

Toxoplasma gondii Overview

ABOUT THE VIRUS

Toxoplasma gondii is an obligate intracellular protozoan ubiquitous in birds and mammals. Toxoplasmosis is the disease that occurs when *T. gondii* invades and multiplies asexually as tachyzoites within the cytoplasm of nucleated cells. When host immunity develops, multiplication of tachyzoites ceases and tissue cysts form, which remain latent, especially in the brain and muscle. Sexual reproduction of *T. gondii* occurs only in the intestinal tract of cats; the resultant oocysts passed in the feces remain infectious up to a year in soil, depending upon the temperature and moisture content.

The two major routes of transmission in humans are oral and congenital. Humans become infected with *T. gondii* through direct contact with oocysts in cat feces or through eating meat contaminated with the extraintestinal form of *T. gondii*. Transmission of the infection from mother to fetus occurs almost solely in women who acquire the infection during pregnancy.

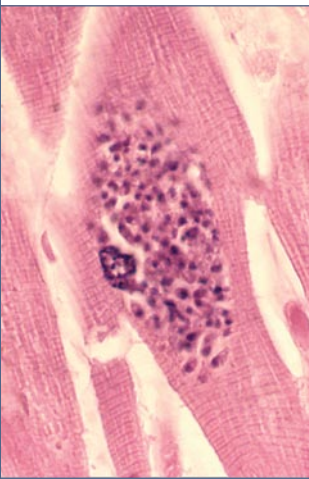
Nearly one quarter of adults and adolescents in the United States have been infected with *T. gondii*; the incidence of seropositivity increases with increasing age. The diagnosis of toxoplasmosis is most critical in four groups of patients: pregnant women who acquire infection during gestation, fetuses and newborns who are congenitally infected, immunocompromised patients and patients with chorioretinitis.

CLINICAL MANIFESTATIONS

Infections in healthy individuals are typically asymptomatic or associated with self-limited symptoms, such as fever, malaise, and lymphadenopathy, which usually resolves within weeks to months and does not require treatment. Infections in pregnant women, also asymptomatic, can be transplacentally transmitted to the fetus. If the fetus is infected in the first trimester, the result ranges from severe disease to spontaneous abortion or stillbirth; if infection occurs afterwards, disease manifestations can include encephalitis, mental retardation, blindness, and epilepsy.

Immunocompromised patients are at risk for primary infection or reactivation of latent infection. Transmission of *T. gondii* by organ transplantation from a seropositive donor to a seronegative recipient is an important potential cause of primary infection in solid organ transplant patients. Hematopoietic stem cell transplant patients and AIDS patients are at most risk for reactivation of a latent infection. Primary toxoplasmosis has been documented between day 1 and 13 months post-transplant; reactivations have been documented up to 7 years post-transplant. Interestingly, toxoplasmosis is sometimes seen only after prophylaxis for pneumocystis pneumonia (PCP) ceases, since the two diseases share therapeutic regimens. Common reactivated infections in transplant patients include disseminated toxoplasmosis, cerebral toxoplasmosis, pulmonary toxoplasmosis, and occasionally, combined ocular and cerebral toxoplasmosis.

Diagnosis is especially difficult in immunocompromised patients, as clinical presentation varies and is often nonspecific. The most common symptoms are fever and altered mental state; pneumonitis and myocarditis are less common presentations. Patients with disseminated toxoplasmosis present with fever that is unresponsive to antibiotics, weakness and fatigue. Chorioretinitis or multiorgan involvement presenting with acute respiratory failure and haemodynamic abnormalities similar to septic shock may also occur. Cerebral toxoplasmosis, the most common form of infection, presents as mental confusion, seizures and typical deep-seated lesions of the brain. Disseminated cerebral infections may present with a radiological image of small miliary lesions. Pulmonary toxoplasmosis presents as respiratory distress and lesions in the lungs.



Histopathology of active toxoplasmosis of myocardium. Numerous tachyzoites of *Toxoplasma gondii* are visible within a pseudocyst in a myocyte.

Image courtesy of CDC.

LABORATORY DIAGNOSIS

T. gondii cannot be cultured in the clinical diagnostic setting, so serological testing has been the mainstay of toxoplasmosis diagnosis, though the method has many significant limitations. For example, IgG antibody detection can be used to identify immunocompromised patients at risk of reactivation, but not for diagnosis of current toxoplasmosis, since any exposure to *T. gondii* at any point in time will result in positive antibodies. Discrimination between recent and more distant infections is not possible using serological methods. In immunocompromised patients, absence of specific antibodies does not rule out active disease since these patients may not be able to mount an appropriate humoral immune response. Risk for congenital toxoplasmosis may go undetected if the pregnant mother was tested during the active phase of infection, when IgG or IgM antibodies may not be detectable. An additional diagnostic method is microscopic examination of tissue, which can be very challenging to obtain. In cases of disseminated toxoplasmosis, the infected tissue could be in almost any organ.

Quantitative real-time PCR overcomes the limitations of serological testing and is a recent and very promising option. It has been shown to be a highly sensitive, specific and rapid method to detect *T. gondii* DNA from a wide variety of specimen sources. In addition, monitoring levels of *T. gondii* DNA in patients correlates well with treatment, enabling physicians to track response to therapy over time and assess outcomes.

TREATMENT

Transplant recipients most likely to acquire infection via the allograft should be tested for baseline toxoplasma IgG antibodies, along with the donor. A seropositive donor and seronegative recipient are at the highest risk; therefore, the transplant recipient should receive prophylaxis.

A combination of pyrimethamine and sulfonamides is the best evaluated therapy and is recommended as first line therapy. However, not all patients can tolerate this combination, therefore, pyrimethamine and clindamycin in combination is recommended as second line therapy. After treatment of the acute phase infection, secondary prophylaxis should be administered as maintenance therapy, which usually consists as the same regimen at half doses until underlying immunosuppression has ceased.

Management of maternal and fetal infection varies widely. Spiramycin is often administered after diagnosis of a recently acquired maternal infection.

Selected References

- Jones J, Kruszon-Moran D, Wilson M. *Toxoplasma gondii* infection in the United States, 1999–2000. *Emerg Infect Dis*. 2003;9(11):1371-1374.
- Jones J, Lopez A, Wilson M, et al. Congenital toxoplasmosis: a review. *Obstet Gynecol Surv*. 2001;56(5):296-305.
- Lin M, Chen T, Kuo T, et al. Real-time PCR for quantitative detection of *Toxoplasma gondii*. *J Clin Microbiol*. 2000;38(11):4121-4125.
- Martino R, Bretagne S, Einsele H, et al. Early detection of toxoplasma infection by molecular monitoring of *Toxoplasma gondii* in peripheral blood samples after allogeneic stem cell transplantation. *Clin Infect Dis*. 2005;(40):67-78.
- Montoya J, Liesenfeld O. Toxoplasmosis. *Lancet*. 2004;(363):1965-1976.
- Remington J, Thulliez P, Montoya J. Recent developments for diagnosis of toxoplasmosis. *J Clin Microbiol*. 2004;2(3):941-945.
- Wulf M, Crevel R, Portier R, et al. Toxoplasmosis after renal transplantation: implications of a missed diagnosis. *J Clin Microbiol*. 2005;43(7):3544-3547.

