Disease Control and Prevention, 3150 Rampart Road, Fort Collins, CO 80522. E-mail: frd3@cdc.gov).

COMMENT. According to the AAP Red Book (2006), the majority of pediatric WNV infections are asymptomatic, 20% have WNF, and <1% develop neuroinvasive disease. Risk of WNND increases with age and is highest in adults >60 years. Patients with WNND present with neck stiffness and headache, typical of aseptic meningitis, mental status changes of encephalitis, movement disorders such as tremor, seizures, or acute flaccid paralysis clinically similar to poliomyelitis or Guillain-Barre syndrome.

SEIZURE DISORDERS

TWINKLE MUTATIONS AND REFRACTORY STATUS EPILEPTICUS

Severe epileptic encephalopathy and refractory status epilepticus are reported in a 20-year follow-up of 23 patients with recessive Twinkle mutations studied at Helsinki University Central Hospital, Finland. Dominant mutations of the C10orf2 gene are linked with progressive external ophthalmoplegia, while recessive mutations cause mitochondrial DNA depletion and encephalopathy or hepatoencephalopathy, similar to phenotypes associated with recessive POLG1 mutations (eg Alpers syndrome). The authors had previously described infantile onset spinocerebellar ataxia caused by Twinkle mutations. On long-term follow-up, further clinical phenotypes developed, including refractory status epilepticus, migraine-like headaches, and psychoses. Myoclonic or focal clonic seizures occurred in 18 patients, progressed to epilepsia partialis continua in 15 and generalized status epilepticus in 13, 8 of whom died. The first episode of status epilepticus occurred between 15 and 34 years of age in homozygotes, and at 2 and 4 years of age in the compound heterozygotes. Status lasted from several days to weeks. Valproate caused elevation of liver enzymes in 2 patients and was discontinued. Phenytoin or fosphenytoin was ineffective and caused an elevation of liver enzymes. Oxcarbazepine, lamotrigine or levetiracetam was of benefit in some. MRI showed focal, stroke-like lesions, some hemispheric, resulting in edema, necrosis, and brain atrophy, including the hippocampus, and confirmed on neuropathology exam. (Lonnqvist T, Paetau A, Valanne L, Pihko H. Recessive twinkle mutations cause severe epileptic encephalopathy. **Brain** June 2009;132:1553-1562). (Respond: Dr Tuula Lonnqvist, Division of Child Neurology, Helsinki University Central Hospital, PO Box 280, Helsinki, 00029 Finland. E-mail: tuula.lonnqvist@hus.fi).

COMMENT. The authors comment that the infantile onset spinocerebellar ataxia (IOSCA) syndrome shares features with other mitochondrial recessive ataxia syndromes, including Friedreich's ataxia, mitochondrial spinocerebellar ataxia-epilepsy (MSCAE) syndrome and mitochondrial DNA polymerase gamma (POLG)-Alpers syndrome. IOSCA, a progressive neurodegenerative disease, is caused by homozygous or compound heterozygous C10orf2 gene mutations that code for the mitochondrial DNA helicase Twinkle. Status epilepticus, migraine-like headaches and psychiatric symptoms are also pathognomonic for the disease. These symptoms should alert the clinician to consider a mitochondrial encephalopathy in differential diagnosis.