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Toxoplasma gondii

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1. INTRODUCTION

Infection with the protozoan parasite *Toxoplasma gondii* is one of the most common parasitic infections of man and other warm-blooded animals *(1)*. It has been found worldwide from Alaska to Australia. Nearly one-third of humanity has been exposed to this parasite *(1)*. In most adults it does not cause serious illness, but it can cause blindness and mental retardation in congenitally infected children, blindness in persons infected after birth, and devastating disease in immunocompromised individuals. Consumption of raw or undercooked meat products and contamination of food or drink with oocysts are the major risk factors associated with *T. gondii* infection.

2. CLASSIFICATION AND IDENTIFICATION

T. gondii is a coccidian parasite with cats as the definitive host, and warm-blooded animals as intermediate hosts *(2)*. It is one of the most important parasites of animals. It belongs to:

Phylum: Apicomplexa; Levine, 1970
Class: Sporozoasida; Leukart, 1879
Subclass: Coccidiasina; Leukart, 1879
Order: Eimeriorina; Leger, 1911
Family: Toxoplasmatidae; Biocca, 1956

There is only one species of *Toxoplasma*, *T. gondii*.

Coccidia in general have complicated life cycles. Most coccidia are host-specific, and are transmitted via a fecal–oral route. Transmission of *T. gondii* occurs via the fecal–oral route, as well as through consumption of infected meat, and by transplacental transfer from mother to fetus *(1,2)*.

The name *Toxoplasma* (toxon = arc, plasma = form) is derived from the crescent shape of the tachyzoite stage (Fig. 1). There are three infectious stages of *T. gondii*: the tachyzoites (in groups), the bradyzoites (in tissue cysts), and the sporozoites (in oocysts).

The tachyzoite is often crescent-shaped and is approximately the size (2×6 μm) of a red blood cell (Fig. 1A). The anterior end of the tachyzoite is pointed, and the posterior end is round. It has a pellicle (outer covering), several organelles including subpellicular

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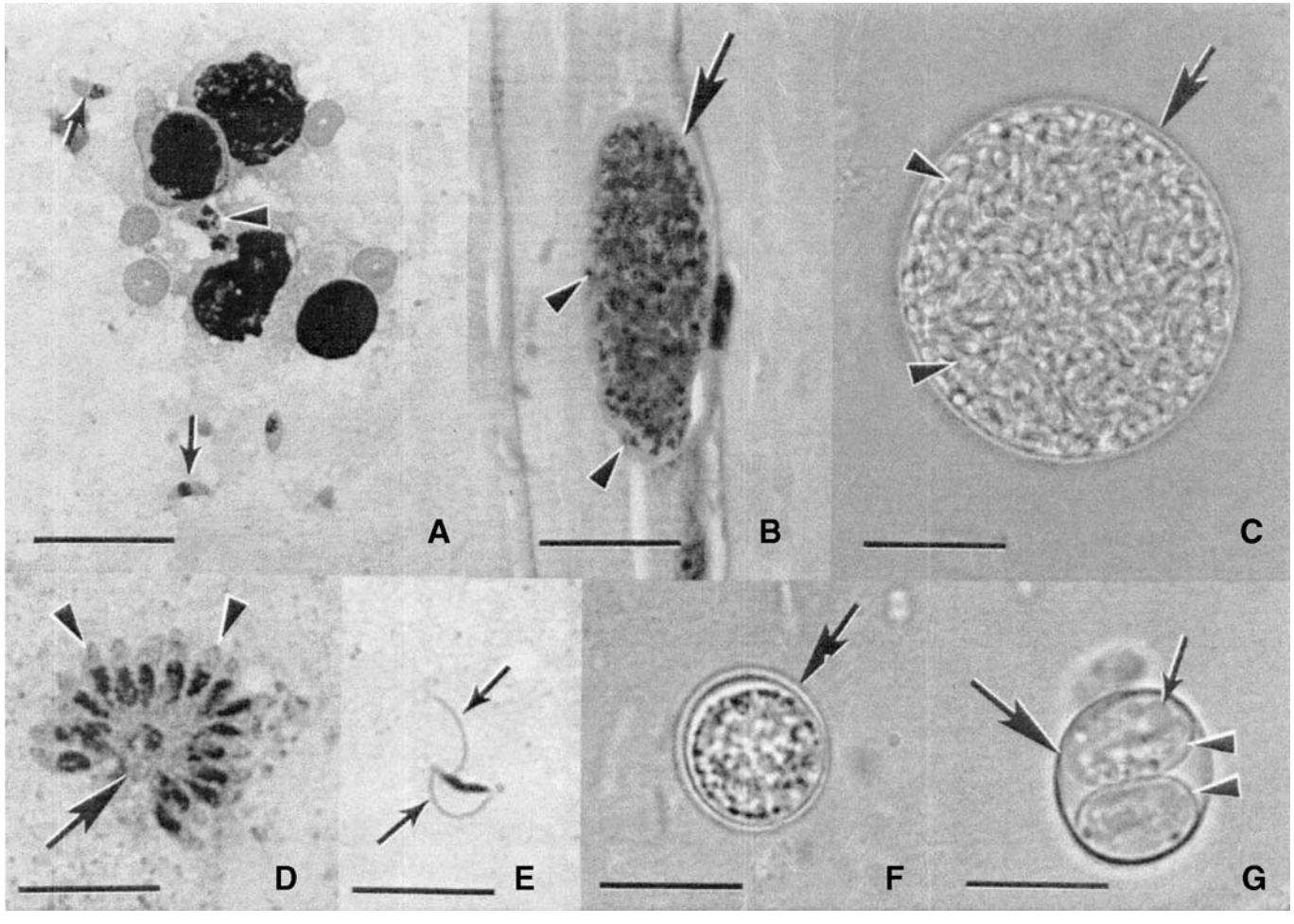

