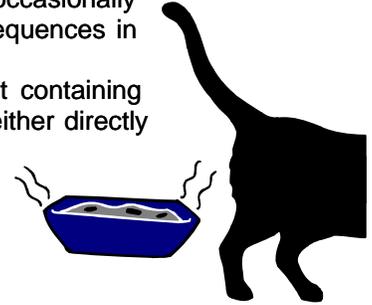




## General Information

- *Toxoplasma gondii* is a protozoal parasite capable of infecting any warm-blooded animal, including humans.
- Wild and domestic cats are the only known definitive hosts of *Toxoplasma*; they shed infective stages of the parasite in their feces. All other animals and humans serve as intermediate hosts in which the parasite may cause systemic infection, which typically results in the formation of tissue cysts.
- In all species, *Toxoplasma* infection is usually subclinical, although it may occasionally cause mild, non-specific signs. Infection may have much more serious consequences in immunocompromised or pregnant animals and people.
- The major modes of transmission include consumption of undercooked meat containing *Toxoplasma* cysts, fecal-oral transfer of *Toxoplasma* oocysts from cat feces (either directly or in contaminated food, water or soil), and vertical transmission from mother to fetus if primary (i.e. first-time) infection occurs during pregnancy.
- The risk of contracting *Toxoplasma* infection from cleaning the litter box of a house cat is actually very small, especially if a few simple precautions such as appropriate hand washing are observed.



## Prevalence of *Toxoplasma*

*Toxoplasma* is one of the most widespread zoonotic pathogens in the world. In most animals and people, primary infection results in a detectable antibody titre for the life of the host, therefore seroprevalence (i.e. previous exposure to the parasite but not necessarily clinical disease) increases with age.

### Humans

- Because toxoplasmosis is not a reportable disease in Ontario and most of North America, it is difficult to estimate the prevalence of infection in animals or people. An average of 15 000 cases of clinical toxoplasmosis are reported annually in the USA, but it has been estimated that the actual number of cases is likely closer to 225 000. It is estimated that 50% of these cases occur due to foodborne transmission of *Toxoplasma*.
- Seroprevalence in the general population in persons over 12 years of age was estimated to be 22.5% in one North American study performed from 1988-1994. Worldwide, seroprevalence ranges from 0-100% depending on country, geographic area and even ethnic group.
- Between 40 to 400 children born in Canada each year are infected with *Toxoplasma* before birth.

### Animals

- The prevalence of oocyst shedding in cats is very low (0-1%), even though serological studies indicate that at least 15-40% of cats have been infected, depending on how the cats are fed and whether they go outdoors.
- Disease and exposure are more common in cats and other pets that go outdoors, hunt, or are fed raw meat.

## Zoonotic Risk & Other Risk Factors

- The risk of transmission of *Toxoplasma* from a household cat can be easily controlled by means of simple infectious disease control procedures (see Infection Control below). In one study from Norway, cleaning a cat litter box was found to be a strong risk factor for exposure to *Toxoplasma*. However the same study, and another European study, showed no association between *Toxoplasma* exposure and living with or near a cat.
  - Contamination of water sources and soil with the feces of wild or domestic cats is more difficult to control, and can lead to infection following ingestion of oocysts on unwashed, uncooked vegetables or in contaminated water. The largest human outbreak of toxoplasmosis ever reported occurred in Victoria, BC in 1995, and was attributed to fecal contamination of the water supply from domestic and wild cats.
  - Cockroaches and flies may also transfer *Toxoplasma* oocysts from cat feces to food, water, utensils or other surfaces.
  - Contact with contaminated soil or sand, such as in a garden or a sandbox, may also be associated with *Toxoplasma* infection.
  - Consumption of undercooked meat is one of the principle risk factors for *Toxoplasma* infection.
- The importance of these various risk factors likely varies considerably between ethnic groups due to differences in cultural habits regarding exposure to undercooked meat, soil and cats.



