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Neurosyphilis presents in several distinct forms.

- **Meningovascular neurosyphilis** is chronic meningitis involving the base of the brain and more variably the cerebral convexities and the spinal leptomeninges. In addition, there may be an associated obliterative endarteritis (Heubner arteritis) accompanied by a distinctive perivascular inflammatory reaction rich in plasma cells and lymphocytes. Cerebral gummas (plasma cell-rich mass lesions) may also occur in the meninges and extend into the parenchyma.
- **Paretic neurosyphilis** is caused by invasion of the brain by *T. pallidum* and is clinically manifested as insidious but progressive cognitive impairment associated with mood alterations (including delusions of grandeur) that terminate in severe dementia **(general paresis of the insane)**. Parenchymal damage of the cerebral cortex is particularly common in the frontal lobe but also occurs in other areas of the isocortex. The lesions are characterized by loss of neurons, proliferation of microglia (rod cells), gliosis, and iron deposits. The latter are demonstrable with the Prussian blue stain perivascularly and in the neuropil, and are presumably the sequelae of small bleeds stemming from damage to the microcirculation. The spirochetes can, at times, be demonstrated in tissue sections.
- **Tabes dorsalis** is the result of damage to the sensory axons in the dorsal roots. This causes impaired joint position sense and ataxia (locomotor ataxia); loss of pain sensation, leading to skin and joint damage (Charcot joints); other sensory disturbances, particularly the characteristic "lightning pains"; and absence of deep tendon reflexes. On microscopic examination there is loss of both axons and myelin in the dorsal roots, with corresponding pallor and atrophy in the dorsal columns of the spinal cord. Organisms are not demonstrable in the cord lesions.

Neuroborreliosis (Lyme Disease)

Lyme disease is caused by the spirochete *Borrelia burgdorferi*, which is transmitted by various species of *Ixodes* tick (Chapter 8). Involvement of the nervous system is referred to as *neuroborreliosis*. Neurologic symptoms are highly variable and include aseptic meningitis, facial nerve palsies and other polyneuropathies, as well as encephalopathy. The rare cases that have come to autopsy have shown a focal proliferation of microglial cells in the brain as well as scattered extracellular organisms.

Viral Meningoencephalitis

Viral encephalitis is a parenchymal infection of the brain almost invariably associated with meningeal inflammation (meningoencephalitis) and sometimes with simultaneous involvement of the spinal cord (encephalomyelitis).

Some viruses have a propensity to infect the nervous system. Such neural tropism takes several forms: some infect specific cell types (e.g., oligodendrocytes), while others preferentially involve particular areas of the brain (e.g., medial temporal lobes or the limbic system). Latency is an important phase of several viral infections of the CNS (e.g., herpes zoster, progressive multifocal leukoencephalopathy). Systemic viral infections in the absence of direct evidence of viral penetration into the CNS may be followed by an immune-mediated disease, such as perivenous demyelination (see "Acute Disseminated Encephalomyelitis and Acute Necrotizing Hemorrhagic Encephalomyelitis"). Intrauterine viral infection may cause congenital malformations, as occurs with rubella. A slowly progressive degenerative disease syndrome may follow many years after a viral illness; an example is postencephalitic parkinsonism after the 1918 viral influenza pandemic.

Arthropod-Borne Viral Encephalitis

Arboviruses are an important cause of epidemic encephalitis, especially in tropical regions of the world, and they are capable of causing serious morbidity and high mortality. In the Western hemisphere the most important types are Eastern and Western equine, West Nile, Venezuelan, St. Louis, and La Crosse; elsewhere in the world, pathogenic arboviruses include Japanese B (Far East), Murray Valley (Australia and New Guinea), and tick-borne (Russia and Eastern Europe).

All these viruses have animal hosts and insect vectors. Clinically, affected individuals develop generalized neurologic deficits, such as seizures, confusion, delirium, and stupor or coma, as well as focal signs, such as reflex asymmetry and ocular palsies. Involvement of the spinal cord in West Nile encephalitis can lead to a polio-like syndrome with paralysis. In general, the CSF is usually colorless, with slightly elevated pressure, an elevated protein level, and a normal glucose. Initially the CSF exhibits a neutrophilic pleocytosis, but this rapidly converts to a lymphocytosis.

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The encephalitides caused by various arboviruses produce similar histopathologic changes that differ only in severity and extent. Characteristically, there is a meningoencephalitis marked by the perivascular accumulation of lymphocytes (and sometimes with neutrophils) (Fig. 28-23*A*). Multiple foci of necrosis of gray and white matter are found; in particular, there is evidence of single-cell neuronal necrosis with phagocytosis of the debris **(neuronophagia)**. Microglial cells form small aggregates around foci of necrosis, called **microglial nodules** (Fig. 28-23*B*). In severe cases there may be a necrotizing vasculitis with associated focal hemorrhages. While some viruses declare their presence by formation of intracellular inclusion bodies, the causative virus is most often identified by a combination of ultrastructural, immunohistochemical, and molecular methods.

Herpes Simplex Virus Type 1

Herpes simplex virus type 1 (HSV-1) encephalitis occurs most commonly in children and young adults. Only about 10% of the affected individuals have a history of prior herpetic infection. The typical presenting symptoms are alterations in mood, memory, and behavior. Polymerase chain reaction (PCR)-based methods for virus detection in CSF samples have increased the ease of diagnosis and the recognition of a subset of patients with less severe disease. Antiviral agents now provide effective treatment in many cases, with a significant reduction in the mortality rate. In some individuals, HSV-1 encephalitis follows a subacute