Toxoplasmosis: Diagnosis, Treatment, and Prevention in Congenitally Exposed Infants

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ABSTRACT

Toxoplasmosis is a rare disease caused by the obligate intracellular protozoan parasite, *Toxoplasma gondii*. Most persons with toxoplasmosis in the United States are asymptomatic, but if a woman is infected during pregnancy, the parasite can cross the placenta and cause congenital toxoplasmosis in the fetus. The severity of congenital toxoplasmosis depends on when in the pregnancy the mother is exposed, but it can cause ocular and central nervous system disease as well as lead to growth failure and hearing and vision abnormalities. Congenital toxoplasmosis is treated with a combination of pyrimethamine, sulfadiazine, and leucovorin. It is important for pediatric nurse practitioners to be aware of the clinical presentation and treatment of congenital toxoplasmosis. J Pediatr Health Care. (2011) *25*, 355-364.

KEY WORDS

Congenital toxoplasmosis, toxoplasmosis, ocular toxoplasmosis, retinochoroiditis, hydrocephalus, pPediatrics, nurse practitioner, congenital infections, TORCH

The TORCH complex refers to five major congenital infections that, when contracted by a fetus in utero, lead to serious and often life-threatening clinical sequelae. The "T" in TORCH stands for toxoplasmosis, an infection by the intracellular parasite *Toxoplasma gondii* (Gerber & Hohlfeld, 2003). *T. gondii* is a member of the phylum Apicomplexa and parasitic subclass coccidian. The primary host of this parasite is the cat (feline family), and it is passed through the feces of felines (Pradhan, Yadav, & Mishra, 2007). Humans can act as an intermediate host in the parasite's life cycle. If a woman is infected while pregnant, this parasite can cross the placenta from mother to fetus and cause damaging effects to the fetal eye, brain, and other tissues leading to congenital toxoplasmosis (Gerber & Hohlfeld, 2003). It is important that pediatric nurse practitioners (PNPs) be aware of this disease, recognize when it should be considered as a differential diagnosis, and understand how it is diagnosed and treated. This article will review the epidemiology, pathophysiology, transmission, risk factors, clinical presentation, diagnostic methods, and treatment of toxoplasmosis and will emphasize the role of the nurse practitioner in clinical education and research.

EPIDEMIOLOGY

The prevalence of toxoplasmosis varies greatly around the world (Jones, Kruszon-Moran, Sanders-Lewis, & Wilson, 2007). Prevalence rates are thought to depend on food production and harvesting practices, water treatment, environment, climate, and exposure to soil or sand (Jones et al., 2007). To gather data regarding the prevalence of this parasite in the United States, serum samples were taken from more than 15,000 volunteers as part of the National Health and Nutrition Examination Survey between 1999 and 2004 (Jones et al., 2007). Results of this study demonstrated that among women of childbearing age (15-44 years), the

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prevalence of women with IgG antibodies to *T. gondii* born within the United States is 11%. For women born outside of the United States, the prevalence was higher, at 28.1% (Jones et al., 2007). The prevalence rates of IgG antibodies to *T. gondii* in women of childbearing age are important to monitor because they provide insight into the prevalence of congenital toxoplasmosis. No large-scale studies have examined the prevalence rates of IgG antibodies to *T. gondii* in pregnant women, and toxoplasmosis is not a nationally reported disease (Lopez, Dietz, Wilson, Navin, & Jones, 2000). According to the Division of Parasitic Diseases of the National Center for Infectious Diseases, it was estimated in the United States in the year 2000, 1 in 10,000 live births results in congenital toxoplasmosis (Brown, Chau, Atashband, Westerberg, & Kozak, 2009; Lopez et al., 2000). The incidence of congenital toxoplasmosis is then estimated to be around 400 to 4000 new cases every year (Lopez et al., 2000; Pinard, Leslie, & Irvine, 2003).