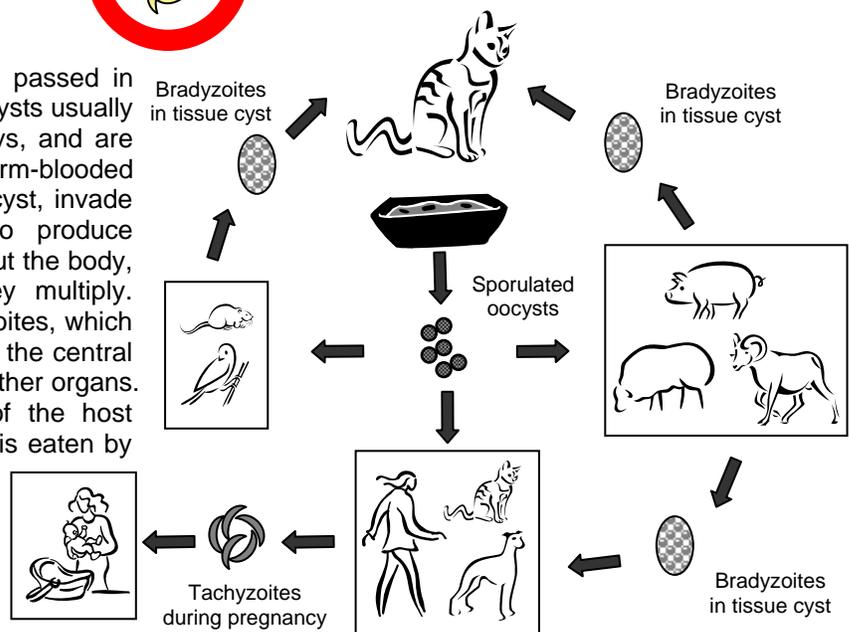


## Life Cycle of *Toxoplasma*

Unsporulated oocysts of *Toxoplasma* are passed in the feces of acutely infected cats. The oocysts usually sporulate (forming sporozoites) in 1-5 days, and are then infective when ingested by any warm-blooded host. In the intestine, the sporozoites excyst, invade intestinal cells and begin to divide to produce tachyzoites. These then migrate throughout the body, invading and destroying tissue cells as they multiply. Eventually the tachyzoites become bradyzoites, which then form microscopic cysts within cells of the central nervous system, muscle, and sometimes other organs. The cysts typically persist until death of the host without causing clinical signs. If the host is eaten by another animal, the bradyzoites excyst in the intestine and the process is repeated, forming tissue cysts in the new host.

If a tissue cyst is eaten by a cat, the bradyzoites invade the intestinal epithelial

cells and undergo a different series of divisions, forming meronts, and finally microgametes and macrogametocytes all within the intestinal wall. The microgametes fertilize the macrogametocytes. These then form a resistant wall to become unsporulated oocysts which are passed in the feces of the cat.



When fed tissue cysts, approximately 97% of cats infected for the first time will produce oocysts, usually within 3-10 days. They may shed for up to 20 days, but the majority of oocysts will be shed in just 1-2 days. Only 20% of cats fed oocysts will develop a patent infection, and the prepatent period may be 18 days or more. Contrary to previous beliefs, studies have shown that oocysts can be shed in low numbers by previously infected cats that are challenged again with the parasite or that become immunosuppressed due to disease or drug therapy.

## Transmission of *Toxoplasma*

Carnivorous animals are often infected with *Toxoplasma* through ingestion of bradyzoites from tissue cysts in infected prey, as are people who **eat undercooked meat**, particularly that of pigs, sheep and goats. *Toxoplasma* cysts are less commonly found in poultry and rarely found in beef. The prevalence of *Toxoplasma* infection in commercial farm animals has decreased significantly with the advent of intensive management practices. Free-range poultry, swine and small ruminants, marsupials (e.g. kangaroos) and some wild game are more likely to harbour cysts.

Oocysts are only shed by cats. **Unsporulated oocysts in fresh feces are not infective**; they need appropriate oxygen, humidity and temperature to sporulate. Sporulated oocysts are the most environmentally resistant life stage of the parasite. Ingestion of as few as ten oocysts may infect an intermediate host, while ingestion of 100 or more oocysts can cause a patent infection in a cat, which may shed tens to hundreds of millions of oocysts.