Fig. 1.

microtubules, mitochondrium, smooth and rough endoplasmic reticulum, a Golgi apparatus, apicoplast, ribosomes, a micropore, and a well-defined nucleus. The nucleus is usually situated toward the central area of the cell.

The tachyzoite enters the host cell by active penetration of the host cell membrane and can tilt, extend, and retract as it searches for a host cell. After entering the host cell, the tachyzoite becomes ovoid in shape and is surrounded by a parasitophorous vacuole. *T. gondii* in a parasitophorous vacuole is protected from host defense mechanisms. The tachyzoite multiplies asexually within the host cell by repeated divisions in which two progeny form within the parent parasite, consuming it (Fig. 1A). Tachyzoites continue to divide until the host cell is filled with parasites. Cells rupture, and free tachyzoites infect neighboring cells and the cycle is repeated. After an unknown number of cycles, *T. gondii* forms tissue cysts. Tissue cysts vary in size from 5 to 70 μm and remain intracellular (Fig. 1B,C). The tissue cyst wall is elastic, thin (< 0.5 μm), and may enclose hundreds of the crescent-shaped, slender *T. gondii* stage known as bradyzoites (*[3]*; Fig. 1C). The bradyzoites are approx 7 × 1.5 μm. Bradyzoites differ structurally only slightly from tachyzoites. They have a nucleus situated toward the posterior end whereas the nucleus in tachyzoites is more centrally located. Bradyzoites are more slender than are tachyzoites and they are less susceptible to destruction by proteolytic enzymes than are tachyzoites. Although tissue cysts containing bradyzoites may develop in visceral organs, including lungs, liver, and kidneys, they are more prevalent in muscular and neural tissues (Fig. 1B), including the brain (Fig. 1C), eye, skeletal, and cardiac muscle. Intact tissue cysts probably do not cause any harm and can persist for the life of the host.

All coccidian parasites have an environmentally resistant stage in their life cycle, called the oocyst. Oocysts of *T. gondii* are formed only in cats, probably in all members of the Felidae (Figs. 2 and 3). Cats shed oocysts after ingesting any of the three infectious stages of *T. gondii*, i.e., tachyzoites, bradyzoites, and sporozoites *(4–6)*. Prepatent periods (time to the shedding of oocysts after initial infection) and frequency of oocyst shedding vary according to the stage of *T. gondii* ingested. Prepatent periods are 3–10 d after ingesting tissue cysts and 18 d or more after ingesting tachyzoites or oocysts *(4–7)*. Less than 50% of cats shed oocysts after ingesting tachyzoites or oocysts, whereas nearly all cats shed oocysts after ingesting tissue cysts *(5)*.

After the ingestion of tissue cysts by cats, the tissue cyst wall is dissolved by proteolytic enzymes in the stomach and small intestine. The released bradyzoites penetrate the

Fig. 1. Stages of *Toxoplasma gondii*. (**A**) Tachyzoites in impression smear of lung. Note crescent-shaped individual tachyzoites (arrows), dividing tachyzoites (arrowheads) compared with size of host red blood cells and leukocytes; Giema stain. (**B**) Tissue cysts in section of muscle. The tissue cyst wall is very thin (arrow) and encloses many tiny bradyzoites (arrowheads); H&E stain. (**C**) Tissue cyst separated from host tissue by homogenization of infected brain. Note tissue cyst wall (arrow) and hundreds of bradyzoites (arrowheads); Unstained. (**D**) Schizont (arrow) with several merozoites (arrowheads) separating from the main mass. Impression smear of infected cat intestine; Giemsa stain. (**E**) A male gamete with two flagella (arrows). Impression smear of infected cat intestine; Giemsa stain. (**F**) Unsporulated oocyst in fecal float of cat feces; Unstained. Note double-layered oocyst wall (arrow) enclosing a central undivided mass. (**G**) Sporulated oocyst with a thin oocyst wall (large arrow), two sporocysts (arrowheads). Each sporocyst has four sporozoites (small arrow) which are not in complete focus; Unstained. Scale bar: A–D = 20 μm; E–G = 10 μm.

