

**FIGURE 247-5** Double-walled cyst of *Acanthamoeba castellanii*, as seen by phase-contrast microscopy. (From DJ Krogstad et al, in A Balows et al [eds]: *Manual of Clinical Microbiology*, 5th ed. Washington, DC, American Society for Microbiology, 1991.)

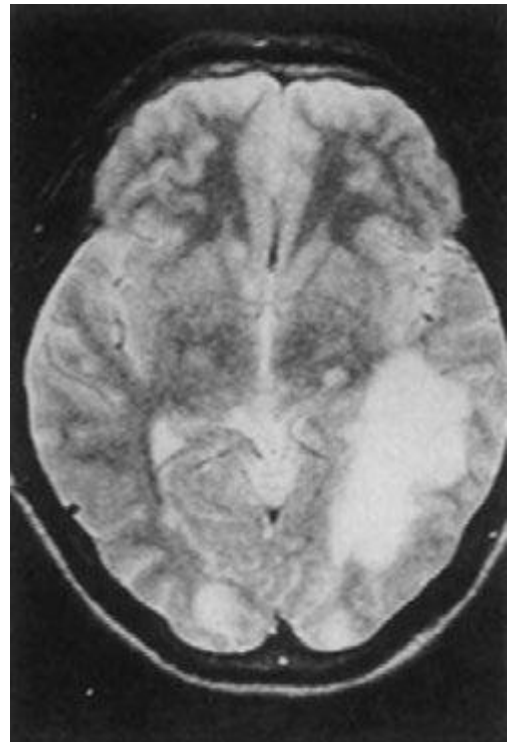
from the CDC for the detection of protozoa in biopsy specimens. Granulomatous amebic encephalitis in patients with AIDS may have an accelerated course (with survival for only 3–40 days) because of poor granuloma formation in these individuals. Various antimicrobial agents have been used to treat *Acanthamoeba* infection, but the infection is almost uniformly fatal. The CDC has now made miltefosine available because of improved survival rates when the drug is included in treatment regimens.

**Keratitis** The incidence of keratitis caused by *Acanthamoeba* has increased in the past 30 years, in part as a result of improved diagnosis. Earlier infections were associated with trauma to the eye and exposure to contaminated water. At present, most infections are linked to extended-wear contact lenses, and rare cases are associated with laser-assisted in situ keratomileusis (LASIK). Risk factors include the use of homemade saline, the wearing of lenses while swimming, and inadequate disinfection. Since contact lenses presumably cause microscopic trauma, the early corneal findings may be nonspecific. The first symptoms usually include tearing and the painful sensation of a foreign body. Once infection is established, progression is rapid; the characteristic clinical sign is an annular, paracentral corneal ring representing a corneal abscess. Deeper corneal invasion and loss of vision may follow.

The differential diagnosis includes bacterial, mycobacterial, and herpetic infection. The irregular polygonal cysts of *Acanthamoeba* (Fig. 247-5) may be identified in corneal scrapings or biopsy material, and trophozoites can be grown on special media. Cysts are resistant to available drugs, and the results of medical therapy have been disappointing. Some reports have suggested partial responses to propamidine isethionate eyedrops. Severe infections usually require keratoplasty.

#### BALAMUTHIA INFECTIONS

*Balamuthia mandrillaris*, a free-living amoeba previously referred to as a leptomyxid amoeba, is an important etiologic agent of amebic meningoencephalitis in immunocompetent hosts. The course is typically subacute, with focal neurologic signs, fever, seizures, and headaches leading to death within 1 week to several months after onset. Examination of CSF reveals mononuclear or neutrophilic pleocytosis, elevated protein levels, and normal to low glucose concentrations. Multiple hypodense lesions are usually detected with imaging studies (Fig. 247-6). This mixed picture of space-occupying lesions with CSF pleocytosis is suggestive of *Balamuthia*. Fluorescent antibody is available from the CDC for brain biopsy specimens. The variety of drugs used to treat the few surviving patients (i.e., fewer than five reported in the United States) includes pentamidine, flucytosine, sulfadiazine, and macrolides. The CDC recommends that miltefosine now be included, as for the other free-living amoebas. The differential diagnosis includes tuberculomas (Chap. 202) and neurocysticercosis (Chap. 260).



**FIGURE 247-6** Brain MRI of amebic meningoencephalitis due to *Balamuthia mandrillaris*. A large lesion in the parieto-occipital lobe and other smaller lesions are seen. (Courtesy of the Department of Radiology, UCSD Medical Center, San Diego.)

## 248 Malaria

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*Humanity has but three great enemies: Fever, famine, and war; of these by far the greatest, by far the most terrible, is fever.*

—William Osler

Malaria is a protozoan disease transmitted by the bite of infected *Anopheles* mosquitoes. The most important of the parasitic diseases of humans, it is transmitted in 106 countries containing 3 billion people and causes approximately 2000 deaths each day; mortality rates are decreasing as a result of highly effective control programs in several countries. Malaria has been eliminated from the United States, Canada, Europe, and Russia; in the late twentieth and early twenty-first centuries, however, its prevalence rose in many parts of the tropics. Increases in the drug resistance of the parasite, the insecticide resistance of its vectors, and human travel and migration have contributed to this resurgence. Occasional local transmission after importation of malaria has occurred in several southern and eastern areas of the United States and in Europe, indicating the continual danger to non-malarious countries. Although there are many successful new control initiatives as well as promising research initiatives, malaria remains today, as it has been for centuries, a heavy burden on tropical communities, a threat to nonendemic countries, and a danger to travelers.

#### ETIOLOGY AND PATHOGENESIS

Six species of the genus *Plasmodium* cause nearly all malarial infections in humans. These are *P. falciparum*, *P. vivax*, two morphologically identical sympatric species of *P. ovale* (as suggested by recent evidence), *P. malariae*, and—in Southeast Asia—the monkey malaria parasite *P. knowlesi* (Table 248-1). While almost all deaths are caused