Tachyzoites are potentially infective, and may be found in the tissues of acutely infected animals, as well as the milk of sheep, goats, cows, and sometimes chicken eggs. However, tachyzoites are killed relatively easily by pasteurization, and uncommonly survive gastric digestion, although this may be more of a concern in infants who have lower concentrations of peptic enzymes. Any kind of cooking will kill tachyzoites in an egg. Toxoplasmosis can also be transmitted by organ transplants and blood transfusions, but this is uncommon.

**In utero transmission of *Toxoplasma*** occurs only if primary infection of the dam/mother occurs during pregnancy. Parasitemia then results in placentitis and infection of the fetus. This is more likely to occur in humans, sheep and goats, and sometimes in mice, cats and dogs. Under normal circumstances, a female that has been exposed to *Toxoplasma* 4-6 months prior to pregnancy will develop sufficient immunity to protect herself and the fetus for the rest of her life. However, if the immune response is suppressed by drug therapy or disease such as HIV/AIDS in humans, both the mother and the fetus may become susceptible to infection again. In humans, the risk of the infection being passed on to the fetus increases from the first trimester (10-25%) to the third trimester (60-90%). However, the potential congenital defects are more severe with earlier infections.



## Symptoms and Signs

Clinical signs of toxoplasmosis are caused by cellular destruction due to multiplying tachyzoites, which most commonly affect the brain, liver, lungs, skeletal muscle and eyes. Oocyst-induced infection may be more severe than that induced by ingestion of tissue cysts. Infection may be associated with other diseases such as HIV/AIDS in humans or immunosuppressive therapy in any species.



### Humans:

- Approximately 15% of cases of *Toxoplasma* infection are associated with clinical signs such as mild fever and lymphadenopathy, and may appear similar to mononucleosis or Hodgkin disease. Signs may persist for 1 to 12 weeks; more severe disease is very rare in immunocompetent individuals. Of clinical cases, 0.2%-0.7% may develop ocular toxoplasmosis (retinitis), but this is more commonly associated with congenital infection. If more severe disease develops, signs may be related to encephalitis, hepatitis, myositis or pneumonia.
- Worldwide, *Toxoplasma* encephalitis develops at some time in approximately 40% of individuals with AIDS, and is fatal in 10-30% of these cases. Individuals with low CD4 counts and high *Toxoplasma* titres are therefore often treated prophylactically for the disease with high-dose trimethoprim-sulfonamide combinations.
- Approximately 10% of congenital *Toxoplasma* infections result in abortion or neonatal death. In 10-23% of congenital infections, signs are present at birth; these may include hydrocephalus, chorioretinitis, hepatosplenomegally, microcephaly, and small size. Clinical signs of congenital *Toxoplasma* infection are not apparent at first in 67-80% of cases. Ocular toxoplasmosis may occur in up to 1/3 of children that survive congenital infection.

### Animals:

- In dogs and cats, primary systemic infection with *Toxoplasma* is typically either subclinical or may cause mild fever and lymphadenopathy. In rare cases when significant clinical disease develops, signs may include fever, lethargy, anorexia, and others signs associated with pneumonia, hepatitis, myositis or encephalitis. The onset of signs may be slow, or the disease may be rapidly fatal. Ocular lesions are much more common in cats than in dogs. Kittens and puppies are often severely affected and may be stillborn or die before weaning.
- Clinical infection in sheep and goats is much more common than in dogs and cats, and is primarily associated with reproductive problems, including abortion and birth of weak, uncoordinated young. The infection can also be common in birds, but it is rarely clinical.



## Diagnosis

Once infected with *Toxoplasma*, people and animals usually develop a life-long protective antibody titre, unless the individual is severely immunocompromised and unable to mount or sustain an appropriate humoral immune response. The organism itself can be detected in tissues or body fluids using either polymerase chain reaction (PCR) or bioassays in mice.