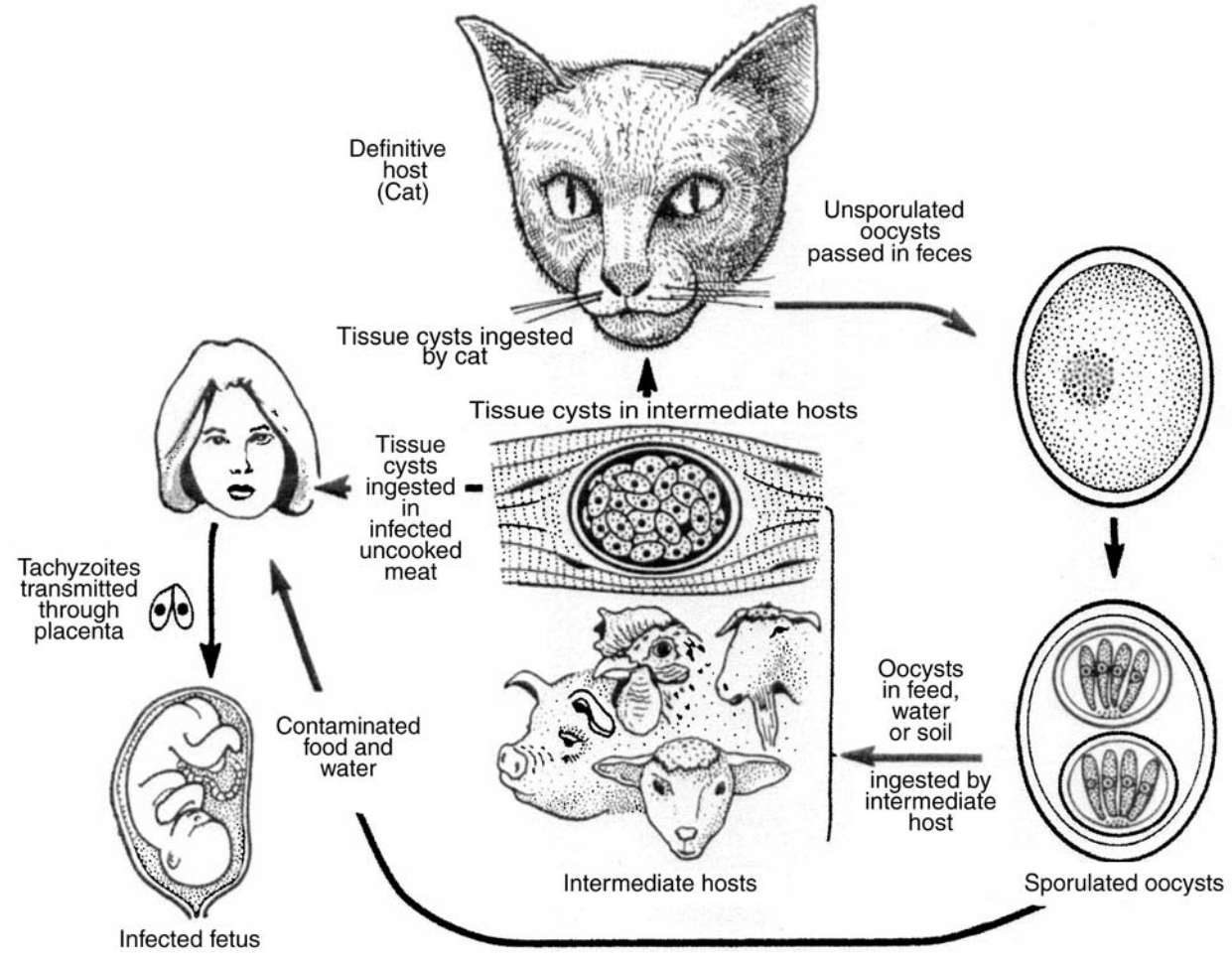

Fig. 2. Life cycle of *Toxoplasma gondii*.

