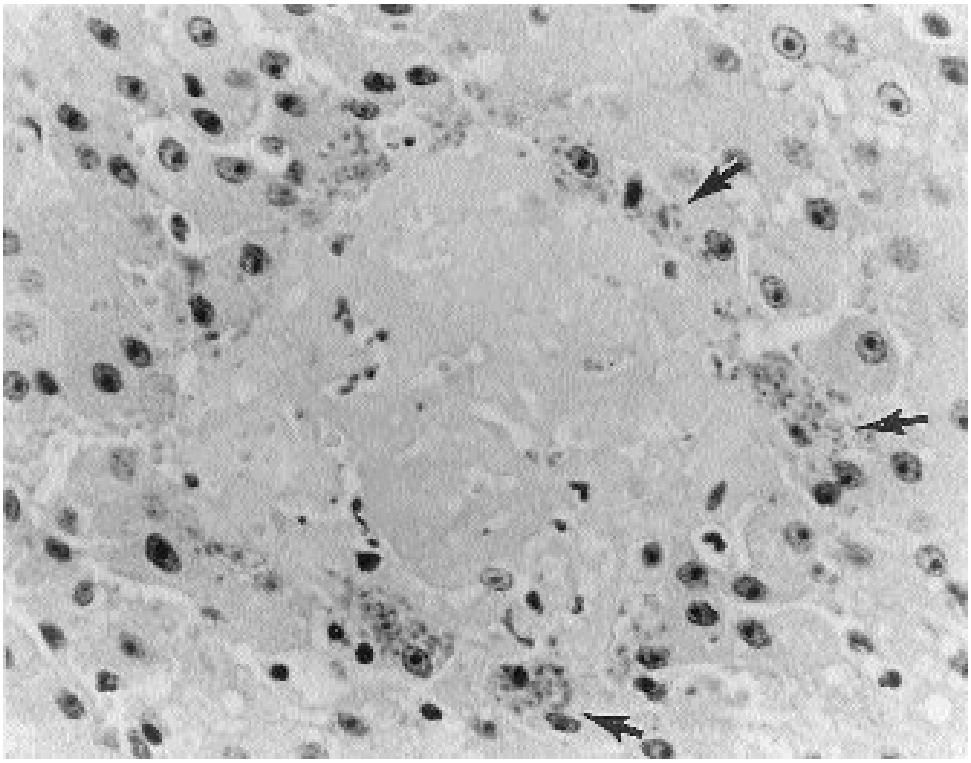

Fig. 1.12. *Toxoplasma gondii.* Focus of necrosis in a cat (H&E-stained histological section, 1000×). Note numerous tachyzoites (*arrows*) at the periphery of the lesion.

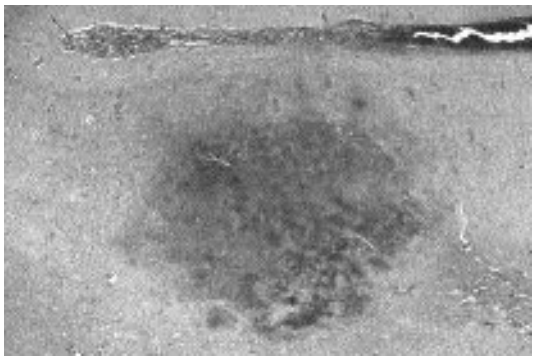

Fig. 1.13. *Toxoplasma gondii.* Necrotizing abscess in the brain of a naturally infected cat that contained numerous dividing tachyzoites.

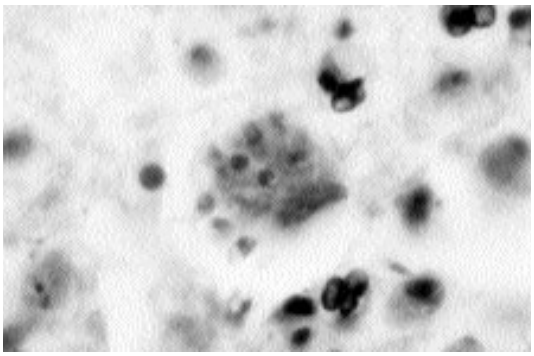

Fig. 1.14. *Toxoplasma gondii.* Higher-power view of abscess in the brain showing the organisms.

most common in the lungs. Gross lesions in the lungs consist of diffuse edema and congestion, failure to collapse, and multifocal areas of firm, white to yellow, discoloration. Pericardial and abdominal effusions may be present. The liver is the most frequently affected abdominal organ, and diffuse necrotizing hepatitis may be visible grossly. Gross lesions associated with necrosis can also be observed in the mesenteric lymph nodes and pancreas.

