Toxoplasmosis is caused by the protozoan parasite Toxoplasma gondii. A recent serologic survey conduced as part of the Third National Health and Nutrition Survey found that 23 percent of adolescents and adults and 15 percent of women of childbearing age in the United States show laboratory evidence of T. gondii infection. Although T. gondii infection in adults is usually asymptomatic or associated with self-limited symptoms (e.g., fever, malaise, lymphadenopathy), infection in a pregnant woman may cause serious health problems if the parasite is transmitted to the fetus.

Based on extrapolation of data from regional studies, 400 to 4,000 cases of congenital toxoplasmosis occur in the United States each year. Congenital toxoplasmosis can have severe sequelae, including mental retardation, blindness, and epilepsy in infancy or much later in life.

Family physicians may be confronted with a number of issues regarding toxoplasmosis. Some of these issues are related to clinical presentation, laboratory testing, and prevention.

Toxoplasma gondii

LIFE CYCLE

The T. gondii life cycle has three stages: tachyzoite, bradyzoite, and sporozoite. During the acute stage of T. gondii infection, tachyzoites invade and replicate within cells and are responsible for congenital infection. The tachyzoites invade all organs, especially the muscles (including the heart), liver, spleen, lymph nodes, and central nervous system (CNS). During latent infection, bradyzoites are present in tissue cysts. Sporozoites are found in environmentally resistant oocysts formed after the sexual stage of the life cycle.

TRANSMISSION

T. gondii is transmitted to humans by three principal routes (Figure 1). First, humans can acquire T. gondii by eating raw or inadequately cooked infected meat, especially pork, mutton, and wild game, or uncooked foods that have come in contact with infected meat. Second, humans can inadvertently ingest oocysts that cats have passed in their feces, either from the acute stage of T. gondii infection, or after a long period of latency. Third, humans can inadvertently ingest oocysts that cats have passed in their feces, either from the acute stage of T. gondii infection, or after a long period of latency.
FIGURE 1. Pathways for Toxoplasma gondii infection. The feline intestinal tract is the only source for the production of T. gondii oocysts. Transmission to humans usually occurs through the ingestion of oocysts from contaminated sources (e.g., soil, cat litter, garden vegetables, water) or the ingestion of tissue cysts in undercooked meat from infected animals. Although fetal infection most often occurs after acute T. gondii infection in a pregnant woman, it also can occur after the reactivation of latent infection in an immunocompromised pregnant woman.

a litter box or from soil (e.g., soil from gardening, on unwashed fruits or vegetables, or in unfiltered water). Third, women can transmit the infection transplacentally to their unborn fetus. In adults, the incubation period for *T. gondii* infection ranges from 10 to 23 days after the ingestion of undercooked meat and from five to 20 days after the ingestion of oocysts from cat feces.

A report from the Economic Research Service of the U.S. Department of Agriculture concluded that one half of toxoplasmosis cases in the United States are caused by eating contaminated meat. This conclusion is supported by the findings of a community-based epidemiologic study.

Women infected with *T. gondii* before conception rarely transmit the parasite to their fetus, but those who become acutely infected or have reactivation of *T. gondii* during pregnancy (i.e., because of immunosuppression) can transmit the organism transplacentally. The risk of congenital disease is lowest (10 to 25 percent) when maternal infection occurs during the first trimester and highest (60 to 90 percent) when maternal infection occurs during the third trimester. However, congenital disease is more severe when infection is acquired in the first trimester. The overall risk of congenital infection from acute *T. gondii* infection during pregnancy ranges from approximately 20 to 50 percent.

Immunosuppression resulting from human immunodeficiency virus (HIV) infection or therapies for malignancies, organ transplantation, and lymphoproliferative disorders can result in the reactivation of latent *T. gondii* infection. Reactivation most often involves the CNS, and symptoms may include those of meningoencephalitis or a mass lesion. Women with reactivated *T. gondii* infection can transmit the organism transplacentally.

**RISK FACTORS**

Recent epidemiologic studies have identified the following risk factors for *T. gondii* infection: owning a cat, cleaning a cat litter box, eating raw or undercooked pork, mutton, lamb, beef, or minced-meat products, gardening, eating raw or unwashed vegetables or fruits, having contact with soil, washing kitchen knives infrequently, having poor hand hygiene, travelling outside of Europe, Canada, or the United States, and drinking municipal water from a contaminated reservoir.