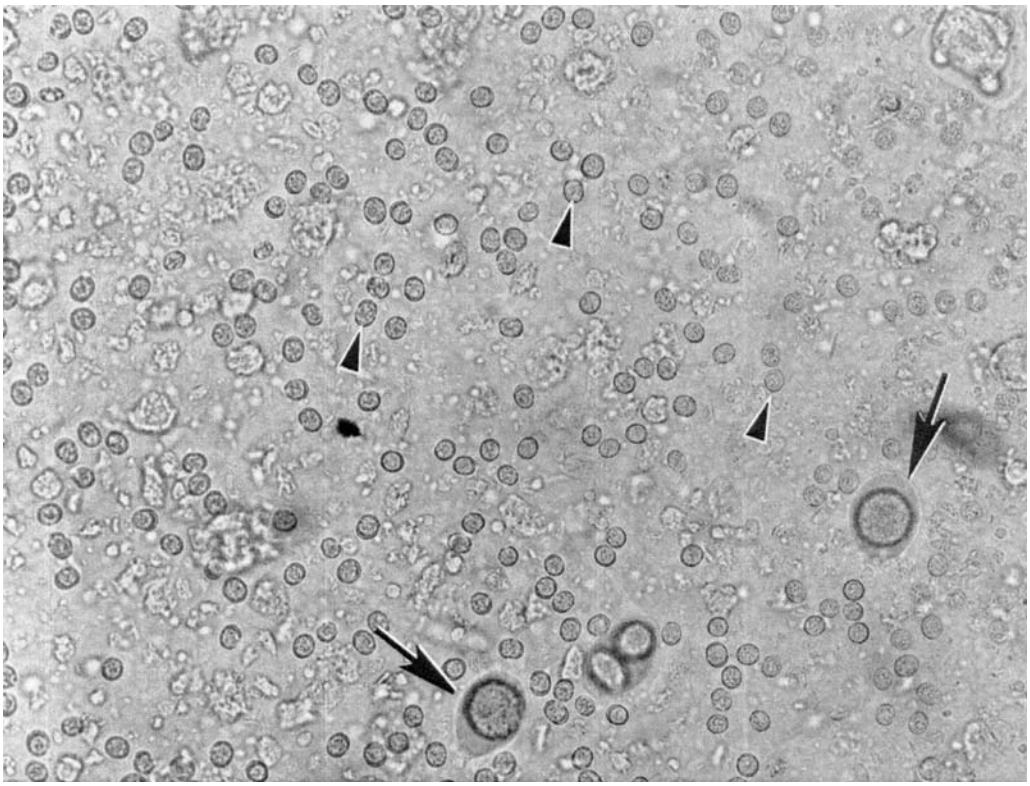

Fig. 3. *Toxoplasma gondii* oocysts in sugar fecal float of an infected cat. Note many spherical *T. gondii* oocysts (arrowheads). Also note oocysts of *Isospora felis* (arrows) which are often present in cat feces and are about four times the size of *T. gondii* oocysts.

epithelial cells of the small intestine and initiate development of numerous generations of asexual and sexual cycles of *T. gondii (4)*. *T. gondii* multiplies profusely in intestinal epithelial cells of cats (entero-epithelial cycle) and these stages are known as schizonts (Fig. 1D). Organisms (merozoites) released from schizonts form male and female gametes. The male gamete has two flagella (Fig. 1E), and it swims to and enters the female gamete. After the female gamete is fertilized by the male gamete (Fig. 1E), oocyst wall formation begins around the fertilized gamete. When oocysts are mature, they are discharged into the intestinal lumen by the rupture of intestinal epithelial cells.

In freshly passed feces, oocysts are unsporulated (noninfective). Unsporulated oocysts are subspherical to spherical and are 10×12 µm in diameter (Fig. 1F). They sporulate (become infectious) outside the cat within 1–5 d depending on aeration and temperature. Sporulated oocysts contain two ellipsoidal sporocysts (Fig. 1G). Each sporocyst contains four sporozoites. The sporozoites are 2×6 to 8 µm in size.

As the entero-epithelial cycle progresses, bradyzoites penetrate the lamina propria of the feline intestine and multiply as tachyzoites. Within a few hours after infection of cats, *T. gondii* may disseminate to extra-intestinal tissues via the lymphatics and the bloodstream. *T. gondii* persists in intestinal and extra-intestinal tissues of cats for at least several months, and possibly for the life of the cat.

Unlike many other microorganisms and in spite of a wide host range and worldwide distribution, *T. gondii* has a low genetic diversity. *T. gondii* strains have been classified into three genetic types (I, II, and III), based on antigens, isoenzymes, and restriction fragment length polymorphism *(8–11)*. Type I strains are considered highly virulent in outbred laboratory mice, whereas types II and III are considered less virulent for mice *(8,12–14)* but there is no correlation between virulence in mice to clinical disease in other animals or humans. Genetic typing of isolates has not provided clues to sources of infection for humans or animals.

3. TRANSMISSION OF *T. GONDII*

Toxoplasmosis may be acquired by ingestion of oocysts or by ingestion of tissue-inhabiting stages of the parasite. Contamination of the environment by oocysts is widespread because oocysts are shed by domestic cats and other felids *(1,2)*. Domestic cats are probably the major source of contamination because oocyst formation is greatest in domestic cats, which are extremely common. Widespread natural infection of the environment is possible because a cat may excrete millions of oocysts after ingesting as few as one bradyzoite or one tissue cyst, and many tissue cysts may be present in one infected mouse *(2,15)*. Sporulated oocysts survive for long periods under most ordinary environmental conditions and even in harsh environment for months. They can survive in moist soil, for example, for months and even years *(1,16)*. Oocysts in soil can be mechanically transmitted by invertebrates such as flies, cockroaches, dung beetles, and earthworms, which can spread oocysts onto human food and animal feeds.

Infection rates in cats are determined by the rate of infection in local avian and rodent populations because cats are thought to become infected by eating these animals. The more oocysts in the environment, the more likely it is that prey animals would be infected, and this in turn would increase the infection rate in cats.

In certain areas of Brazil, approx 60% of 6–8-yr-old children have antibodies to *T. gondii* linked to the ingestion of oocysts from the environment heavily contaminated with *T. gondii* oocysts *(17)*. Infection in aquatic mammals indicates contamination and survival of oocysts in sea water *(16,18–20)*. The largest recorded outbreak of clinical toxoplasmosis in humans was epidemiologically linked to drinking water from a municipal water reservoir in British Columbia, Canada *(21)*. This water reservoir was thought to be contaminated with *T. gondii* oocysts excreted by cougars (*Felis concolor*). Although attempts to recover *T. gondii* oocysts from water samples in the British Columbia outbreak were unsuccessful, methods to detect oocysts were reported *(22)*. At present there are no commercial reagents available to detect *T. gondii* oocysts in the environment.