Ocular lesions are also common in cats, but the actual prevalence is not known. Most lesions are

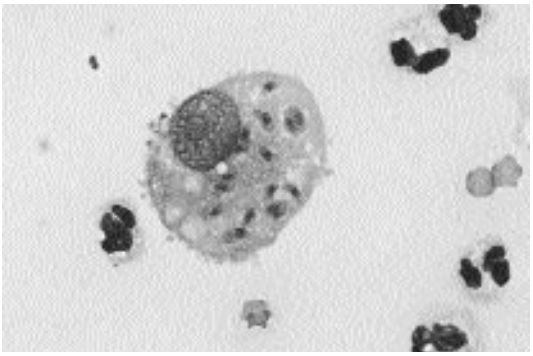

Fig. 1.15. *Toxoplasma gondii.* Macrophage from the abdominal cavity of a naturally infected cat containing numerous tachyzoites.

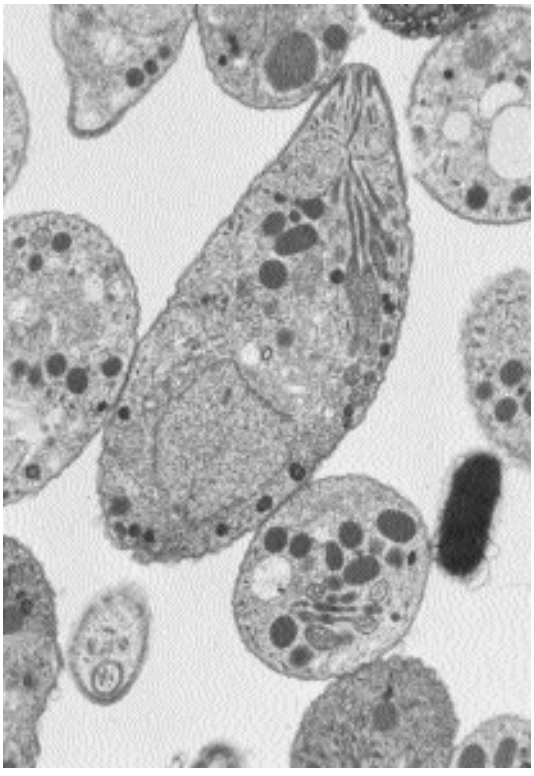

Fig. 1.16. *Toxoplasma gondii.* Electron micrograph of a tachyzoite of the RH strain showing the structures typical of this apicomplexan parasite, e.g., apical complex, rhoptries, and dense granules. (Image kindly supplied by the late Dr. John Cummings.)

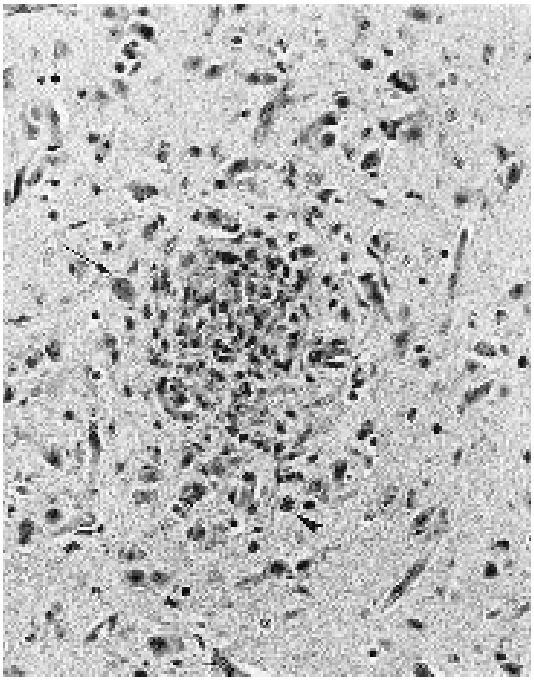

Fig. 1.17. *Toxoplasma gondii.* Glial nodule in the cerebrum of a congenitally infected kitten (H&E-stained histological section). A tissue cyst (*arrow*) and tachyzoites (*arrowhead*) are present at the periphery of the nodule.

in the anterior segment (Lappin et al., 1989c). Cats with ocular lesions have a higher seroprevalence than cats with normal eyes. Ocular findings are varied: They include aqueous flares, hyphema, velvety iris, mydriasis, anisocoria, retinal hemorrhages, retinal atrophy, retinochoriditis, and slow pupillary reflex.