It is important to note that recent epidemiologic studies have not shown cat ownership to be a consistent risk factor for *T. gondii* infection. The risk of infection is not related to owning a cat but to being exposed to feces from a cat that is shedding oocysts. When cats become infected with *T. gondii*, they generally shed oocysts only for a few weeks during their lifetime. Indoor cats that do not hunt and are not fed raw meat are unlikely to acquire *T. gondii* infection and therefore pose little risk. Furthermore, a study of cats induced to shed oocysts found no oocysts on the cats’ fur after they shed the oocysts. Therefore, the possibility of *T. gondii* transmission through touching a cat is considered to be minimal or nonexistent.

Because cats often do not develop antibodies to *T. gondii* during the oocyst-shedding period, serologic testing does not provide useful information about the ability of a particular cat to transmit toxoplasmosis. A cat that tests positive for *T. gondii* probably has shed oocysts previously and therefore may pose less of a risk than a serologically negative cat. Because cats can shed oocysts more than once, serologic testing is not helpful if a cat is seropositive to *T. gondii* antibody. Testing a cat’s stool to determine human risk is also of little value, because cats shed oocysts for only a short period of time.

**Toxoplasmosis in Pregnant Women**

**SCREENING**

A practice bulletin from the American College of Obstetricians and Gynecologists on perinatal viral and parasitic infections recommends toxoplasmosis screening only in high-risk persons or those in whom routine ultrasound examination (or ultrasonography
performed for other reasons) shows findings such as hydrocephalus, intracranial calcifications, microcephaly, fetal growth retardation, ascites, or hepatosplenomegaly.\textsuperscript{18} [Evidence level C, consensus/expert guidelines] Screening tests may have equivocal or false-positive results that could lead to inappropriate treatment or the termination of pregnancy.\textsuperscript{19,20} Because of the low incidence of toxoplasmosis in the United States, some investigators\textsuperscript{21} have determined that the risk to the fetus would be greater from routine screening than from no screening. However, women with HIV infection should be screened for toxoplasmosis because of the risk of \textit{T. gondii} reactivation and toxoplasmic encephalitis.\textsuperscript{18}

**DIAGNOSTIC TESTS**

When acute \textit{T. gondii} infection is suspected in a pregnant woman, the diagnosis should be pursued. Toxoplasmosis usually is diagnosed on the basis of antibody detection. In acute infection, IgG and IgM antibody levels generally rise within one to two weeks of infection.\textsuperscript{22} The presence of elevated levels of \textit{T. gondii}–specific IgG antibodies indicates that

**TABLE 1**

<table>
<thead>
<tr>
<th>General Interpretation of \textit{Toxoplasma gondii} Serologic Results Obtained with Commercial Assays</th>
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infection has occurred but does not distin-
guish between recent infection and infection
acquired in the distant past. Detection of
*T. gondii*—specific IgM antibodies has been
used as an aid in determining the time of
infection: a negative IgM test result with a
positive IgG result usually indicates infection
at least six months previously. However, the
interpretation of *T. gondii*—specific IgM-posi-
tive results is complicated by the persistence of
IgM antibodies up to 18 months after infec-
tion5 and by false-positive reactions in com-
mercial tests.19 A guide for interpreting labo-
ratory tests is provided in Table 1,5 and an
algorithm for *T. gondii* serologic testing in
patients older than one year is presented in
Figure 2.5

IgM-positive test results should be con-
firmed by a Toxoplasma reference labora-
tory.19 The laboratory may also be able to nar-
row the time of infection through the use of
specific tests (e.g., IgG avidity test)23 or a sero-
logic profile (e.g., Sabin-Feldman dye test,
IgM enzyme-linked immunosorbent assay
[ELISA], IgA ELISA, IgE ELISA, differential
agglutination).24

When a pregnant woman is found to be
infected with *T. gondii*, the next step is to
determine whether the fetus is infected. Physi-
cians most often use polymerase chain reac-
tion (PCR) testing of amniotic fluid to diag-
nose congenital toxoplasmosis. PCR testing of
amniotic fluid is safer and more sensitive than
fetal blood sampling,25 and it allows earlier
confirmation of fetal infection.26 However,
false-positive and false-negative tests may
occur with PCR tests.