Increased risk for *T. gondii* infection has been associated with many food-related factors, including: eating raw or undercooked pork, mutton, lamb, beef, or mincemeat products *(23–26)*, eating raw or unwashed vegetables, raw vegetables outside the home, or fruits *(23)*, washing kitchen knives infrequently *(25)*, and having poor hand-hygiene *(23)*. Decreased risk for *T. gondii* infection has been found to be associated with eating a meat-free diet *(27)*. Outbreaks of toxoplasmosis have been attributed to ingestion of raw or undercooked beef, lamb, pork, and venison *(28–34)*; and consumption of raw goat's milk *(35)*.

In the United States, infection in humans is probably most often the result of ingestion of tissue cysts contained in undercooked meat *(1,27,36)*, though the exact contribution

of foodborne toxoplasmosis vs oocyst induced toxoplasmosis to human infection is currently unknown. *T. gondii* infection is common in many animals used for food, including sheep, pigs, goats, and rabbits. Birds and other domesticated and wild animals can also become infected *(1)*. Animals that survive infection harbor tissue cysts, and can therefore transmit *T. gondii* infection to human consumers *(37,38)*. In one study, viable *T. gondii* tissue cysts were isolated from 17% of 1000 adult pigs (sows) from a slaughter plant in Iowa *(39)*. Serological surveys of pigs from pig farms in Illinois indicate an infection rate of about 3% in market weight animals and 20% for breeding pigs, suggesting that age is a factor for pigs acquiring *Toxoplasma* infection *(40)*. Serological surveys of pigs on New England farms revealed an overall infection rate of 47% *(41)*, and from one farm *T. gondii* was isolated from 51 of 55 market age (feeder) pigs *(42)*. Infection in cattle is less prevalent than in sheep or pigs in the United States, however, recent surveys in several European countries using serology and PCR to detect parasite DNA have shown that the infection rates in pigs and horses are negligible, compared to sheep and cattle that ranges from 1 to 6% *(43,44)*. Serological surveys in eastern Poland revealed that 53% of cattle, 15% of pigs, and 0–6% of chickens, ducks, and turkeys were positive for *T. gondii* infection; nearly 50% of the people in the region were also serologically positive for *T. gondii* infection *(45)*. The prevalence of *T. gondii* infection in commercially raised chickens in the United States and elsewhere has not been investigated; however, most chicken meat in the United States is cooled to near freezing or is completely frozen at the packing plant *(46)*, which would kill organisms in tissue cysts *(47)*. The relative contributions of undercooked pork, beef, and chicken to *T. gondii* infection in humans was unknown; a nationwide retail meat survey was conducted to determine the risk to US consumers of purchasing pork, beef, and chicken containing viable *T. gondii* tissue cysts at the retail level *(95)*. The national retail meats survey for *T. gondii* collected 6,282 meat samples; 2094 each of beef, chicken, and pork, from 698 randomly selected retail outlets in 28 major geographic regions in the U.S. The survey determined that viable *T. gondii* was present in 0.4% of retail pork. There was little risk of acquiring *T. gondii* after ingestion of beef and chicken.

T. gondii infection is also prevalent in game animals. Among wild game, *T. gondii* infection is most prevalent in black bears and in white-tailed deer. Serological surveys of white-tailed deer in the United States have demonstrated seropositivity of 30–60% *(48–50)*, and viable *T. gondii* can be demonstrated in half of seropositive deer *(51)*. A recent study reported the occurrence of clinical toxoplasmosis and necrotizing retinitis in deer hunters with a history of consuming undercooked or raw venison *(34)*. Approx 80% of black bears are infected in the United States *(52)*, and about 60% of raccoons have antibodies to *T. gondii (53,54)*. Because raccoons and bears scavenge for their food, infection in these animals is a good indicator of the prevalence of *T. gondii* in the environment.

Virtually all edible portions of an animal can harbor viable *T. gondii* tissue cysts, and tissue cysts can survive in food animals for years. The number of *T. gondii* in meat from food animals is very low. It is estimated that as few as one tissue cyst may be present in 100 g of meat. Since it is not practical to detect this low level of *T. gondii* infection in meat samples, digestion of meat samples in trypsin or pepsin is used to concentrate *T. gondii* for detection *(55)*. Digestion in trypsin and pepsin ruptures the *T. gondii* tissue cyst wall, releasing hundreds of bradyzoites. The bradyzoites survive