Central nervous system toxoplasmosis is not common in cats. Neurological signs including hypothermia, partial or total blindness, stupor, incoordination, circling, torticollis, anisocoria, head bobbing, ear twitch, atypical crying, and increased affectionate behavior have been reported (Dubey and Carpenter, 1993a).

Congenital toxoplasmosis occurs in cats, but the frequency is not known (Dubey and Carpenter, 1993b) (Figs. 1.17 and 1.18).

Clinical Signs of Feline Toxoplasmosis. The severe central nervous system involvement observed in congenitally infected infants and AIDS patients and the tendency of tissue cysts to

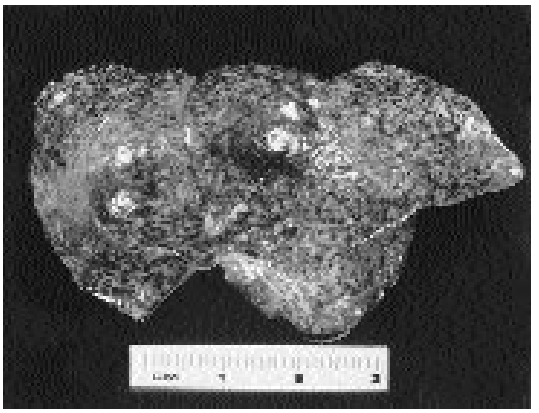

Fig. 1.18. *Toxoplasma gondii.* Liver of a congenitally infected 8-day-old kitten.

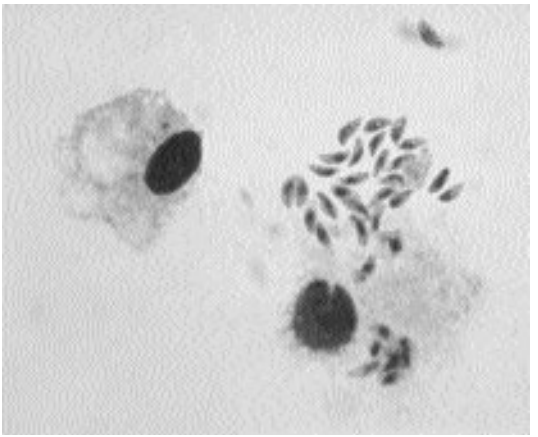

Fig. 1.19. *Toxoplasma gondii.* Alveolar macrophage of a cat with tachyzoites after 40 hours of in-vitro co-culture.

develop in the brains of humans and mice have led to the erroneous assumption by many that toxoplasmosis in all animals is a central nervous system disease. Central nervous system infections do occur in cats but neurologic signs are not the most common clinical sign of infection in cats (Dubey and Carpenter, 1993a).

Fever (40 to 41.7°C) is present in many cats with toxoplasmosis. Clinical signs of dyspnea, polypnea, and icterus and signs of abdominal discomfort were the most frequent findings in 100 cats with histologically confirmed toxoplasmosis (Dubey and Carpenter, 1993a). Uveitis and retinochoroiditis are also common clinical signs in cats with toxoplasmosis. Gross and microscopic lesions are found in many organs but are most common in the lungs. Gross lesions in the lungs consist of edema and congestion, failure to collapse, and multifocal areas of firm, white to yellow, discoloration. Pericardial and abdominal effusions may be present. The liver is the most frequently affected abdominal organ and diffuse necrotizing hepatitis may be visible grossly. Gross lesions associated with necrosis can also be observed in the mesenteric lymph nodes and pancreas.

Ocular lesions of toxoplasmosis are common in cats. The actual prevalence is not known, but antibodies to *Toxoplasma gondii* were observed in the sera of 80 percent of cats with uveitis in one study (Chavkin et al., 1992), indicating a high prevalence in infected cats. Most lesions are in the anterior segment (Lappin et al., 1992c). Ocular findings are varied: they include aqueous flare, hyphema, iritis, mydriasis, anisocoria, retinal hemorrhages, retinal atrophy, retinochoroiditis, and slow pupillary reflex.