Because of the high likelihood of fetal dam-
age, abortion may be considered if *T. gondii*
infection is confirmed and infection is
thought to have occurred before the 16th
week of pregnancy or if the fetus shows evi-
dence of hydrocephalus.10

**TREATMENT**

If the presence of acute *T. gondii* infection in
a pregnant woman is confirmed, treatment
with spiramycin (Rovamycine) can be initi-
ated in an effort to prevent transmission to the
fetus. If fetal infection is confirmed through
amniocentesis, the woman may be switched to
pyrimethamine (Daraprim) and sulfadiazine

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**Serologic Testing for Toxoplasma gondii**

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**FIGURE 2.**
after the first trimester or, according to some experts, after the 18th week of gestation. [Reference 27—Evidence level B, non-randomized study] Folinic acid (leucovorin) is given with pyrimethamine and sulfadiazine to protect bone marrow from the suppressive effects of pyrimethamine.

Spiramycin is an investigational drug in the United States and can only be obtained through the manufacturer (Aventis Pharmaceuticals, Bridgewater, N.J.) with approval from the U.S. Food and Drug Administration. Pyrimethamine generally is not recommended for use in pregnant women because it is a folic acid antagonist (pregnancy category C drug) and can cause bone marrow suppression in both mother and infant.

The treatment of acute *T. gondii* infection in pregnancy has not been evaluated in randomized prospective studies. Questions have been raised about the effectiveness of treatment in preventing congenital infection or sequelae in infants. Nevertheless, historical observational studies suggest that treatment is beneficial, and a recent multicenter observational study found that treatment in pregnancy was associated with a reduction of sequelae in infants but not a reduction in maternal-fetal transmission.

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### TABLE 2
**Possible Signs and Symptoms of Congenital Toxoplasmosis in Infancy and Later in Life***

<table>
<thead>
<tr>
<th>Abnormal spinal fluid</th>
<th>Anemia</th>
<th>Chorioretinitis†</th>
<th>Convulsions</th>
<th>Deafness</th>
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*Most neonates with congenital toxoplasmosis are asymptomatic as determined by routine newborn examination.
†—Sign in the classic triad suggesting the presence of congenital toxoplasmosis.

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**Congenital Toxoplasmosis**

**CLINICAL MANIFESTATIONS**

The classic triad of signs suggestive of congenital toxoplasmosis includes chorioretinitis, hydrocephalus, and intracranial calcifications. However, other clinical manifestations also are associated with the disease (Table 2).

Because clinical manifestations may be nonspecific, *T. gondii* infection must be considered in a large variety of presentations. Congenital toxoplasmosis can mimic disease caused by organisms such as herpes simplex virus, cytomegalovirus, and rubella virus.

Premature infants with toxoplasmosis may develop CNS and ocular disease in the first three months of life. In contrast, *T. gondii*–infected full-term infants more often have milder disease, with hepatosplenomegaly and lymphadenopathy in the first two months of life. Although most infants infected in utero are born with no obvious signs of toxoplasmosis on routine newborn examination, up to 80 percent develop learning or visual disabilities later in life. With congenital infection, reduction of visual acuity and new eye lesions may occur through the third decade of life or even later. Ocular problems require a complete ophthalmologic evaluation.
TREATMENT

Pyrimethamine and sulfadiazine generally are used to treat infants with congenital toxoplasmosis. Infants treated with these drugs have been shown to have improved outcomes compared with untreated infants and children from studies in the past.10,34 [Reference 34—Evidence level B, uncontrolled study] Drug therapy usually is continued for one year. Active and recurrent toxoplasmic eye disease also frequently responds to antiparasitic drugs, which may be given with steroids.

Prevention of Toxoplasmosis in Pregnant Women

Recommendations for the prevention of toxoplasmosis in pregnant women are presented in Table 3.35 In addition, pregnant women who travel abroad should avoid eating undercooked meat or drinking untreated water.

Programs that educate women of childbearing age about the prevention of toxoplasmosis have demonstrated some success in changing risk behaviors36 and have been associated with a decrease in T. gondii seroconversion over time.37 Finally, newborn screening for toxoplasmosis has been used in two states (Massachusetts and New Hampshire) in an attempt to identify and treat T. gondii–infected infants.4

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REFERENCES

Congenital Toxoplasmosis