Virology and Pathogenesis

West Nile virus (WNV) is a mosquito-borne virus belonging to the genus *Flavivirus* in the *Flaviviridae* family. The viral genome is approximately 11,000 nucleotides in length coding for three structural (C, capsid protein; prM, the membrane precursor protein that is proteolytically cleaved by a cellular protease to form the M protein in mature virions; and E, envelope protein) and seven nonstructural (NS) proteins (NS1, NS2a, NS2b, NS3, NS4a, NS4b and NS5). The E glycoprotein is the most immunologically important protein.

Serologically, West Nile virus is a member of the Japanese encephalitis serocomplex, which includes antigenic related viruses as Murray valley encephalitis (MVE), St. Louis encephalitis (SLE), Kunjin (KUN), Usutu (USU), Koutango (KOU), Cacipacore (CPC), Alfuy (ALF) and Yaounde (YAO).

Different genetic lineages have been identified worldwide but the strains responsible for serious epidemics are attributable to Lineage 1 and Lineage 2. Phylogenetic analyses revealed that all European WNV lineage 1 and 2 strains are derived from a

limited number of independent introductions, most likely from Africa, followed by local spread and evolution. Other lineages have been identified but not associated so far with human or animal diseases.

WNV is rapidly inactivated in the environment outside hosts. Low temperatures preserve infectivity, with stability being greatest below -60°C. It is inactivated by heat (50 to 60°C for at least 30 minutes), ultraviolet light, and gamma irradiation (Burke and Monath, 2001). The virus is also susceptible to disinfectants such as 3 to 8% formaldehyde, 2% glutaraldehyde, 2 to 3% hydrogen peroxide, 500 to 5,000 ppm available chlorine, alcohol, 1% iodine, and phenol iodophors.

Mosquito salivary components introduced at the site of infection in vertebrates modulate initial infection of target cells such as keratinocytes, Langerhans cell and skin-resident dendritic cells (Lim et al., 2011). The infected cells migrate to draining lymph nodes generating a viremia responsible for the infection of visceral organs and potentially to the central nervous system. How Flavivirus neuroinvasion occurs is still poorly understood. Postulated mechanisms include the direct viral crossing of the blood-brain barrier due to cytokine-mediated increased vascular permeability; the passage through the endothelium of the blood-brain barrier; a Trojan horse mechanism in which infected tissue macrophages are trafficked across the blood-brain barrier; and the retrograde axonal transport of the virus to the central nervous system via infection of olfactory or peripheral neurons (Cho and Diamond, 2012).