Central nervous system toxoplasmosis is not common in cats. In one study, only 7 of 100 cases of histologically confirmed cases of toxoplasmosis had neurological signs (Dubey and Carpenter, 1993a). Neurological signs including hypothermia, partial or total blindness, stupor, incoordination, circling, torticollis, anisocoria, head bobbing, ear twitch, atypical crying, and increased affectionate behavior have been reported.

Congenital toxoplasmosis occurs in cats, but the frequency is not known. Disease in congenitally infected kittens can be severe and fatal (Dubey and Carpenter, 1993b). The most common clinical signs are anorexia, lethargy, hypothermia, and sudden death (Dubey et al., 1995b).

Diagnosis of Feline Toxoplasmosis. The diagnosis of clinical toxoplasmosis requires that three criteria be fulfilled (Lappin, 1990). The cat must have clinical signs consistent with toxoplasmosis and serological evidence of recent or active infection, and the patient must respond to anti-*Toxoplasma gondii* treatment or have *Toxoplasma gondii* demonstrated in its tissues or body fluids.

Toxoplasmosis should be suspected in cats with anterior uveitis, retinochoroiditis, fever, dyspnea, polypnea, abdominal discomfort, icterus, anorexia, seizures, ataxia, and weight loss. Fecal

Table 1.5—Serological tests for the demonstration of *Toxoplasma gondii* antibodies in cats

Test	Antibody first detected	Comments (cutoff titer)
IgG-ELISA	2 weeks	Test detects IgG, 4 fold increase in titer over 2 to 3 weeks indicates active infection (1:64)
IgM-ELISA	1–2 weeks	Test detects IgM, titer of >1:256 indicative of active infection, positive IgM with negative IgG indicates active infection. (1:64)
Modified direct agglutination	—	—
Formalin fixed (FF) antigen	2 weeks	Test detects IgG, 4 fold increase in titer over 2 to 3 weeks indicates active infection, titers remains high. (1:25)
Acetone fixed (AC) antigen	1–2 weeks	Test detects IgG, titers high during acute infection. High AC and low FF titer indicates active infection. (1:100)
Indirect hemagglutination test (IHT), latex agglutination test (LAT), IgG indirect fluorescent antibody (IgG-IFA)	2 weeks	Tests detect IgG, IHT is insensitive, 4 fold increase in titer over 2 to 3 weeks indicates active infection. (1:64)
IgM-IFA	1–2 weeks	Detects IgM, positive IgM with negative or low IgG indicates active infection. (1:64)
Sabin-Feldman dye test	1–2 weeks	Detects IgG and IgM, 4 fold increase in titer over 2 to 3 weeks indicates active infection. (1:16)

Note: Titers on paired serum samples should be examined on the same day to avoid test variability. (Adapted from Lindsay et al., 1997a.)

examination only rarely detects oocysts in cats, and most cats with clinical toxoplasmosis will not be excreting oocysts at the time of presentation. Thoracic radiographs may be helpful. Diffusely disseminated and poorly demarcated foci of increased radiodensity caused by interstitial and alveolar pneumonia are suggestive of but not definitive for *Toxoplasma gondii* in febrile cats.

Serological Tests for Active Toxoplasmosis. Several serological tests are available for the diagnosis of active toxoplasmosis in cats (Table 1.5). Titers obtained in one type of test may not correlate with titers obtained in other tests (Patton et al., 1991; Dubey and Thulliez, 1989; Lappin and Powell, 1991). Most tests rely on the detection of IgG antibodies, which do not develop until about 2 weeks postinfection and may remain at high levels for several years to the life of the cat (Dubey et al., 1995a). Therefore, diagnosis of active toxoplasmosis in cats using an IgG-based test requires that a rising titer be demonstrated (Lindsay et al., 1997a).

