



## **Pathophysiology of neurological manifestations of HIV infection**

Avindra Nath

*Department of Neurology, Johns Hopkins University, Baltimore, Maryland, USA*

HIV infection causes a wide variety of neurological syndromes that can involve the entire neuraxis. These include a subacute dementia, cerebellar degeneration, vacuolar myelopathy, a peripheral neuropathy, and a polymyositis. Dementia is the most feared manifestation and its pathophysiology is the best understood. Infection occurs productively in invading macrophages and in resident microglia and latently in astrocytes. The infected cells release viral proteins termed “virotoxins” that are either directly toxic to neurons or initiate a cascade of events via activation of glial cells and chemotaxis of monocytes leading to neurotoxicity. Oxidative stress may be a final common pathway and a potential therapeutic target. Likely similar cascades are involved in the pathogenesis of HIV peripheral neuropathy aggravated by the treatment of HIV infection with nucleoside analogs. Vacuolar myelopathy may be secondary to alterations in vitamin B12 pathway although B12 levels themselves are normal. The pathophysiology of the other manifestations is poorly understood.