from 3 weeks to 6 months. Some patients show clinical improvement despite worsening radiographic findings.

**Congenital Infection** The issue of concern when a pregnant woman has evidence of recent *T. gondii* infection is whether the fetus is infected. PCR analysis of the amniotic fluid for the B1 gene of *T. gondii* has replaced fetal blood sampling. Serologic diagnosis is based on the persistence of IgG antibody or a positive IgM titer after the first week of life (a time frame that excludes placental leak). The IgG determination should be repeated every 2 months. An increase in IgM beyond the first week of life is indicative of acute infection. Up to 25% of infected newborns may be seronegative and have normal routine physical examinations. Thus assessment of the eye and the brain, with ophthalmologic testing, CSF evaluation, and radiologic studies, is important in establishing the diagnosis.

**Ocular Toxoplasmosis** The serum antibody titer may not correlate with the presence of active lesions in the fundus, particularly in cases of congenital toxoplasmosis. In general, a positive IgG titer (measured in undiluted serum if necessary) in conjunction with typical lesions establishes the diagnosis. Antibody production in ocular fluids, expressed in terms of the Goldmann-Witmer coefficient, has been described for diagnosis of ocular disease but does not always correlate with PCR results. If lesions are atypical and the serum antibody titer is in the low-positive range, the diagnosis is presumptive. The parasitic antigen–specific polyclonal IgG assay as well as parasite-specific PCR may facilitate the diagnosis. Accordingly, the clinical diagnosis of ocular toxoplasmosis can be supported in 60–90% of cases by laboratory tests, depending on the time of anterior chamber puncture and the panel of antibody analyses used. In the remaining cases, the possibility of a falsely negative laboratory diagnosis or of an incorrect clinical diagnosis cannot be clarified further.



## TREATMENT TOXOPLASMOSIS

### CONGENITAL INFECTION

Congenitally infected neonates are treated with daily oral pyrimethamine (1 mg/kg) and sulfadiazine (100 mg/kg) with folinic acid for 1 year. Depending on the signs and symptoms, prednisone (1 mg/kg per day) may be used for congenital infection. Some U.S. states and some countries routinely screen pregnant women (France, Austria) and/or newborns (Denmark, Massachusetts). Management and treatment regimens vary with the country and the treatment center. Most experts use spiramycin to treat pregnant women who have acute toxoplasmosis early in pregnancy and use pyrimethamine/sulfadiazine/folinic acid to treat women who seroconvert after 18 weeks of pregnancy or in cases of documented fetal infection. This treatment is somewhat controversial: clinical studies, which have included few untreated women, have not proven the efficacy of such therapy in preventing congenital toxoplasmosis. However, studies do suggest that treatment during pregnancy decreases the severity of infection. Many women who are infected in the first trimester elect termination of pregnancy. Those who do not terminate pregnancy are offered prenatal antibiotic therapy to reduce the frequency and severity of *Toxoplasma* infection in the infant. The optimal duration of treatment for a child with asymptomatic congenital toxoplasmosis is not clear, although most clinicians in the United States would treat the child for 1 year in light of cohort investigations conducted by the National Collaborative Chicago-Based, Congenital Toxoplasmosis Study.

### INFECTION IN IMMUNOCOMPETENT PATIENTS

Immunologically competent adults and older children who have only lymphadenopathy do not require specific therapy unless they have persistent, severe symptoms. Patients with ocular toxoplasmosis are usually treated for 1 month with pyrimethamine plus either sulfadiazine or clindamycin and sometimes with prednisone. Treatment should be supervised by an ophthalmologist familiar with *Toxoplasma* disease. Ocular disease can be self-limited without treatment, but therapy is typically considered for lesions that are severe or close to the fovea or optic disc.

### INFECTION IN IMMUNOCOMPROMISED PATIENTS

**Primary Prophylaxis** Patients with AIDS should be treated for acute toxoplasmosis; in immunocompromised patients, toxoplasmosis is rapidly fatal if untreated. Before the introduction of cART, the median survival time was >1 year for patients who could tolerate treatment for TE. Despite their toxicity, the drugs used to treat TE were required for survival prior to cART. The incidence of TE has declined as the survival of patients with HIV infection has increased through the use of cART.

In Africa, many patients are diagnosed with HIV infection only after developing opportunistic infections. Hence, the optimal management of these opportunistic infections is important if the benefits of subsequent cART are to be realized. The incidence of TE in under-resourced settings is not clear because of a lack of facilities for serologic testing and imaging. AIDS patients who are seropositive for *T. gondii* and who have a CD4+ T lymphocyte count of <100/μL should receive prophylaxis against TE.

Of the currently available agents, trimethoprim-sulfamethoxazole (TMP-SMX) appears to be an effective alternative for treatment of TE in resource-poor settings where the preferred combination of pyrimethamine plus sulfadiazine is not available. The daily dose of TMP-SMX (one double-strength tablet) that is recommended as the preferred regimen for prophylaxis of PcP is effective against TE. If patients cannot tolerate TMP-SMX, the recommended alternative is dapsone-pyrimethamine, which likewise is effective against PcP. Atovaquone with or without pyrimethamine also can be considered. Prophylactic monotherapy with dapsone, pyrimethamine, azithromycin, clarithromycin, or aerosolized pentamidine is probably insufficient. AIDS patients who are seronegative for *Toxoplasma* and are not receiving prophylaxis for PcP should be retested for IgG antibody to *Toxoplasma* if their CD4+ T cell count drops to <100/μL. If seroconversion has taken place, then the patient should be given prophylaxis as described above.

**Discontinuing Primary Prophylaxis** Current studies indicate that prophylaxis against TE can be discontinued in patients who have responded to cART and whose CD4+ T lymphocyte count has been >200/μL for 3 months. Although patients with CD4+ T lymphocyte counts of <100/μL are at greatest risk for developing TE, the risk that this condition will develop when the count has increased to 100–200/μL has not been established. Thus, prophylaxis should be discontinued when the count has increased to >200/μL. Discontinuation of therapy reduces the pill burden; the potential for drug toxicity, drug interaction, or selection of drug-resistant pathogens; and cost. Prophylaxis should be recommenced if the CD4+ T lymphocyte count again decreases to <100–200/μL.

Individuals who have completed initial therapy for TE should receive treatment indefinitely unless immune reconstitution, with a CD4+ T cell count of >200/μL, occurs as a consequence of cART. Combination therapy with pyrimethamine plus sulfadiazine plus leucovorin is effective for this purpose. An alternative to sulfadiazine in this regimen is clindamycin.

**Discontinuing Secondary Prophylaxis (Long-Term Maintenance Therapy)** Patients receiving secondary prophylaxis for TE are at low risk for recurrence when they have completed initial therapy for TE, remain asymptomatic, and have evidence of restored immune function. Individuals with HIV infection should have a CD4+ T lymphocyte count of >200/μL for at least 6 months after cART. This recommendation is consistent with more extensive data indicating the safety of discontinuing secondary prophylaxis for other opportunistic infections during advanced HIV disease. A repeat MRI brain scan is recommended. Secondary prophylaxis should be reintroduced if the CD4+ T lymphocyte count decreases to <200/μL.

### PREVENTION

All HIV-infected persons should be counseled regarding sources of *Toxoplasma* infection. The chances of primary infection with *Toxoplasma* can be reduced by not eating undercooked meat and