Diagnostic tests based on detection of IgM antibodies (Lappin et al., 1989a, 1989c; Lin and Bowman, 1991), circulating parasite antigens (AG) (Lappin et al., 1989b), or acetone-fixed (AF) tachyzoite antigens (Dubey et al., 1995a) can detect early infections at 1 to 2 weeks postexposure. The *Toxoplasma gondii*–specific IgM levels in cats peak at 3 to 6 weeks and drop to negative by 12 weeks postexposure in the IgM-ELISA test. However, some cats will have sporadic low IgM-ELISA levels for up to 1 year postexposure. Peak detection of circulating *Toxoplasma gondii* antigens occurs about 21 days postexposure, but some cats will have circulating *Toxoplasma gondii* antigens for at least 1 year in the AG-ELISA; overall, the test is not very useful in diagnosis (Lappin et al., 1989b). Reactivity to AF tachyzoites in the modified direct agglutination test (MAT, normally formalin-fixed [FF] tachyzoites are used) remains present for up to 70 months (Dubey et al., 1995a). The IgA-ELISA produces variable results in detecting serum antibodies in cats and is not used to detect early infections (Burney et al., 1995). The use of an early detection test coupled with an IgG detection test can provide valuable information on the kinetics of the *Toxoplasma gondii* infection. For example, a high IgM-ELISA titer and a negative or low IgG-ELISA titer would indicate active infection.

The reverse would be true for a chronic infection. Serology can often be difficult to interpret and should never be the sole basis for diagnosis.

Serological Tests for Ocular and CNS Toxoplasmosis. Detection of *Toxoplasma gondii* antibodies in aqueous humor has been used as an aid in the diagnosis of ocular toxoplasmosis in cats (Patton et al., 1991; Lappin et al., 1992c, 1995; Lin et al., 1992b). Calculating the Goldman-Witmer coefficient (C-value) helps correct for antibodies that may have leaked across a damaged vasculature and not been produced directly in the eye (Lappin et al., 1992c). Experimentally infected cats begin to have detectable IgA and IgG levels in aqueous humor at 4 weeks postexposure, while IgM is either not present or at levels too low to detect (Lappin et al., 1995); however, all three antibody isotypes have been found in the aqueous humor of naturally infected cats. Cats with C-values <1 are considered to have antibodies that have leaked across a damaged vasculature, while C-values of 1 to 8 are highly suggestive of clinical ocular toxoplasmosis (Lappin et al., 1992c, 1995). Cats with C-values >8 are considered to have conclusive evidence of ocular antibody production due to *Toxoplasma gondii* infection (Chavkin et al., 1994). Most cats with C-values >1 will respond to specific antitoxoplasmal treatment (Lappin et al., 1992c). Although not conclusive, a trend toward association of *Toxoplasma gondii*–specific IgA in the serum of cats with ocular disease has been reported (Burney et al., 1995).

Using the FF-MAT (Patton et al., 1991), a modified ELISA (Lin et al., 1992b), and IgG-ELISA (Muñana et al., 1995), *Toxoplasma gondii* antibodies have been demonstrated in the cerebrospinal fluid (CSF) of cats with experimental infections but no clinical signs of encephalitis. No IgM was detected in the CSF of experimentally infected cats using the IgM-ELISA. Little else is available on the diagnosis of toxoplasmic encephalitis in cats using CSF. Because *Toxoplasma gondii*–specific IgG has been observed in the CSF of clinically normal cats, it has been suggested that the diagnosis of central nervous system toxoplasmosis in cats not be based solely on detection of intrathecally synthesized *Toxoplasma gondii*–specific IgG (Muñana et al., 1995).

Serological Tests for Neonatal Toxoplasmosis. Neonatal toxoplasmosis is difficult to diagnosis antemortem because the clinical signs are vague and kittens will have nursed prior to examination. Serological indications can be inferred in some cases by comparing titers in queens with their kittens (Dubey et al., 1995b) Transplacental transfer of *Toxoplasma gondii* antibodies does not occur in cats (Dubey et al., 1995b). If the queen is seronegative, then it is unlikely that the kittens have toxoplasmosis because transplacental transmission is unlikely if the queen has acquired the infection with less than 2 weeks left in pregnancy, which is the time it takes for a detectable antibody response. If the queen has a positive IgM titer or the queen and kittens have rising IgG titers, then transplacental or lactogenic transmission is possible. Western blot analysis of serum from the queen and kitten can be helpful in diagnosing neonatal toxoplasmosis in kittens (Cannizzo et al., 1996). Antigen recognition patterns are different for congenitally infected kittens when compared with queens or kittens that have maternally acquired antibody. Serum for congenitally infected kittens will usually recognize an antigen with a molecular mass between 27 and 29 kD (Cannizzo et al., 1996).

