

# Toxoplasmosis



## Case Definition

**Confirmed Case:** Case definition depends on the age and immunocompetency of the patient. See **Diagnosis**, directly excerpted from the 1997 Red Book (see ref. 2).

## Reporting Requirements

- All positive tests (including IgG) are reportable by laboratory.
- All cases determined through any combination of clinical and laboratory evidence are reportable by attending health care professional.

## Clinical Presentation/Natural History

Infections are frequently asymptomatic or present as an acute disease with one or more of fever, lymphadenopathy and/or lymphocytosis persisting for days or weeks. It sometimes resembles mononucleosis. With development of an immune response, the parasitemia decreases, but *Toxoplasma* cysts remaining in the tissues contain viable organisms. These tissue cysts may reactivate if the immune system becomes compromised. Among immunodeficient persons, primary or reactivated infection may cause cerebritis, chorioretinitis, pneumonia, generalized skeletal muscle involvement, myocarditis, a maculopapular rash and/or death. Cerebral toxoplasmosis is a frequent complication of AIDS.

A primary infection during early pregnancy may lead to fetal infection with death of the fetus or chorioretinitis, brain damage with intracerebral calcification, hydrocephaly, microcephaly, fever, jaundice, rash, hepatosplenomegaly, xanthochromic CSF and convulsions evident at birth or shortly thereafter. Later in pregnancy, maternal infection results in mild or sub-clinical fetal disease with delayed manifestations, such as recurrent or chronic chorioretinitis. In immunosuppressed pregnant women who are *Toxoplasma* seropositive, there may be reactivation of the latent infection that may

rarely result in congenital toxoplasmosis. Dormant organisms from a latent infection can reactivate and cause cerebral toxoplasmosis, particularly among immunodeficient persons, such as AIDS patients.

## Etiology

*Toxoplasma gondii*, an intracellular coccidian protozoan of cats, belonging to the family *Sarcocystidae*, grouped in the class *Sporozoa*.

## Epidemiology

**Reservoir and Source:** The definitive hosts of *T. gondii* are cats and other felines, which acquire infection mainly from eating infected mammals (especially rodents) or birds and rarely from feces of infected cats. Only felines harbour the parasite in the intestinal tract where the sexual stage of its life cycle takes place. This results in the excretion of the oocysts in feces for 10 to 20 days or, rarely, longer.

The intermediate hosts of *T. gondii* include sheep, goats, rodents, swine, cattle, chickens and birds. These hosts may carry an infective stage (cystozoite or bradyzoite) of *T. gondii* encysted in tissue, especially muscle and brain. Tissue cysts remain viable for long periods, perhaps for the life of the animal.

**Transmission:** Transplacental infection in humans occurs when a pregnant woman has rapidly dividing tachyzoites circulating in her bloodstream, usually in the primary infection. Children may become infected by ingesting infective oocysts from dirt in sandboxes, playgrounds and yards in which cats have defecated. Infections may be acquired by eating raw or undercooked infected meat (pork or mutton, more rarely beef) containing tissue cysts, or by the ingestion of infective oocysts in food or water contaminated with feline feces. Inhalation of sporulated oocysts was associated with one reported outbreak. Milk of infected goats and cattle may contain tachyzoites; one reported outbreak was associated epidemiologically with consumption of raw goat's milk. Infection may rarely be acquired by

blood transfusion or organ transplantation from an infected donor.

## Occurrence:

**General:** Worldwide in mammals and birds. Infection in humans is common.

**Manitoba:** Toxoplasmosis first became reportable in January 1999. Fifty persons tested positive for IgM and/or IgG in 1999.

**Incubation Period:** From 10 to 23 days in one common-source outbreak from ingestion of undercooked meat; five to 20 days in an outbreak associated with cats.

**Susceptibility and Resistance:** Susceptibility to infection is general, but immunity is readily acquired and most infections are asymptomatic. Duration and degree of immunity are unknown but assumed to be long lasting or permanent; antibodies persist for years, probably for life. Persons undergoing cytotoxic or immunosuppressive therapy or persons with AIDS are at increased risk of developing illness from reactivated infection.