PATHOPHYSIOLOGY

T. gondii is an obligate intra-cellular protozoan parasite that is responsible for the disease toxoplasmosis (Tamma & Serwint, 2007). This parasite has a complex life cycle that is relatively host specific and is divided into three infectious stages (Dubey, 2004; Kravetz & Federman, 2005). The preferred primary host for *T. gondii* is felines (cats), but humans can become infected when they act as an intermediate host. When an intermediate host ingests *T. gondii,* the first stage, tachyzoites, enter a cell and create a vacuole to protect themselves from the host's immune system (Dubey, 2004). Tachyzoites are resilient and are capable of entering and reproducing in almost any mammalian or avian cell (Rorman, Zamir, Rilkis, & Ben-David, 2006). Tachyzoites contained within certain immune cells can be disseminated throughout the body until an adequate immune response is mounted between 7 and 10 days after infection (Kravetz & Federman, 2005). In response to the host's immune system, tachyzoites multiply asexually and produce cysts, each of which contains the next stage, bradyzoites (Dubey, 2004). Each individual cyst can contain hundreds of bradyzoites and can be found within many different types of tissue (Dubey, 2004). The most common tissues include tissue in the eye, heart, brain, lungs, liver, and lymph nodes. The intact cysts can persist for life in a dormant stage in an intermediate host (Kravetz & Federman, 2005). If the immune system becomes compromised, these bradyzoites can begin replicating asexually again and will exit the cyst as tachyzoites and be spread through the body in blood and lymph systems (Kravetz & Federman, 2005).

When a cat ingests a tissue cyst in meat it consumed, enzymes in the stomach and intestine degrade the cyst and bradyzoites are released. Through asexual reproduction these bradyzoites will become tachyzoites again, the first aforementioned stage (Dubey, 2004.) Some bradyzoites will invade the epithelial tissue of the feline intestine and will begin to multiply through sexual reproduction to form a fertilized oocyst (Kravetz & Federman, 2005). These oocysts can only be formed in the intestine of a wild or domestic member of the feline family and cannot be formed in an intermediate host such as humans (Dubey, 2004).

Oocysts pass out of the feline host through feces and become sporulated in the environment, forming the third stage, sporozoites (Jones, Lopez, & Wilson, 2003). Any host that ingests sporozoites from the environment or acquires tissue cysts from eating infected meat will become infected with *T. gondii* (Jones, Lopez et al., 2003). In humans, contaminated fruit, vegetables, or water that has been in contact with cat feces is the source of ingestion of sporozoites from the environment. Tissue cysts are usually acquired through the ingestion of undercooked infected meat (Jones, Lopez et al., 2003; Pradhan et al., 2007). Bradyzoites released from an ingested tissue cyst or sporozoites released from an ingested oocyst penetrate the human intestine and become tachyzoites again. These tachyzoites then follow the cycle described previously (Dubey, 2004).

T. gondii has been shown to be a highly mobile parasite and actively travels through blood and lymph fluid and across biological barriers such as the intestinal wall, blood-brain barrier, and the placenta (Rorman et al., 2006). In humans, the transplacental passage of tachyzoites from mother to fetus leads to congenital toxoplasmosis (Dubey, 2004). In healthy adults, an infection of *T. gondii* is asymptomatic in most cases. The immune system will prevent replication of the parasite and destroy any bradyzoites that are released from dormant tissue cysts (Dubey, 2004). However, if a woman is infected during pregnancy, tachyzoites can cross the placenta and infect the fetus (Dubey, 2004). The symptoms and course of infection depend on many factors including inoculation factors, virulence of the particular organism, gestational age at time of infection, sex, genetic factors, and immune status of the mother and fetus (Pradhan et al., 2007). The cycle of exposure that leads to congenital toxoplasmosis is illustrated in Figure 1.

VERTICAL TRANSMISSION

Transplacental transmission of *T. gondii* occurs in approximately 40% of pregnancies in which the mother is exposed for the first time during the course of the pregnancy (Bonfioli & Orefice, 2005). In 90% of cases, the mother will be asymptomatic at the time of infection (Kravetz & Federman, 2005). It is estimated that 50% of expectant mothers who give birth to infants congenitally infected with *T. gondii* have no recollection of symptoms or any obvious exposure to the parasite