### Humans:



- There are several different serological tests used to diagnose toxoplasmosis in humans that are intended to help differentiate between latent and acute infections. Serum IgM titres indicate recent infection, whereas serum IgG titres persist longer and therefore typically indicate previous infection. However, both types of antibodies are usually detectable within 1-2 weeks of infection.
- Some *Toxoplasma* IgM test kits have relatively high false-positive rates, and results must therefore be interpreted carefully.
- Measurement of IgG avidity can also help "age" the antibody response.
- The modified latex agglutination test (MAT) detects IgG, but can help differentiate acute and chronic infections based on reactivity with acetone versus formalin-fixed antigen. It is considered extremely sensitive.

Serological screening of pregnant women is not generally recommended in the USA and Canada, as it is in some European countries such as Belgium and France, because the risk of exposure to *Toxoplasma* is comparatively low. Diagnosis of *in utero* infection is most commonly accomplished by detecting *Toxoplasma* DNA in amniotic fluid using PCR. A positive test should be followed up by a fetal ultrasonographic examination to look for physical congenital defects.



## Animals:

- Compared to humans, development and persistence of IgM in systemically infected cats is very inconsistent, and is not a reliable marker of acute *Toxoplasma* infection. Furthermore, some cats may not develop IgG titres until 4-6 weeks after infection, well after they have stopped shedding oocysts, and the titre may peak in as little as 2-3 weeks and remain high for years.
- **A cat that is IgG seropositive is unlikely to be shedding oocysts, and is unlikely to shed oocysts if it is exposed to the parasite.** Nonetheless, exposure should be minimized as some seropositive cats may shed low numbers of oocysts if re-exposed. **A cat that is seronegative is unlikely to be shedding oocysts, but is likely to develop a patent infection if it is exposed to *Toxoplasma*.**
- Cats typically only shed oocysts in their feces for 1-3 weeks following their first exposure to *Toxoplasma*, therefore fecal examination is usually unrewarding.



## Treatment of Toxoplasmosis

### Humans:

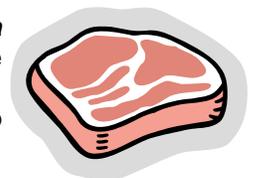
- Traditional drug therapy for clinical toxoplasmosis consists of a combination of pyrimethamine and sulfonamides. Spiramycin is one of the current drugs of choice for treatment of pregnant women. It is readily available in Europe, but must be purchased from the manufacturer in the USA.
  - Since the effectiveness of drug therapy for toxoplasmosis during pregnancy is actually unknown, the cost effectiveness of such therapy is often debated. Treatment may decrease the severity of congenital toxoplasmosis or long term consequences, but possibly not the risk of transmission.
- Early treatment of prenatally infected children has been shown to reduce or prevent clinical problems later in life, therefore neonatal screening programs, particularly those that are piggy-backed on existing screening programs for disease such as phenylketonuria, can be quite cost effective.
- Transplant patients (especially heart transplant patients) should be treated prophylactically with antimicrobials for six weeks to help prevent infection following the operation.
- Antimicrobial prophylaxis is also recommended to prevent reactivation of infection from encysted bradyzoites in patients who develop HIV/AIDS and have had a high antibody titre to *Toxoplasma*.

**Animals:** Clindamycin and pyrimethamine/sulfonamide combinations are typically used to treat clinical toxoplasmosis in dogs and cats. The same drugs, as well as anticoccidials such as monensin and toltrazuril can be used to help decrease oocyst shedding in cats if the animal is exposed to the parasite or becomes immunosuppressed. An oral vaccine to reduce oocyst shedding in cats has been developed, but is not currently commercially available.