in the digests for several hours. Even in the digested samples, only a few *T. gondii* are present and their identification by direct microscopic examination is not practical. Therefore, the digested material is bioassayed in mice *(55)*. The mice inoculated with digested material have to be kept for 6–8 wk before *T. gondii* infection can be detected reliably—this procedure is not practical for mass scale samples. The detection of *T. gondii* DNA in meat samples by PCR has been reported *(56)*, but there are no data on specificity and sensitivity of this method to detect *T. gondii*. A highly sensitive method using a Real-Time PCR and fluorogenic probes was found to detect *T. gondii* DNA from as few as four bradyzoites in meat samples *(57)*. This method is now being tested to detect *T. gondii* in meat samples obtained from slaughtered animals. Cultural habits of people may affect the acquisition of *T. gondii* infection *(26)*. For example, in France the prevalence of antibody to *T. gondii* is very high in humans. Though 84% of pregnant women in Paris have antibodies to *T. gondii*, only 32% of pregnant women in New York City and 22% in London have such antibodies *(1)*. Jones et al. *(58)* have shown a seroprevalence of 23% in the United States in the National Health and Nutrition Examination Survey (NHANES), which is a representative sample of the US noninstitutionalized civilian population. The high incidence of *T. gondii* infection in humans in France appears to be related in part to the French habit of eating some of their meat products undercooked or uncooked. In contrast, the high prevalence of *T. gondii* infection in Central and South America is probably due to high levels of contamination of the environment with oocysts *(1,17,59,60)*. Having said this, it should be noted that the relative frequency of acquisition of toxoplasmosis from eating raw meat and that related to ingestion of food or water contaminated by oocysts from cat feces is very difficult to determine and as a result, statements on the subject are at best controversial. There are no tests at the present time to determine the source of infection in a given person. There is little, if any, danger of *T. gondii* infection by drinking cow's milk and, in any case, cow's milk is generally pasteurized or even boiled, but infection has followed drinking unboiled goat's milk *(1)*. Raw hens' eggs, although an important source of *Salmonella* infection, are extremely unlikely to transmit *T. gondii* infection.

4. PATHOGENICITY

T. gondii can multiply in virtually any cell in the body. How *T. gondii* is destroyed in immune cells is not completely known *(61)*. All extracellular forms of the parasite are directly affected by antibody but intracellular forms are not. It is believed that cellular factors, including lymphocytes and lymphokines, are more important than humoral factors in immune-mediated destruction of *T. gondii (61)*.

Immunity does not eradicate infection. *T. gondii* tissue cysts persist several years after acute infection. The fate of tissue cysts is not fully known. Whether bradyzoites can form new tissue cysts directly without transforming into tachyzoites is not known. It has been proposed that the tissue cysts may at times rupture during the life of the host. The released bradyzoites may be destroyed by the host's immune responses, or there may be formation of new tissue cysts.

In immunosuppressed patients, such as those given large doses of immunosuppressive agents in preparation for organ transplants and in those with AIDS, rupture of a tissue cyst may result in transformation of bradyzoites into tachyzoites and renewed

multiplication. The immunosuppressed host may die from toxoplasmosis unless treated. It is not known how corticosteroids cause relapse, but it is unlikely that they directly cause rupture of the tissue cysts.

Pathogenicity of *T. gondii* is determined by the virulence of the strain and the susceptibility of the host species. *T. gondii* strains may vary in their pathogenicity in a given host. Certain strains of mice are more susceptible than others and the severity of infection in individual mice within the same strain may vary. Certain species are genetically resistant to clinical toxoplasmosis. For example, adult rats do not become ill, while young rats can die of toxoplasmosis. Mice of any age are susceptible to clinical *T. gondii* infection. Adult dogs, like adult rats, are resistant, whereas puppies are fully susceptible to clinical toxoplasmosis. Cattle and horses are among the hosts more resistant to clinical toxoplasmosis, whereas certain marsupials and New World monkeys are highly susceptible to *T. gondii* infection *(1)*. Nothing is known concerning genetically determined susceptibility to clinical toxoplasmosis in higher mammals, including humans.

5. CLINICAL CHARACTERISTICS

T. gondii infection is widespread in humans though its prevalence varies widely from place to place. In the United States and in the United Kingdom, it is estimated that 16–40% of people are infected *(58)*, whereas in Central and South America and continental Europe, estimates of infection range from 50 to 80% *(1,17)*. Most infections in humans are asymptomatic but at times the parasite can produce devastating disease. Infection may be congenitally or postnatally acquired. Congenital infection occurs only when a woman becomes infected during pregnancy. Congenital infections acquired during the first trimester are more severe than those acquired in the second and third trimester *(62,63)*. While the mother rarely has symptoms of infection, she does have a temporary parasitemia. Focal lesions develop in the placenta and the fetus may become infected. At first there is generalized infection in the fetus. Later, infection is cleared from the visceral tissues and may localize in the central nervous system. Although most children are asymptomatic at birth *(64)*, a wide spectrum of clinical diseases can occur in congenitally infected children *(62,65)* or develop later in life *(66)*. Mild disease may consist of slightly diminished vision, whereas severely diseased children may have the full tetrad of signs: retinochoroiditis (inflammation of the inner layers of the eye), hydrocephalus (big head), convulsions, and intracerebral calcification. Of these, hydrocephalus is the least common but most dramatic result of toxoplasmosis (Fig. 4). By far the most common sequela of congenital toxoplasmosis is ocular disease *(62,63)*. In addition to ocular infection that occurs with congenital disease, up to 2% of adults newly infected with *T. gondii* develop ocular lesions, and because most people are infected with *T. gondii* after birth, authorities now believe that the majority of Toxoplasma-induced ocular disease is a result of infection with *T. gondii* after birth *(67)*.

