

**TABLE 247-1 DRUG THERAPY FOR AMEBIASIS**

Indication	Therapy
Asymptomatic carriage	Luminal agent: iodoquinol (650-mg tablets), 650 mg tid for 20 days; or paromomycin (250-mg tablets), 500 mg tid for 10 days
Acute colitis	Metronidazole (250- or 500-mg tablets), 750 mg PO or IV tid for 5–10 days; or tinidazole, 2 g/d PO for 3 days <b>plus</b> Luminal agent as above
Amebic liver abscess	Metronidazole, 750 mg PO or IV for 5–10 days; or tinidazole, 2 g PO once; or ornidazole, <sup>a</sup> 2 g PO once <b>plus</b> Luminal agent as above

<sup>a</sup>Not available in the United States.

asymptomatic individuals who pass cysts are colonized with *E. dispar*, which does not warrant specific therapy. However, it is prudent to treat asymptomatic individuals who pass cysts unless *E. dispar* colonization can be definitively demonstrated by specific antigen-detection tests.

*Tissue* amebicides reach high concentrations in the blood and tissue after oral or parenteral administration. The development of nitroimidazole compounds, especially metronidazole, was a major advance in the treatment of invasive amebiasis. Patients with amebic colitis should be treated with IV or oral metronidazole. Side effects include nausea, vomiting, abdominal discomfort, and a disulfiram-like reaction. Another longer-acting imidazole compound, tinidazole, is also effective and available in the United States. All patients should also receive a full course of therapy with a luminal agent, since metronidazole does not eradicate cysts. Resistance to metronidazole has been selected in the laboratory but has not been found in clinical isolates. Relapses are not uncommon and probably represent reinfection or failure to eradicate amebas from the bowel because of an inadequate dosage or duration of therapy.

#### AMEBIC LIVER ABSCESS

Metronidazole is the drug of choice for amebic liver abscess. Longer-acting nitroimidazoles (tinidazole and ornidazole) have been effective as single-dose therapy in developing countries. With early diagnosis and therapy, mortality rates from uncomplicated amebic liver abscess are <1%. There is no evidence that combined therapy with two drugs is more effective than the single-drug regimen. Studies of South Africans with liver abscesses demonstrated that 72% of patients without intestinal symptoms had bowel infection with *E. histolytica*; thus, all treatment regimens should include a luminal agent to eradicate cysts and prevent further transmission. Amebic liver abscess recurs rarely.

More than 90% of patients respond dramatically to metronidazole therapy with decreases in both pain and fever within 72 h. Indications for aspiration of liver abscesses are (1) the need to rule out a pyogenic abscess, particularly in patients with multiple lesions; (2) the lack of a clinical response in 3–5 days; (3) the threat of imminent rupture; and (4) the need to prevent rupture of left-lobe abscesses into the pericardium. There is no evidence that aspiration, even of large abscesses (up to 10 cm), accelerates healing. Percutaneous drainage may be successful even if the liver abscess has already ruptured. Surgery should be reserved for instances of bowel perforation and rupture into the pericardium.

#### PREVENTION

Amebic infection is spread by ingestion of food or water contaminated with cysts. Since an asymptomatic carrier may excrete up to 15 million cysts per day, prevention of infection requires adequate sanitation and eradication of cyst carriage. In high-risk areas, infection can be minimized by the avoidance of unpeeled fruits and vegetables

and the use of bottled water. Because cysts are resistant to readily attainable levels of chlorine, disinfection by iodination (tetraglycine hydroperoxide) is recommended. There is no effective prophylaxis.

### INFECTION WITH FREE-LIVING AMEBAS

#### EPIDEMIOLOGY



Free-living amebas of the genera *Acanthamoeba* and *Naegleria* are distributed throughout the world and have been isolated from a wide variety of fresh and brackish water, including that from lakes, taps, hot springs, swimming pools, and heating and air-conditioning units, and even from the nasal passages of healthy children. Encystation may protect the protozoa from desiccation and food deprivation. The persistence of *Legionella pneumophila* in water supplies may be attributable in part to chronic infection of free-living amebas, particularly *Naegleria*. Free-living amebas of the genus *Balamuthia* have been isolated from soil samples, including a sample from a flowerpot linked to a fatal infection in a child.

#### NAEGLERIA INFECTIONS

Primary amebic meningoencephalitis caused by *Naegleria fowleri* follows the aspiration of water contaminated with trophozoites or cysts or the inhalation of contaminated dust, leading to invasion of the olfactory neuroepithelium. Infection is most common among otherwise healthy children or young adults, who often report recent swimming in lakes or heated swimming pools. Rarely, some cases occur when contaminated water is used for nasal irrigation. After an incubation period of 2–15 days, severe headache, high fever, nausea, vomiting, and meningismus develop. Photophobia and palsies of the third, fourth, and sixth cranial nerves are common. Rapid progression to seizures and coma may follow. The prognosis is uniformly poor: most patients die within a week. Recently, two surviving children were treated with miltefosine, an investigational drug that is available through the Centers for Disease Control and Prevention (CDC) for the treatment of *Naegleria* infections.

The diagnosis of *Naegleria* infection should be considered in any patient who has purulent meningitis without evidence of bacteria on Gram's staining, antigen detection assay, and culture. Other laboratory findings resemble those for fulminant bacterial meningitis, with elevated intracranial pressure, high white blood cell counts (up to 20,000/ $\mu$ L), and elevated protein concentrations and low glucose levels in cerebrospinal fluid (CSF). Diagnosis depends on the detection of motile trophozoites in wet mounts of fresh spinal fluid. Antibodies to *Naegleria* species have been detected in healthy adults; serologic testing is not useful in the diagnosis of acute infection.

#### ACANTHAMOEBA INFECTIONS

**Granulomatous Amebic Encephalitis** Infection with *Acanthamoeba* species follows a more indolent course and typically occurs in chronically ill or debilitated patients. Risk factors include lymphoproliferative disorders, chemotherapy, glucocorticoid therapy, lupus erythematosus, and AIDS. Infection usually reaches the central nervous system hematogenously from a primary focus in the sinuses, skin, or lungs. In the central nervous system, the onset is insidious, and the syndrome often mimics a space-occupying lesion. Altered mental status, headache, and stiff neck may be accompanied by focal findings such as cranial nerve palsies, ataxia, and hemiparesis. Cutaneous ulcers or hard nodules containing amebas are frequently detected in AIDS patients with disseminated *Acanthamoeba* infection and can be an important diagnostic site.

Examination of the CSF for trophozoites may be diagnostically helpful, but lumbar puncture may be contraindicated because of increased intracerebral pressure. CT frequently reveals cortical and subcortical lesions of decreased density consistent with embolic infarcts. In other patients, multiple enhancing lesions with edema may mimic the computed tomographic appearance of toxoplasmosis (Chap. 253). Demonstration of the trophozoites and cysts of *Acanthamoeba* on wet mounts or in biopsy specimens establishes the diagnosis. Culture on nonnutrient agar plates seeded with *Escherichia coli* also may be helpful. Fluorescein-labeled antiserum is available