Other Methods of Detection of *Toxoplasma gondii* Infections. Direct demonstration of *Toxoplasma gondii* stages can be used to make a method of antemortem diagnosis. Examination of brocheolavage material or material collected by abdominocentesis can be used to detect suspected cases of disseminated toxoplasmosis in cats or neonatal toxoplasmosis in kittens. Examination of CSF may also demonstrate organisms in cases of encephalitis.

The polymerase chain reaction (PCR) has been widely used in human medicine to detect *Toxoplasma gondii* in secretions and fluids, and methods are currently under development for use in cats (Stiles et al., 1996; Lappin et al., 1996b; Burney et al., 1998). The primers have been developed that amplify portions of the parasites B1 gene and used to detect tachyzoites in serum, blood, aqueous humor, and CSF. The PCR test can detect DNA from as few as 10 tachyzoites in serum, CSF, and aqueous humor (Stiles et al.,

Table 1.6—Treatment of feline toxoplasmosis

Product	Treatment regimen
Clindamycin hydrochloride	Oral, 10–2 mg/kg BID for 4 weeks
Clindamycin phosphate	IM, 12.5–25 mg/kg BID for 4 weeks
Pyrimethamine plus sulfonamide	Oral, 0.25–0.5 mg/kg combined with 30 mg/kg sulfonamide BID for 2 to 4 weeks
Trimethoprim + sulfadiazine	Oral 15 mg/kg BID for 4 weeks

1996; Lappin et al., 1996b) and DNA from as few as 100 tachyzoites in blood (Stiles et al., 1996). The use of PCR combined with traditional antibody testing may be useful in the antemortem diagnosis of toxoplasmosis in cats. Results of PCR testing alone should never be used as the sole method of diagnosis of toxoplasmosis.

Postmortem diagnosis can be made by demonstration of the parasite in tissue sections using routine methods or by supplementing histopathologic examinations with immunohistochemical staining for specific *Toxoplasma gondii.* Other methods, such as bioassays in cats or mice, can be used but are not practical.

Vaccination against Oocyst Excretion. A vaccine that prevents oocyst excretion in cats would be beneficial for both veterinary and public health reasons (Fishback and Frenkel, 1990; Frenkel et al., 1991; Freyre et al., 1993). Vaccination of cats would decrease environmental contamination with oocysts. This would aid in preventing exposure of animals and humans to oocysts and lead to a decreased prevalence of the encysted parasite in food animals.

Killed or recombinant tachyzoite–based vaccines do not stimulate intestinal immunity and are of no value in preventing oocyst excretion. Technically it is not presently possible to produce sufficient numbers of bradyzoites or enteroepithelial stages to develop killed or recombinant vaccines based on these stages.

Intestinal immunity can be induced by infecting cats with an oocyst-producing strain of *Toxoplasma gondii* and by prophylactically treating the cats for 8 to 19 days with anti–*Toxoplasma gondii* chemotherapy (Frenkel and Smith, 1982a, 1982b). Oocyst excretion can be prevented during the immunizing phase, and 80 to 85 percent of the cats become immune. Although effective, this method of vaccination is impractical for many technical and safety reasons.

The life cycle of *Toxoplasma gondii* can be manipulated by extensive passage of the parasite in mice (Frenkel et al., 1976) or in cell cultures (Lindsay et al., 1991) so that the bradyzoites lose the ability to produce oocyst excretion in cats. Unfortunately, none of these oocyst-less strains of *Toxoplasma gondii* stimulate sufficient intestinal immunity, and the cats will excrete oocysts when challenged with an oocyst-producing strain.

Vaccination of cats against intestinal *Toxoplasma gondii* infection has been successfully achieved using a chemically induced mutant strain (T-263) of the parasite (Frenkel et al., 1991; Freyre et al., 1993). Oral administration of strain T-263 bradyzoites results in intestinal infection but does not result in oocyst production in cats. These vaccinated cats do not excrete oocysts when challenged with oocyst-producing strains of *Toxoplasma gondii.* The T-263 strain is safe to use in healthy cats. It would not be recommended for use in pregnant cats or feline leukemia virus (FeLV) positive cats or immunocompromised cats (Choromanski et al., 1994, 1995). It has only limited ability to persist in the tissues of cats and cannot survive more than three back-passages in cats. No reversion to oocyst excretion or increase in virulence has been observed in over 200 inoculated cats. The T-263 strain is rapidly cleared from the mouth of inoculated cats.