The socio-economic impact of toxoplasmosis in human suffering and the cost of care of sick children, especially those with mental retardation and blindness, are enormous *(68,69)*. The testing of all pregnant women for *T. gondii* infection is compulsory in some European countries including France and Austria. The cost benefits of such mass screening are being debated in many other countries *(63)*. A number of recent studies have raised questions about the effectiveness of treating acutely infected pregnant

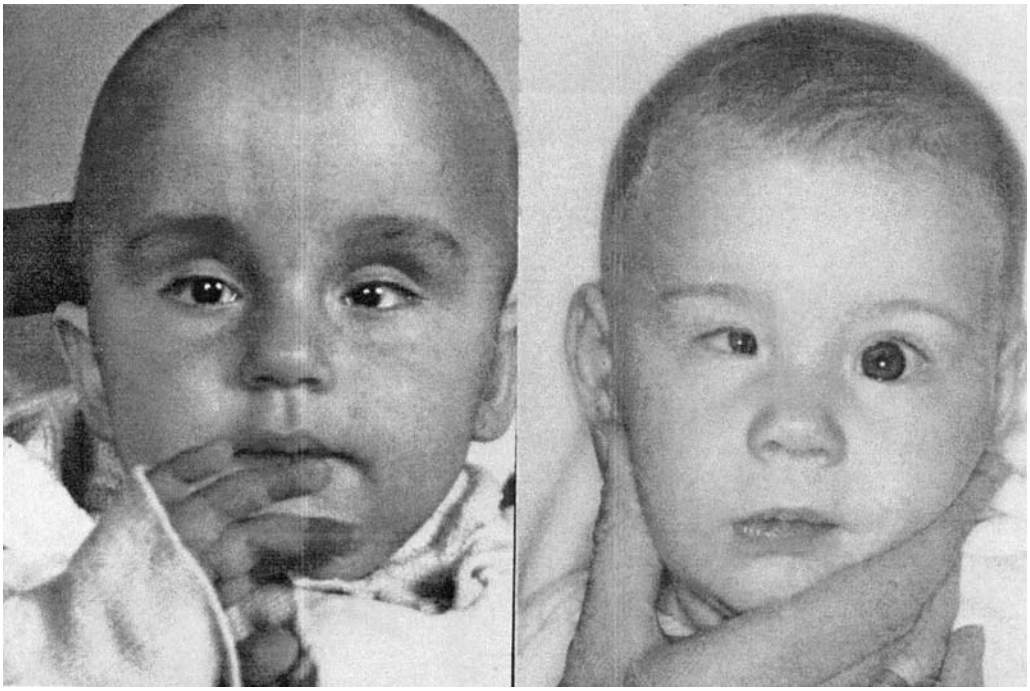

Fig. 4. Congenital toxoplasmosis in children. Hydrocephalus with bulging forehead (left) and microophthalmia of the left eye (right).

women to prevent transmission to the fetus and or prevent sequela in infants *(70–72)*. Newborn screening is another option for identifying infected infants and has been used in two states in the United States *(64)*, but infected newborns that are identified by screening require a year of follow-up and treatment with potentially toxic drugs and the efficacy of treating infants with congenital toxoplasmosis has not been documented in well-controlled studies *(73)*.

Postnatally acquired infection may be localized or generalized. Oocyst-transmitted infections may be more severe than tissue cyst-induced infections *(1,74–76)*. Enlarged lymph nodes are the most frequently observed clinical form of toxoplasmosis in humans (Table 1). Lymphadenopathy may be associated with fever, fatigue, muscle pain, sore throat, and headache. Although the condition may be benign, diagnosis of *T. gondii*-associated lymphadenopathy is important in pregnant women because of the risk to the fetus. In a British Columbia outbreak, of 100 people who were diagnosed with acute infection, 51 had lymphadenopathy and 20 had retinitis *(21,77)*. Encephalitis is an important manifestation of toxoplasmosis in immunosuppressed patients because it causes the most severe damage to the patient *(1,78)*. Infection may occur in any organ. Patients may have headache, disorientation, drowsiness, hemiparesis, reflex changes, and convulsions, and many become comatose.

Toxoplasmosis ranked high on the list of diseases which lead to death of patients with acquired immunodeficiency syndrome (AIDS) in the United States; approx 10% of AIDS patients in the United States and up to 30% in Europe were estimated to die from toxoplasmosis *(78)* before prophylactic medications such as trimethoprim-sulfamethoxazole,

Table 1
Frequency of Symptoms in People With Postnatally Acquired Toxoplasmosis From Oocyst Ingestion[a]

Symptoms	Patients with symptoms (%)	
	Atlanta outbreak[b] (35 Patients)	Panama outbreak[c] (35 Patients)
Fever	94	90
Lymphadenopathy	88	77
Headache	88	77
Myalgia	63	68
Stiff neck	57	55
Anorexia	57	NR[d]
Sore throat	46	NR
Artharlgia	26	29
Rash	23	0
Confusion	20	NR
Earache	17	NR
Nausea	17	36
Eye pain	14	26
Abdominal pain	11	55

[a]Both the outbreaks thought to be caused by infection with oocysts.
[b]From ref. *(74)*.
[c]From ref. *(75)*.
[d]Not reported.

and the treatment for HIV infection with highly active antiretroviral therapy (HAART) were widely available. However, since use of prophylactic therapy and HAART became common in the mid-1990s, the number of persons with AIDS dying of toxoplasmosis has markedly declined *(79)*. Although in AIDS patients any organ may be involved, including the testis, dermis, and the spinal cord, infection of the brain is most frequently reported. Most AIDS patients suffering from toxoplasmosis have bilateral, severe, and persistent headache which responds poorly to analgesics. As the disease progresses, the headache may give way to a condition characterized by confusion, lethargy, ataxia, and coma. The predominant lesion in the brain is necrosis, especially of the thalamus *(61)*.

