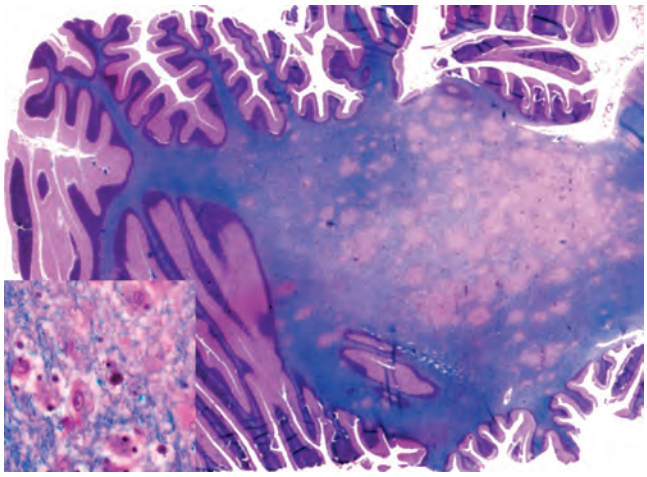

Figure 28-27 Progressive multifocal leukoencephalopathy. Section stained for myelin showing irregular, poorly defined areas of demyelination, which become confluent in places. *Inset*, Enlarged oligodendrocyte nucleus represents the effect of viral infection.

enlarged oligodendrocyte nuclei containing glassy amphophilic viral inclusions (Fig. 28-27, *inset*), which can be identified by immunohistochemistry. Within the lesions, there may be bizarre giant astrocytes with one to several irregular, hyperchromatic nuclei mixed with more typical reactive astrocytes. Infection of granule cell neurons in the cerebellum been demonstrated in rare instances.

neurologic symptoms and signs, and imaging studies show extensive, often multifocal, lesions in the hemispheric or cerebellar white matter.

Subacute Sclerosing Panencephalitis

Subacute sclerosing panencephalitis (SSPE) is a rare progressive clinical syndrome characterized by cognitive decline, spasticity of limbs, and seizures. It occurs in children or young adults, months or years after an initial, early-age acute infection with measles. The disease stems from persistent, but nonproductive, infection of the CNS by an altered measles virus; changes in several viral genes have been associated with the disease. It is characterized by widespread gliosis and myelin degeneration; viral inclusions, largely within the nuclei of oligodendrocytes and neurons; variable inflammation of white and gray matter; and neurofibrillary tangles. Ultrastructural study shows that the inclusions contain nucleocapsids characteristic of measles and immunohistochemistry for measles virus antigen is positive. The incidence of the disease has fallen sharply due to vaccination programs, but it persists in nonimmunized populations.

Fungal Meningoencephalitis

Fungal infections of the CNS are encountered primarily in immunocompromised individuals. The brain is usually involved following widespread hematogenous dissemination of fungi; the most frequent offenders are *Candida albicans*, Mucor species, *Aspergillus fumigatus*, and *Cryptococcus neoformans*. In endemic areas, pathogens such as *Histoplasma capsulatum*, *Coccidioides immitis*, and *Blastomyces dermatitidis* may involve the CNS after a primary pulmonary or cutaneous infection; again, this often follows immunosuppression. Although most fungi reach the brain by hematogenous dissemination, direct extension may also occur, particularly in mucormycosis in the setting of diabetes mellitus.

The three main forms of injury in fungal infection in the CNS are chronic meningitis, vasculitis, and parenchymal invasion. Vasculitis is most frequently seen with *Mucormycosis* and *Aspergillosis*, both of which directly invade blood vessel walls, but it occasionally occurs with other infections such as candidiasis. The resultant vascular thrombosis produces infarction that is often strikingly hemorrhagic and that subsequently becomes septic from ingrowth of the causative fungus.

Parenchymal infection, usually in the form of granulomas or abscesses, can occur with most of the fungi and often coexists with meningitis. The most commonly encountered fungi that invade the brain are *Candida* and *Cryptococcus*. Candidiasis usually produces multiple microabscesses, with or without granuloma formation.

Cryptococcal meningitis, a common opportunistic infection in the setting of AIDS, may be fulminant and fatal in as little as 2 weeks or indolent, evolving over months or years. The CSF may contain few cells but usually has a high concentration of protein. The mucoid-encapsulated yeasts can be visualized in the CSF with special stains or detected indirectly using assays for cryptococcal antigens.

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With cryptococcal infection, there is a chronic meningitis affecting the basal leptomeninges, which are opaque and thickened by reactive connective tissue that may obstruct the outflow of CSF from the foramina of Luschka and Magendie, giving rise to hydrocephalus. Sections of the brain disclose a gelatinous material within the subarachnoid space and small cysts within the parenchyma ("soap bubbles"), which are especially prominent in the basal ganglia in the distribution of the lenticulostriate arteries (Fig. 28-28*A*). Parenchymal lesions consist of aggregates of organisms within expanded perivascular (Virchow-Robin) spaces associated with minimal or absent inflammation or gliosis (Fig. 28-28*B*). The meningeal infiltrates consist of chronic inflammatory cells and fibroblasts admixed with cryptococci.

Other Infectious Diseases of the Nervous System

Protozoal diseases (including malaria, toxoplasmosis, amebiasis, and trypanosomiasis), rickettsial infections (e.g., typhus and Rocky Mountain spotted fever), and metazoal diseases (especially cysticercosis and echinococcosis) may also involve the CNS and are discussed in Chapter 8.

- *Cerebral toxoplasmosis* is an opportunistic infection commonly found in the setting of HIV-associated immunosuppression. The clinical symptoms of infection of the brain by *Toxoplasma gondii* are subacute, evolving during a 1- or 2-week period, and may be both focal