form virus encephalopathies. Although these diseases have been shown to be of infectious etiology by the transmission of viral origin since its initial description by Dawson in 1932. Measles virus or a virus closely related to measles virus has been recovered from the brains of patients with the disease. The disorder may be considered to be a slow form of measles encephalitis (see Chap. 200).

SUBACUTE SCLEROSING PANENCEPHALITIS (INCLUSION-BODY ENCEPHALITIS) This progressive and ultimately fatal disease of children and adolescents had been suspected to be of viral nature, but has been confirmed by recent studies. Measles virus or a virus closely related to measles virus has been recovered from the brains of patients with the disease. The disorder may be considered to be a slow form of measles encephalitis (see Chap. 200).

Measles virus is the etiologic agent. Electron-microscopic studies show that the intranuclear inclusions in brain cells are composed of hollow tubular filaments resembling the internal nucleocapsid component of a paramyxovirus. Staining of brain sections with specific hyperimmune rabbit serum. Serologic diagnosis using the complement fixation test shows that the intranuclear inclusions in oligodendrocytes first suggested that the disease was of a viral etiology. Electron-microscopic observations show the intranuclear inclusion bodies to be composed of closely packed spheres, which have the physical dimensions and properties of the polyomavirus genus of the papovaviruses.

Abundant virus particles are present in brain. Rapid identification of the virus in brain is possible using fluorescent antibody technique with the virus when a disease which interferes with the patient's initial rubella infection. A few reported cases may have been related to measles vaccination. The risk of SSPE following measles vaccination is far less, however, than the risk of encephalitis or SSPE following natural measles.

SSPE patients lack antibody to one of the measles virus proteins (the M or matrix protein) despite high titer of antibodies to the other viral proteins. The M protein is a nonglycosylated protein localized to the inner surface of the viral membrane; it is important in the assembly of the virus particle at the cell surface. SSPE brain cells do not appear capable of synthesizing the M protein even in normal amounts. The reason for this selective defect in a single viral protein has not been ascertained.

Isoprinosine has been reported by some to affect the course of the disease favorably in an open therapeutic trial, but there is controversy about the drug's effectiveness.

PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY This rare neurological condition, first described in 1958, usually occurs in patients who have leukemia, malignant lymphoma, carcinomatosis, immunosuppressive therapy, or a variety of other chronic disease processes. The disease is consistently associated with disorders of cell-mediated immunity with which deficits in humoral antibody response may or may not coexist.

The disease affects adults of both sexes, and its duration from onset of symptoms to death is 1 to 6 or more months. The neurological signs and symptoms reflect a diffuse, asymmetric involvement of the cerebral hemispheres. Hemiplegia, hemianopsia, aphasia or dysarthria, and organic mental changes are frequent; visual field abnormalities and complete or incomplete transverse myelitis may develop. Headache and convulsive seizures are rare, but EEG abnormalities consisting of diffuse or focal abnormalities are often present. Lesions in the white matter may be recognized on CT scans. CSF is normal.

The pathologic changes consist of multiple areas of demyelination with little or no perivascular infiltration and abnormal mitotic figures in astrocytes. The presence of distinctive intranuclear inclusions in oligodendrocytes first suggested that the disease was of a viral etiology. Electron-microscopic observations show the intranuclear inclusion bodies to be composed of closely packed spheres, which have the physical dimensions and properties of the polyomavirus genus of the papovaviruses.

By employing tissue cultures derived from human fetal brain it has been possible to recover a new human polyomavirus serotype (JC virus) from the brains of PML patients. Abundant virus particles are present in brain. Rapid identification of the virus in brain is possible using fluorescent antibody staining or electron-microscopic agglutination with monospecific hyperimmune rabbit serum. Serologic diagnosis using the patient's serum is unreliable. The virus has not been demonstrated in tissues other than brain; the disease has not been transmitted to animals.

There are isolated reports of clinical remission with cytosine arabinoside, but no cure. Death usually occurs within 6 months of onset.

PML may result from the activation of a polyomavirus which has been latent in brain or other tissues since childhood infection. Alternatively, there may be certain individuals who fail to acquire immunity in childhood and have their first encounter with the virus when a disease which interferes with cell-mediated immunity develops. The demyelination which

from patients with the disease develop a nonfatal neurological disorder with EEG changes.

There is evidence that SSPE patients have clinical measles at an unusually early age, but SSPE appears many years after the patient's initial rubella infection. A few reported cases may have been related to measles vaccination. The risk of SSPE following measles vaccination is far less, however, than the risk of encephalitis or SSPE following natural measles.

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