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## **Toxoplasmosis Update**

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Toxoplasmosis infection is caused by the *Toxoplasmosis gondii* parasite. This parasite can be found in undercooked meat, soil, and cat feces. The life cycle of the parasite is completed in a cat host, and when the cat releases feces (into the litter box or soil) the parasite becomes infectious after several days to weeks. Oocytes can remain infectious in cat feces buried in warm, moist soil for up to one year (Jones et al., 2002). Transmission to humans occurs by three principle routes. About 50% of infection cases are attributed to persons ingesting undercooked infected meat (particularly pork, mutton, wild game) or foods that have come into contact with infected meat (Jones et al., 2002). Secondly, persons can unknowingly ingest infectious oocytes from coming into contact with feces in the cat litter box or in the soil (while gardening or eating unwashed fruits and vegetables). Finally, there can be maternal-fetal transplacental transmission.

Symptoms of toxoplasmosis infection can include swollen lymph nodes, fatigue, muscle aches, malaise, fever, and other flu or mononucleosis-type symptoms. However, up to 90% of immunocompetent persons are asymptomatic (Jones et al., 2002).

### **Congenital Toxoplasmosis**

In the United States it is estimated that between 1-10/ 10,000 infants are born annually with congenital toxoplasmosis (Lopez et al., 2000). Symptoms of infection may not be evident on ultrasound or at birth, but can occur months or several years or more after birth. Nonspecific ultrasound findings can include the most common finding of hydrocephalus (Hohlfeld et al., 1991), intracranial calcifications, microcephaly, intrauterine growth retardation, hydrops, and echogenic bowel. Symptoms in the neonate can include chorioretinitis (most common finding), pneumonia, myocarditis, erythroblastosis, anemia, jaundice, nephritis, myositis, and rash. Possible long-term effects seen in infants with congenital toxoplasmosis include seizures, mental retardation, spasticity, deafness, and blindness. Two states (MA and NH) currently perform newborn screening for congenital toxoplasmosis. For over two decades France (and several other European countries) have been performing universal prenatal screening for congenital toxoplasmosis with monthly repeated serologic testing of nonimmune women (Romand et al., 2001). This practice has not been adopted by the United States. Opponents of universal screening in the United States point out that the frequency of congenital infection in the United States is 10 fold lower than France, and they note the inherent limitations in both diagnostic and therapeutic options (Bader et al., 1997). Screening in the United States is typically initiated following suspicious ultrasound findings.

### **Timing in Pregnancy for Infection**

The placental infection transmission rate is variable depending on the gestational age at the time of maternal infection. Women infected before conception, with rare exception, do not transmit the

infection to the fetus, whereas women infected closer to term have a transmission rate estimated to be as high as 90% (Friedman and Polifka, 1994). Following a primary infection, the transmission rates in the 1st trimester ranges from <1-15%, approximately 30% for the second trimester, and approximately 60% for the 3rd trimester (Antsaklis et al., 2002). While fetal infection is more likely later in pregnancy, the severity of congenital infection is inversely related to the age at maternal infection. For example, one small prospective study noted that severe congenital toxoplasmosis occurred in 6% of infants and perinatal death in 5% of infants when infection occurred in the first trimester, while there were no cases of severe symptoms in the infants of 128 women infected in the third trimester (Friedman and Polifka, 1994). This study, however, does not rule out the possibility of severe symptoms with third trimester exposure.

### **Prenatal Diagnosis**

The first step prior to prenatal diagnosis is to confirm maternal infection typically with antibody detection. Maternal serum is tested for the presence of toxoplasmosis-specific IgG and IgM antibodies. If IgG is negative, there is no evidence of maternal infection. However, if an acute infection is suspected, samples can be retested in three weeks. If IgG is positive, maternal infection has occurred at some time, and in order to determine the approximate time of infection, maternal serum is tested for the presence of toxoplasmosis-specific IgM antibodies (see Table 1 adapted from Jones et al., 2002). If IgG is positive, and IgM is negative, then maternal infection occurred more than a year ago (no increased risk to the fetus). If both IgG and IgM are positive, maternal infection occurred within the last year, or it is a false-positive IgM result.