**Period of Communicability:** Not directly transmitted from person-to-person except in utero. Oocysts shed by cats sporulate and become infective one to five days later and may remain infective in water or moist soil for about one year. Cysts in the flesh of an infected animal remain infective as long as the meat is edible and uncooked.

## Diagnosis

Serologic tests are the primary means of diagnosis, but results must be interpreted carefully. IgG-specific antibodies are measured by enzyme immunoassay (EIA) in most clinical laboratories. IgG-specific antibodies peak in concentration one to two months after infection and remain positive indefinitely. To determine acute infection, the Centres for Disease Control and Prevention recommend a capture-EIA for IgM antibodies. IgM-specific antibodies can be detected two weeks after the onset of infection, reach peak concentrations in one month, decline thereafter,

and usually become undetectable within six to nine months. On rare occasions, IgM-specific antibodies are detectable for as long as two years following acute infection. Tests to detect IgA antibodies, which fall to undetectable concentrations sooner than IgM antibodies, are useful in diagnosing congenital infections and when more precise information about the duration is needed. These tests are available only in reference laboratories. Tests for specific IgM antibodies should be performed by an experienced laboratory; test kits used by some laboratories can give false-positive and false-negative results.

Serconversion or a four-fold rise in specific IgG antibody titre suggests recently acquired infection, but the results can be misleading if serum specimens are not tested concurrently to control for day-to-day laboratory variability. Persons with seroconversion or a four-fold rise in IgG antibody titre should have specific IgM antibody determinations performed by a reference laboratory.

**Prenatal:** A definitive diagnosis of congenital toxoplasmosis can be made prenatally by (1) detecting the parasite in fetal blood or amniotic fluid or (2) documenting the presence of *Toxoplasma* IgM and IgA antibodies in fetal blood. The parasite can be isolated by mouse inoculation or its genomic material can be detected by the polymerase chain reaction (PCR) in a reference laboratory. Suspicion of infection is increased by documenting maternal seroconversion during pregnancy. However, maternal seroconversion does not lead to inevitable fetal infection. Serial fetal ultrasounds should be performed in cases of suspected congenital infection to detect and increase in size of the lateral ventricles of the central nervous system or other signs of fetal infection.

**Postnatal:** If the diagnosis is unconfirmed at the time of delivery in an infant with suspected toxoplasmosis, ophthalmologic, auditory, and neurologic examinations and computed tomography of the head should be performed. An attempt should be made to isolate *T. gondii* from the placenta, cord, and/or the infant's peripheral blood by mouse inoculation. Alternatively, the buffy coat from 1 ml of blood or the cell pellet from the

cerebrospinal fluid may be tested by PCR for genetic evidence of the parasite. Congenital toxoplasmosis also can be diagnosed serologically by the detection of *Toxoplasma*-specific IgM or IgA or the persistence of *Toxoplasma* IgA beyond 12 months of age. Cadham Provincial Laboratory should be requested to forward samples to a reference laboratory that performs the mouse inoculation and the *Toxoplasma* IgM and IgA assays by the double-sandwich IgM EIA (DS-IgM EIA) or IgM immunosorbent agglutination assay (ISAGA). The DS-IgM EIA and the ISAGA detect *Toxoplasma* IgM in approximately 75-80% of infants with congenital infection. The sensitivity of both the immunofluorescent and capture-EIA assays for *Toxoplasma* IgM are significantly less than that of the DS-IgM, IgA EIA or ISAGA assays, and negative results with these assays do not exclude congenital infection. Circulating maternal *Toxoplasma* IgG antibodies in an uninfected infant usually become undetectable by six to 12 months of age.

Infants should be evaluated for congenital toxoplasmosis if they are born to women who are infected concurrently with HIV and *Toxoplasma* or to women who have evidence of primary *Toxoplasma* infection during gestation.

