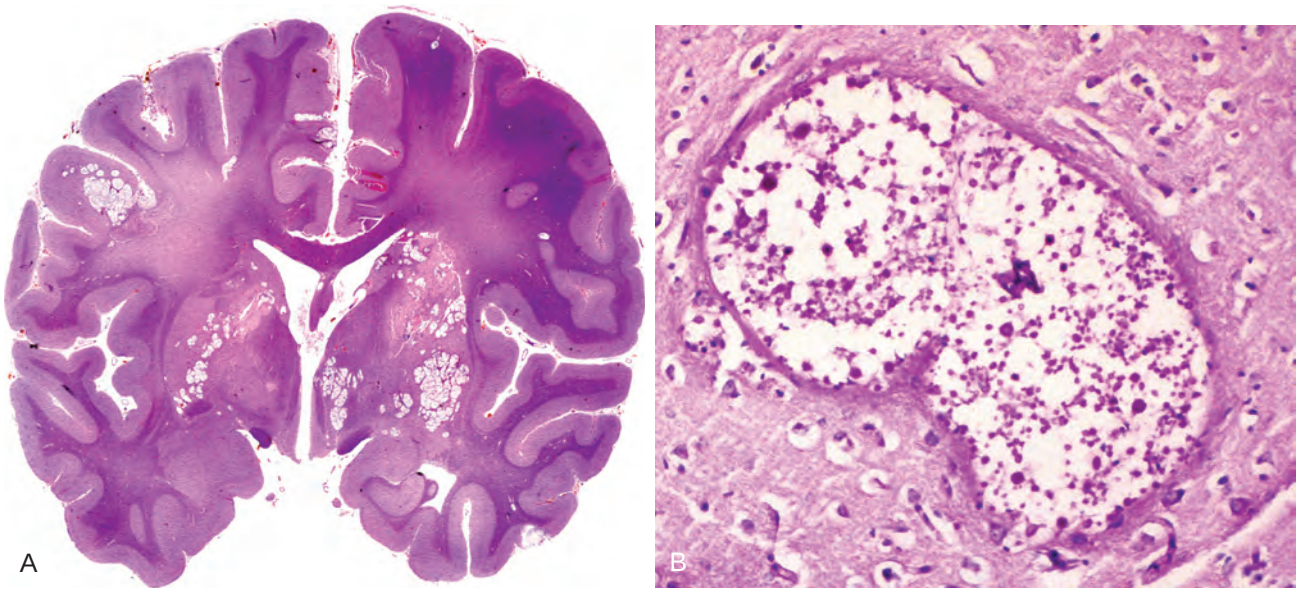

Figure 28-28 Cryptococcal infection. **A,** Whole-brain section showing the numerous areas of tissue destruction ("soap bubbles") associated with the spread of organisms in the perivascular spaces. **B,** At higher magnification it is possible to see the cryptococci in the lesions.

and diffuse. Computed tomography and magnetic resonance imaging studies may show multiple ring-enhancing lesions; however, this radiographic appearance is not specific, as CNS lymphoma, tuberculosis, and fungal infections produce similar findings. In non-immunosuppressed hosts, the impact of toxoplasmosis on the brain is most often seen when primary maternal infection occurs early in pregnancy. Such infections often spread to the brain of the developing fetus and cause severe damage in the form of multifocal necrotizing lesions that may calcify.

MORPHOLOGY

Toxoplasmosis of the CNS produces brain abscesses, which are found most often in the cerebral cortex (near the gray-white junction) and deep gray nuclei, less often in the cerebellum and brainstem, and rarely in the spinal cord (Fig. 28-29). Acute lesions exhibit central necrosis, petechial hemorrhages surrounded by acute and chronic inflammation, macrophage infiltration, and vascular proliferation. Both free tachyzoites and encysted bradyzoites (Fig. 28-29*B*) may be found at the periphery of the necrotic foci. The organisms are often seen on routine hematoxylin and eosin (H & E) or Giemsa stains, but are more easily recognized by immunohistochemical methods. The blood vessels near these lesions may show marked intimal proliferation or even frank vasculitis with fibrinoid necrosis and thrombosis. After treatment, the lesions consist of large, well-demarcated areas of coagulative necrosis surrounded by lipid-laden macrophages. Cysts and free tachyzoites can also be found adjacent to these lesions but may be considerably reduced in number or absent if effective therapy has been received. Chronic lesions consist of small cystic spaces containing scattered lipid- and hemosiderin-laden macrophages that are surrounded by gliotic brain. Organisms are difficult to detect in these older lesions.

- *Cerebral amebiasis.* A rapidly fatal necrotizing encephalitis results from infection with *Naegleria* species, and a chronic granulomatous meningoencephalitis has been associated with infection with *Acanthamoeba.* The amebae may be difficult to distinguish morphologically from activated macrophages (Fig. 28-30). Methenamine silver or PAS stains are helpful in visualizing the organisms, although definitive identification ultimately depends on immunofluorescence studies, culture, and molecular methods.
- *Cerebral malaria.* A rapidly progressive encephalitis, cerebral malaria is the complication of infection by *Plasmodium falciparum* with the highest mortality. Most likely the result of vascular dysfunction, cerebral involvement by malaria is accompanied by reduced cerebral blood flow and results in ataxia, seizures, and coma in the acute phase, with long-term cognitive deficits in up to 20% of children after cerebral malaria (Chapter 8).

KEY CONCEPTS

Infections

- Pathogens from viruses through parasites can infect the brain. Different pathogens use distinct routes to reach the brain and cause different patterns of disease.
- Routes of access of organisms to the brain include: hematogenous spread (e.g., abscess formation in the setting of endocarditis), direct extension (following trauma or with extension from the sinuses with Mucor) and retrograde transport along nerves (as with rabies).
- Bacterial infections may cause meningitis, cerebral abscesses, or a chronic meningoencephalitis. The distribution of pathogens is influenced by various host factors, such as age and level of immune function.
- Viral infections can cause meningitis or meningoencephalitis. Some viruses have characteristic patterns of