### **Treatment**

Maternal infection during pregnancy is treated with spiramycin from the time of diagnosis until term, unless fetal infection is detected. If fetal infection is detected, mothers can be treated with pyrimethamine and sulfadiazine or sulfadoxine (Jones et al., 2002). It has been suggested that this treatment reduces the transmission rate of infection by 50%, but this has also been refuted (Foulon et al., 1999, Gilbert et al., 2003). For example, one multicenter European study evaluated 140 infants (at birth and at one year of age) of women with confirmed seroconversion during pregnancy. Only 25 women-infant pairs hadn't received treatment. When gestational age at infection was accounted for, prenatal antibiotic treatment did not reduce the rate of fetal transmission. However, treatment was associated with a significantly reduced rate of serious sequelae among infected infants (Foulon et al., 1999).

Infants diagnosed prenatally or postnatally are treated with pyrimethamine and sulfadiazine for the first year of life, and then are screened periodically for associated problems. This has been documented to provide a much more favorable outcome compared to infected infants who were not treated or only treated for one month (McAuley et al., 1994).

### **Possible Teratogenicity of Spiramycin, Pyrimethamin, and Sulfonamides**

Spiramycin is a macrolide antibiotic used in pregnancy to treat maternal toxoplasmosis infections. No adequate pregnancy studies have been published. A Hungarian case-control study of macrolide antibiotics used in pregnancy did not identify an increased risk of congenital abnormalities. However, since this study included only 12 cases with exposure to spiramycin, it had little potential to detect an increased teratogenic risk with the individual macrolide antibiotics (Briggs, 2002) (REPROTOX-spiramycin). Spiramycin has not been approved for use in the United States by the Food and Drug Administration (FDA) and is therefore considered an experimental drug (orphan). It can be obtained from the FDA. Physicians who are interested in obtaining the drug, should contact the FDA at 301-827-2335 (March of Dimes, 2001).

Pyrimethamine is a folic acid antagonist used in combination with sulfonamides for treatment and

prophylaxis of malaria and toxoplasmosis. Human doses have been found to be teratogenic in rats and include cleft palate, mandibular hypoplasia, limb defects, and neural tube defects) (Shepard, 1995). However, limited studies on pyrimethamine in human pregnancy has not identified this medicine as teratogenic. If this drug is used during pregnancy, folic acid supplementation is recommended, especially during the first trimester (Briggs, 2002) (REPROTOX- pyrimethamine).

Sulfonamides are a group of antimicrobial agents with primarily bacteriostatic effects on microorganisms. Sulfonamides readily cross the placenta during all stages of gestation. Human birth defects have not been associated with this group of drugs even when administered during the first trimester. The number of human case studies available for the sulfonamides is still small, however, and there are animal data suggesting that sulfonamides can cause malformations in some species. There are also concerns for use of these agents near term because of possible effects on newborns including jaundice, hemolytic anemia, and theoretically, kernicterus (Briggs, 2002) (REPROTOX- sulfonamides).

### **Prevention**

Preventative strategies for pregnant women (Lopez et al., 2000) include:

- Cook their meat until it is no longer pink and the juices run clean
- Wear gloves when gardening
- Wash and peel all fruits and vegetables
- Clean cooking surfaces and utensils after they have contacted raw meat, poultry, seafood, and unwashed fruits and vegetables
- Wash hands carefully after handling raw meat, fruit, vegetables, and soil
- Do not change a cat's litter, or if you must, use gloves and then wash hands thoroughly
- Do not feed cats raw or undercooked meat, and keep cats inside

### **Health Education Recommendations (Pawlowski, 2001) include:**

- Provide health education materials in waiting rooms in outpatient clinics, clubs for pregnant women, ladies weekly magazines, and television
- Promote the educational role of medical personnel
- Preventative education should especially be targeted for pregnant women 20 years old or younger (this age group had the lowest levels of knowledge and highest frequency of congenital toxoplasmosis)

### **Helpful Websites:**

Center for Disease Control: Fact Sheet on Toxoplasmosis

[www.cdc.gov](http://www.cdc.gov)

ITIS (1994 ) Original Toxoplasmosis Newsletter

[www.fetal-exposure.org](http://www.fetal-exposure.org)

March of Dimes: Fact Sheet on Toxoplasmosis

[www.modimes.org](http://www.modimes.org)

Organization of Teratology Information Services: Patient Fact Sheet on Toxoplasmosis

[www.otispregnancy.org](http://www.otispregnancy.org)

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