Treatment of Feline Toxoplasmosis. No chemotherapeutic agents are approved for the treatment of toxoplasmosis in cats. Table 1.6 lists agents that are used to treat toxoplasmosis in cats.

Clindamycin is the drug of choice for the treatment of disseminated toxoplasmosis in cats (Lappin et al., 1989c). Clinically, the drug has been widely used with good response.

Table 1.7—Prevention of *Toxoplasma gondii* infection in cats and humans

Recommendation/Reason
Cats
1. Do not feed raw or rare meat to cats/*Prevent exposure to tissue cysts.*
2. Keep cats indoors and do not allow cats to hunt/*Prevent exposure to tissue cysts in prey animals.*
3. Vaccination (if it becomes available)/*Prevent oocyst excretion.*
Humans
1. Do not eat raw or rare meat/*Prevent ingestion of viable tissue cysts.*
2. Wash hands and food preparation surfaces with warm soapy water after handling and preparing raw meat/*Inactivate tissue cysts.*
3. Wear gloves while gardening or wash hands after gardening/*Prevent exposure to oocysts in the soil.*
4. Wash all fruits and vegetables before eating/*Remove any oocysts that may be present.*
5. Change litter box daily. Pregnant women and immunosuppressed individuals should not change litter box/*Remove oocysts before they become infective and prevent exposure of high risk individuals.*

Cats can also be treated with pyrimethamine or trimethoprim combined with a sulfonamide. Pyrimethamine is active at lower concentrations than is trimethoprim. Sulfadiazine and sulfamethoxazole are the sulfonomides most often used. Bone marrow suppression can occur with the use of pyrimethamine- or trimethoprim-sulfonamide combinations and can be corrected with the addition of folinic acid (5 mg per day) or the addition of yeast (100 mg/kg) to the cat's diet.

Prevention of *Toxoplasma gondii* Infection in Cats and Humans. Measures can be taken to prevent or lower the risk of exposure of cats and humans to *Toxoplasma gondii.* They are based on a detailed knowledge of the parasite's life cycle and are presented in Table 1.7. They are based on preventing exposure to sporulated oocysts or tissue cysts.

Pork is the most likely source of tissue cysts for people in the United States. This is because cattle are naturally resistant, and other *Toxoplasma gondii*–infected meats such as sheep and goat are not consumed in significant amounts (Dubey, 1994). Chickens are susceptible to *Toxoplasma gondii* infection, but because chicken is often frozen and seldom eaten rare, it is not considered a primary source of infection. Tissue cysts in meat are killed by cooking to temperatures of 58°C for 10 minutes or 61°C for 4 minutes (Dubey et al., 1990). Tissue cysts are believed to be killed instantaneously by exposure to −13°C; however, they will survive for up to 3 weeks at −3°C and 11 days at −6°C (Kotula et al., 1991). Gamma irradiation at an absorbed dose of 0.4 kGy is lethal for tissue cysts in meat (Dubey and Thayer, 1994).

Cutting boards, knives, and other surfaces that raw meat has contacted should be washed in warm soapy water to kill the tissue cysts and any bradyzoites that may have been liberated during handling. Hands should also be washed in warm soapy water after contact with raw meat.

Cat Ownership and the Risk of Toxoplasmosis. It is logical to assume that veterinarians, who have more exposure to cats (both sick and healthy) than the general public, would be at a greater risk for developing toxoplasmosis. However, serological studies do not confirm this assumption (Behymer et al., 1973; Sengbusch and Sengbusch, 1976; DiGiacomo et al., 1990). In one study of AIDS patients it was conclusively shown that owning cats did not increase the risk of developing toxoplasmosis (Wallace et al., 1993). However, the role of cat ownership and exposure to *Toxoplasma gondii* is not completely clear at present. Many studies have been conducted to determine the association between cat ownership or cat exposure and the prevalence of *Toxoplasma gondii* infection in humans. Many studies do not find a positive relationship (Partono and Cross, 1975; Ulmanen and Leinikki, 1975; Durfee et al., 1976; Zigas, 1976; Tizard et al., 1977; Gandahusada, 1978; Sedaghat et al., 1978; Ganley and Comstock, 1980; Stray-Pedersen and Lorentzen-Styr, 1980; Konishi and Takahashi, 1987; Arias et al., 1996; Bobic et al., 1998; Flegr et al., 1998), while many find a positive relationship (Clarke et al., 1975; Frenkel and Ruiz, 1980, 1981; Barbier et al., 1983; Martinez Sanchez et al., 1991; Ahmed, 1992; MacKnight and Robinson, 1992; Etheredge and Frenkel,