Diagnosis is made by biologic, serologic, or histologic methods or by a combination of the above. Clinical signs of toxoplasmosis are nonspecific and are not sufficiently characteristic for a definite diagnosis. Detection of *T. gondii* antibody in patients may aid diagnosis. There are numerous serologic procedures available for detection of humoral antibodies. These include the Sabin–Feldman dye test, the indirect hemagglutination assay, the indirect fluorescent antibody assay (IFA), the direct agglutination test, the latex agglutination test, the enzyme-linked immunoabsorbent assay (ELISA), and the immunoabsorbent agglutination assay test (IAAT). The IFA, IAAT and ELISA have been modified to detect IgM antibodies *(63)*. The IgM antibodies appear sooner after infection than the IgG antibodies and the IgM antibodies disappear faster than IgG antibodies after recovery *(63)*. Detection of IgM and IgG antibodies, along with a panel of other serologic tests including the avidity test, have been found to be

very helpful in diagnosing acute infection in pregnant women when conducted at a reference laboratory *(80,81)*.

6. CHOICE OF TREATMENT

In general, physicians are most likely to consider treatment for *T. gondii* infection in four circumstances: (1) pregnant women with acute infection to prevent fetal infection, (2) congenitally infected infants, (3) immunosuppressed persons, usually with reactivated disease, and (4) acute and recurrent ocular disease *(82)*. Although well-designed clinical trials have demonstrated the effectiveness of treatment in immunosuppressed persons for reactivated disease *(83–86)*, there is less evidence for the effectiveness of treatment in the other circumstances listed above *(70–73,87,88)*.

Sulfadiazine and pyrimethamine (Daraprim) are two drugs widely used for treatment of toxoplasmosis *(64,89)*. While these drugs have a beneficial action when given in the acute stage of the disease process when there is active multiplication of the parasite, they will not usually eradicate infection. It is believed that these drugs have little effect on subclinical infections, but the growth of tissue cysts in mice has been restrained with sulfonamides. Certain other drugs, diaminodiphenylsulfone, atovaquone, azithromycin, clarithromycin, dapson, spiramycin, and clindamycin are also used to treat toxoplasmosis in difficult cases, often in combination with pyrimethamine. Medications are also prescribed for preventive or suppressive treatment in HIV-infected persons and have been quite effective when used for this purpose *(90)*.

7. PREVENTION AND CONTROL

To prevent infection of human beings by *T. gondii*, the hands of people handling meat should be washed thoroughly with soap and water before they go to other tasks *(1,36)*. All cutting boards, sink tops, knives, and other materials coming in contact with uncooked meat should be washed with soap and water also. Washing is effective because of the physical removal of material from the hands and because the stages of *T. gondii* in meat are killed by contact with soap and water *(1)*.

T. gondii organisms in meat can be killed by exposure to extreme cold or heat. Tissue cysts in meat are killed by heating the meat throughout to 67°C *(91)*. *T. gondii* in meat is killed by cooling to −13°C *(47)*. *Toxoplasma* in tissue cysts are also killed by exposure to 0.5 krad of γ irradiation *(92)*. Meat should be cooked to 145°F for beef, 160°F for pork, ground meat, and wild game, and 180°F for poultry (in thigh, to ensure doneness) before consumption, and tasting meat while cooking or while seasoning should be avoided. Pregnant women, especially, should avoid contact with cats, soil, and raw meat. Pet cats should be fed only dry, canned, or cooked food. The cat litter box should be emptied every day, preferably not by a pregnant woman or an immunosuppressed person. Pregnant women and immunosuppressed persons should wear gloves while gardening or changing cat litter (if no one else can change the litter) and wash their hands thoroughly afterwards. Fruits and vegetables should be washed thoroughly before eating because they may have been contaminated with cat feces or soil containing oocysts from cat feces. Untreated water should not be consumed, particularly in developing countries. Women of childbearing age and expectant mothers should be aware of the dangers of toxoplasmosis *(36,93,94)*. At present there is no vaccine to prevent toxoplasmosis in humans.

8. SUMMARY

Infection by the protozoan parasite *T. gondii* is widely prevalent in humans and animals. Although it usually causes asymptomatic infection in immune competent adults, *T. gondii* can cause devastating disease in congenitally infected children and those with depressed immunity. To prevent human infection, all meat should be cooked well and fruits and vegetables washed before consumption, precautions such as wearing gloves and washing hands should be taken during and after gardening to prevent exposure to soil contaminated with *T. gondii* oocysts excreted in cat feces, and ingestion of untreated water should be avoided, especially in developing countries.

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