**HIV Infection:** Persons with HIV infection, latently infected with *Toxoplasma*, have variable titres of IgG antibody to *Toxoplasma* but rarely have IgM antibody. While seroconversion and four-fold rises in IgG antibody titres may occur, the ability to diagnose active disease in AIDS patients is commonly impaired by immunosuppression. In many cases, a presumptive diagnosis of *Toxoplasma* encephalitis is based on the presence of the characteristic clinical and roentgenographic findings in an HIV-infected patient who is seropositive for *Toxoplasma* IgG. If the patient does not respond to an empiric trial of anti-*Toxoplasma* therapy, demonstration of *T. gondii* organisms, antigen, or DNA in biopsied tissue, blood, and/or cerebrospinal fluid may be necessary to confirm the diagnosis.

Infants born to women who are dually infected with HIV and *Toxoplasma*, or who have evidence of

primary *Toxoplasma* infection during gestation, should be evaluated for congenital toxoplasmosis.

Diagnosis of ocular toxoplasmosis is based on observation of characteristic retinal lesions in conjunction with serum *Toxoplasma*-specific IgG or IgM antibodies.

## Key Investigations

None, except in outbreaks when possible sources of infection should be investigated.

## Control

### Management of Cases:

#### Treatment:

- Most cases of acquired infection do not require specific antimicrobial therapy.
- When indicated, the combination of pyrimethamine and sulfadiazine, which is synergistic against *Toxoplasma*, is the most widely accepted regimen for children and adults with acute, symptomatic disease. Pyrimethamine, 1 mg/kg per day (maximum daily dose, 25 mg) orally once a day in combination with sulfadiazine, 85 to 100 mg/kg per day in four divided doses (maximum daily dose, 8g) should be given for three to six weeks. Supplemental folic acid (calcium leucovorin) must be administered concurrently (5-10 mg every three days orally or parenterally) to prevent hematologic toxic effects. Alternatively, pyrimethamine can be used in combination with clindamycin if the patient does not tolerate sulfadiazine. The use of corticosteroids in the management of ocular complication and of central nervous system disease is controversial.
- Persons infected with HIV who have had toxoplasmic encephalitis should receive suppressive therapy. Regimens for primary treatment are also effective for suppressive therapy.

- For HIV-infected adults, primary chemoprophylaxis against toxoplasmosis has been recommended for those who are *Toxoplasma*-seropositive and have low CD4+ T-lymphocyte counts. The recommended drug is trimethoprim-sulfamethoxazole. Current data are insufficient for formulation of specific guidelines for children. Based on recommendations for adults, chemoprophylaxis in some circumstances should be considered and is recommended by some experts.
- For both symptomatic and asymptomatic congenital infection, pyrimethamine combined with sulfadiazine (supplemented with folinic acid) also is recommended as initial therapy. Duration of therapy is prolonged and often is one year. However, the optimal dosage and duration are not definitely established and should be decided in consultation with appropriate specialists.
- Treatment of primary *Toxoplasma* infection in pregnant women, including those with HIV infection, should be decided in consultation with appropriate specialists. Spiramycin treatment of primary infection during gestation reduces the frequency of congenital infection, but maternal therapy will not prevent sequelae in the fetus once congenital toxoplasmosis has occurred.

#### **Public Health Measures:**

- Cases in hospital should be managed with routine infection control precautions.

#### **Management of Contacts:**

- The Public Health Branch will monitor the occurrence of outbreaks. When these occur, all cases will be referred for investigation to determine risk factors for infection.
- In an outbreak family members should undergo serological testing and have exposure histories taken to identify possible common sources of infection.

#### **Management of Outbreaks:**

- Search for and remedy common sources of infection such as food, water or soil.

#### **Preventive Measures:**

- Cook meat to 150°F before eating. Freezing reduces, but does not eliminate, infectivity.
- Pregnant women should not clean up cat litter unless they are known to have been infected previously and are immunocompetent. Gloves should be worn when cleaning litter and gardening. Cat litter should be disposed of daily so sporocysts do not have time to become infective. Care should be taken not to aerosolize cat litter dust. Litter pans should be disinfected via scalding.
- Wash hands after cleaning litter, handling raw meat and before eating.
- Feed cats dry, canned or boiled food and discourage hunting.
- Control stray cats.
- Prevent access by cats to sandboxes and sand piles at all times.