## Infection Control

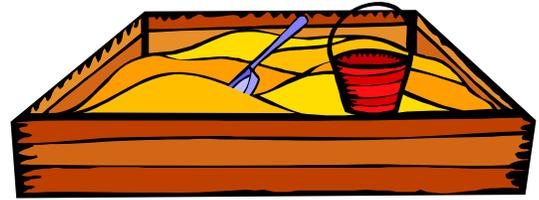


- **In the majority of studies, no direct association has been found between cat ownership and the risk of toxoplasmosis in people.** Given the emotional benefits associated with owning a cat, and the minimal risk of transmission of *Toxoplasma* if appropriate hygiene is practiced, even immunocompromised or pregnant individuals do NOT need to give up their cats.
- Such individuals should avoid contact with cat feces and cat litter whenever possible by having someone else clean their cat's litter box.
- If a cat is found to be shedding oocysts, it should be removed from the premises temporarily and treated to eliminate shedding. Because cats are usually meticulous groomers, it is unlikely that oocysts will be found on their fur, so regular handling is not a significant risk.
- **Always wash your hands thoroughly after contact with cat stool, litter or a litter box.**
- Microwave cooking, salting and smoking do not consistently kill all infective *Toxoplasma* organisms. Freezing meat to  $-12^{\circ}\text{C}$  for at least 24 hours will kill most *Toxoplasma* tissue cysts, but sporulated oocysts can survive at  $-20^{\circ}\text{C}$  for up to 28 days.
- Washing kitchen utensils and surfaces that have come in contact with raw meat with soap and scalding hot water ( $>70^{\circ}\text{C}$ ) will kill any bradyzoites or tachyzoites present.





- Oocysts take longer to sporulate under cooler conditions. For example, at room temperature sporulation may occur within 1-5 days, but it may take 3 weeks at 11°C.
- Once sporulated, oocysts can survive even longer in the environment. They are resistant to most disinfectants, therefore immersion of litter boxes and other potentially contaminated instruments in boiling or scalding water is the preferred means of decontamination. Even sporulated oocysts are killed by heating to 55-60°C for 1-2 minutes.
- Cat feces should be disposed of daily to reduce the risk of transmission. Feces and dirty litter can be disposed of in a septic system if the litter is biodegradable, sealed tightly in a plastic bag and placed in the garbage, or incinerated. Backyard compost units do not produce sufficient heat to destroy oocysts and other pathogens potentially present in fecal material.
- Keep cats out of sandboxes (e.g. cover sandboxes when not in use) and other areas where children play that cats may be inclined to defecate.



## Zoonotic Disease Risk

The zoonotic risk to the general population posed by *Toxoplasma* in cats is:

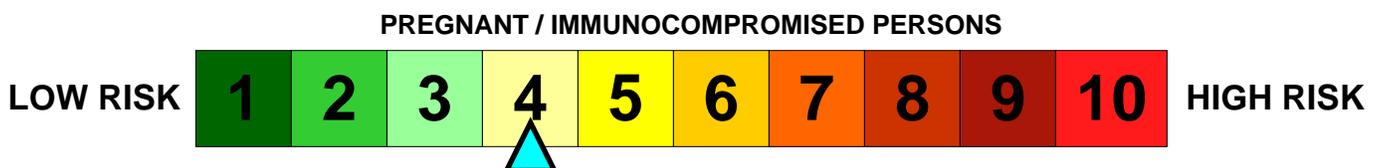


### Pregnant Women and Individuals with Compromised Immune Systems:

Education of individuals in these high risk groups about how to decrease the transmission of *Toxoplasma* is an important tool in the prevention of this disease. The following recommendations are particularly important for these individuals, but also apply to the prevention of toxoplasmosis in general:

- ▶ Cook all meat to a minimum internal temperature of 67°C/153°F.
- ▶ Peel or thoroughly wash fruit and vegetables prior to consumption.
- ▶ Clean all surfaces and objects that come in contact with raw meat or unwashed fruit and vegetables.
- ▶ **Avoid contact with cat litter and garden soil**, otherwise wear gloves and wash hands thoroughly after.
- ▶ Avoid feeding raw meat to cats.
- ▶ Keep cats indoors so they do not become infected by eating small prey.

For these groups, the zoonotic risk posed by *Toxoplasma* in cats is likely:



## Additional Reading

- Bowie WR, King AS, Werker DH, et al. Outbreak of toxoplasmosis associated with municipal drinking water. The BC *Toxoplasma* investigation team. *Lancet*. 1997;350:173-177.
- Lopez A, Dietz VJ, Wilson M, et al. Preventing congenital toxoplasmosis. *MMWR Recomm Rep*. 2000;49:59-68.
- Tenter AM, Heckeroth AR, Weiss LM. *Toxoplasma gondii*: From animals to humans. *Int J Parasitol*. 2000;30:1217-1258.