1995; del Castillo and Herruzo, 1998; Rey and Ramalho, 1999). It must be remembered that preventing exposure to cats is not the same as preventing exposure to *Toxoplasma gondii* oocysts. One study indicated that exposure to dogs was more of a risk factor than exposure to cats (Frenkel et al., 1995). If dogs are fed sporulated *Toxoplasma gondii* oocysts, many will pass out in the dogs feces and remain infectious (Lindsay et al., 1997b), and it has been suggested that dogs consume cat feces or roll in cat feces and thereby increase human contact with *Toxoplasma gondii* oocysts when they return home (Frenkel and Parker, 1996). Pregnant women or immunocompromised individuals should not change the cat's litter box. If feces are removed daily this will also help prevent exposure by removing oocysts before they can sporulate. Oocysts can survive in the soil for years and can be disseminated from the original site of deposition by erosion, other mechanical means, and phoretic vectors. Inhalation of oocysts stirred up in the dust by horses has been associated with an outbreak of human toxoplasmosis at a riding stable (Teutsch et al., 1979). Oocysts are not likely to remain in the air for extended periods of time. Washing fruits and vegetables and wearing gloves while gardening are means of preventing exposure to oocysts. Oocysts are killed by exposure to 0.25 kGy gamma irradiation, and this is a potential means of killing oocysts on contaminated fruit and vegetables (Dubey et al., 1996).

Toxoplasma gondii oocysts were not isolated from the fur of oocyst-excreting cats (Dubey, 1995). Therefore, it is unlikely that infection can be obtained by petting a cat. Tachyzoites are not likely to be present in the oral cavity of cats with active *Toxoplasma gondii* infection, and none would be in a chronic infection; therefore, it is unlikely that a cat bite would transmit *Toxoplasma gondii* infection. Cat scratches are also unlikely to transmit *Toxoplasma gondii* infection.

Important Aspects of Human Maternal Toxoplasmosis. Pregnant women and immunocompromised patients should follow the prevention guidelines in Table 1.7. Immunocompetent women with *Toxoplasma gondii* antibody titers prior to becoming pregnant are considered immune and will not transmit the parasite to the fetus if exposed during pregnancy. It is important for a pregnant woman to know her titer because it can serve as a baseline if exposure is suspected during pregnancy. About 60 percent of women infected with *Toxoplasma gondii* during pregnancy will transmit the infection to the fetus. The age at which the fetus becomes infected determines the severity of subsequent disease. Few cases of fetal infection occur when the mother is infected during weeks 1 to 10; however, severe disease occurs in the infants that do become infected (Remington et al., 1995). Pregnant women are at greatest risk of delivering a severely infected infant if infected during weeks 10 to 24 of gestation (Remington et al., 1995). If *Toxoplasma gondii* infection of the mother occurs at weeks 26 to 40, there is a low risk of delivery of a severely infected infant, but most infants will be infected and have mild symptoms (Remington et al., 1995).

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Unclassified *Toxoplasma gondii*-Like Organism

Etymology

This organism has not been named.

History

This parasite was first reported in the early 1990s (Dubey et al., 1992; Dubey and Carpenter, 1993; Dubey and Fenner, 1993). It closely resembles *Toxoplasma gondii,* but the tissue cysts of this organism are about twice as large as those of *Toxoplasma gondii* (Figs. 1.20–1.22).

Geographic Distribution and Prevalence

Dubey and Carpenter (1993) found this organism in 3 of 103 cats examined in a retrospective study of feline toxoplasmosis. The subjects had been examined at necropsy at the Angell Memorial Animal Hospital, Boston, Massachusetts, between 1952 to 1991.