with CSF pleocytosis in whom parasites are not found, tuberculous meningitis and HIV-associated CNS infections such as cryptococcosis should be considered in the differential diagnosis.

A number of serologic assays, such as the card agglutination test for trypanosomes (CATT) for *T. b. gambiense*, are available to aid in the diagnosis of HAT. Their ease of use makes them valuable for epidemiologic surveys, but their variable sensitivity and specificity mandate that decisions about treatment be based on demonstration of the parasite. Accurate PCR assays for detecting African trypanosomes in humans have been developed, but the lack of the necessary technical and human resources in most endemic areas stands in the way of their widespread use.

TREATMENT SLEEPING SICKNESS

The drugs used for treatment of HAT are suramin, pentamidine, eflornithine, and the organic arsenical melarsoprol. In the United States, these drugs can be obtained from the CDC. Therapy for HAT must be individualized on the basis of the infecting subspecies, the presence or absence of CNS disease, adverse reactions, and occasionally drug resistance. The choices of drugs for the treatment of HAT are summarized in **Table 252-2**.

Suramin is highly effective against stage 1 *rhodesiense* HAT. However, it can cause serious adverse effects and must be administered under the close supervision of a physician. A 100- to 200-mg IV test dose should be given to detect hypersensitivity. The dosage for adults is 20 mg/kg on days 1, 5, 12, 18, and 26. The drug is given by slow IV infusion of a freshly prepared 10% aqueous solution. Approximately 1 patient in 20,000 has an immediate, severe, and potentially fatal reaction to the drug, developing nausea, vomiting, shock, and seizures. Less severe reactions include fever, photophobia, pruritus, arthralgias, and skin eruptions. Renal damage is the most common important adverse effect of suramin. Transient proteinuria often appears during treatment. A urinalysis should be done before each dose, and treatment should be discontinued if proteinuria increases or if casts and red cells appear in the sediment. Suramin should not be given to patients with renal insufficiency.

Pentamidine is the first-line drug for treatment of stage 1 *gambiense* HAT. The dose for both adults and children is 4 mg/kg per day, given IM or IV for 7–10 days. Frequent, immediate adverse reactions include nausea, vomiting, tachycardia, and hypotension. These reactions are usually transient and do not warrant cessation of therapy. Other adverse reactions include nephrotoxicity, abnormal liver function tests, neutropenia, rashes, hypoglycemia, and sterile abscesses. Suramin is an alternative agent for stage 1 *T. b. gambiense* disease.

Eflornithine is highly effective for treatment of both stages of *gambiense* sleeping sickness. In the trials on which the FDA based its approval, this agent cured >90% of 600 patients with stage 2 disease. The recommended treatment schedule is 400 mg/kg per day, given IV in four divided doses, for 2 weeks. Adverse reactions include diarrhea, anemia, thrombocytopenia, seizures, and hearing loss. The high dosage and duration of therapy required are disadvantages that make widespread use of eflornithine difficult. A randomized trial comparing the standard eflornithine regimen (400 mg/kg per day infused over 6 h for 14 days) with nifurtimox-eflornithine combination therapy (NECT; oral nifurtimox, 15 mg/kg per day in three divided doses, plus IV eflornithine, 200 mg/kg per day in two divided doses, both for 7 days) in adults with stage 2 *gambiense* HAT showed improved efficacy and reduced adverse effects with combination therapy, making this drug suitable for first-line use.

The arsenical melarsoprol is the drug of choice for the treatment of *rhodesiense* HAT with CNS involvement and is an alternative agent for stage 2 *gambiense* disease. The "short course" of melarsoprol that is currently recommended has been shown to be noninferior to the decades-old treatment course for *T. b. rhodesiense*, which was administered over several weeks and was much more toxic. The short-course regimen consists of 10 daily doses of 2.2 mg/kg IV, each given with prednisolone (1 mg/kg).

Melarsoprol is highly toxic and should be administered with great care. As noted, all patients receiving melarsoprol should be given prednisolone to reduce the likelihood of drug-induced encephalopathy. Without prednisolone prophylaxis, the incidence of reactive encephalopathy has been as high as 18% in some series. Clinical manifestations of reactive encephalopathy include high fever, headache, tremor, impaired speech, seizures, and even coma and death. Treatment with melarsoprol should be discontinued at the first sign of encephalopathy but may be restarted cautiously at lower doses a few days after signs have resolved. Extravasation of the drug results in intense local reactions. Vomiting, abdominal pain, nephrotoxicity, and myocardial damage can occur.

TABLE 252-2 TREATMENT OF HUMAN AFRICAN TRYPANOSOMIASIS[a]

	Clinical Stage	
Causative Organism	**1 (Normal CSF)**	**2 (Abnormal CSF)**
T. b. gambiense (West African)	Pentamidine Alternative: Suramin	Eflornithine Alternatives: NECT Melarsoprol[b]
T. b. rhodesiense (East African)	Suramin Alternative: Pentamidine	Melarsoprol[b]

[a]For doses and duration, see text. [b]Short course.

Abbreviations: CSF, cerebrospinal fluid; NECT, nifurtimox-eflornithine combination therapy.

PREVENTION

HAT poses complex public-health and epizootic problems in Africa. Considerable progress has been made in many areas through control programs that focus on eradication of vectors and drug treatment of infected humans. People can reduce their risk of acquiring trypanosomiasis by avoiding areas known to harbor infected insects, by wearing protective clothing, and by using insect repellent. Chemoprophylaxis is not recommended, and no vaccine is available to prevent transmission of the parasites.

253 *Toxoplasma* Infections

Kami Kim, Lloyd H. Kasper

DEFINITION

Toxoplasmosis is caused by infection with the obligate intracellular parasite *Toxoplasma gondii*. Acute infection acquired after birth may be asymptomatic but is thought to result in the lifelong chronic persistence of cysts in the host's tissues. In both acute and chronic toxoplasmosis, the parasite is responsible for clinically evident disease, including lymphadenopathy, encephalitis, myocarditis, and pneumonitis. *Congenital* toxoplasmosis is an infection of newborns that results from the transplacental passage of parasites from an infected mother to the fetus. These infants may be asymptomatic at birth, but most later manifest a wide range of signs and symptoms, including chorioretinitis, strabismus, epilepsy, and psychomotor retardation. In immunocompetent individuals, toxoplasmosis can also present as acute disease (typically chorioretinitis) associated with food- or waterborne sources.

ETIOLOGY

T. gondii is an intracellular coccidian that infects both birds and mammals. There are two distinct stages in the life cycle of *T. gondii* that yield transmissible forms of the parasite **(Fig. 253-1)**. In the *asexual* stages, tissue cysts that contain bradyzoites or sporulated oocysts that contain sporozoites are ingested by an intermediate host (e.g., a human, mouse, sheep, pig, or bird). The cyst is rapidly digested by the