Supplemental content for advanced practice nurses

# Alpers-Huttenlocher Syndrome

Alpers-Huttenlocher syndrome (AHS) is a mitochondrial disease that typically onsets in childhood. The specific alterations are with multiple gene mutations in the mitochondrial DNA replicase, polymerase gamma 1 (POLG1) gene.8 There are 180 known mutations. POLG1 mutations have been noted in every ethnic group. 6,8 Distribution is also noted equally in each gender. Age of onset is variable. The most common occurrence is at 2-3 years of age, with some dominant gene mutations not exhibiting signs until adulthood. Seizures are often the first signaling event of the syndrome. The clinical course varies in progression from months up to 10 years. Death occurs from multiple organ system failure. The diagnostic triad for this syndrome is listed as epilepsy, refractory to medication intervention, psychomotor regression, and liver disease. Some of the most commonly cited additional symptoms are areflexia, atonia, and an EEG pattern revealing occipital-predominant epileptiform discharges. If the triad is recognized, it is recommended that the patient gene be sequenced and the patient switched to another AED. If VPA is chosen as the treatment for AHS-related seizures, liver failure ensues, leading to death within 2-3 months of initialization of therapy. 6,8

# Leigh Syndrome

Leigh syndrome is a neurodegenerative disorder associated with over 60 different genetic mutations.9 This type of disease is described as a phenocopies disease. Phenocopies disease means that multiple gene mutations lead to the same clinical presentation. It is one of the most common mitochondrial disorders. The hallmark diagnostic criteria are bilateral symmetric hypodensities in the basal ganglia on computed tomography (CT) or bilateral symmetric hyperintense lesions in the brainstem and/or basal ganglia seen on a magnetic resonance imaging (MRI). Blood testing reveals high levels of circulating lactic acid. Leigh syndrome is frequently associated with epilepsy, making it vital not to choose VPA in this subset of patients. 3

# Myoclonic epilepsy (MERRF) disorder

Myoclonic epilepsy with ragged-red fibers (MERRF) is a disorder characterized by myoclonus, generalized epilepsy, ataxia, hearing loss, exercise intolerance, and lactic acidosis. In approximately 90% of cases, MERRF is due to a mutation in the mitochondrial DNA. The most frequently occurring mutation is m.8344A>G, associated with 80% of the cases. This diagnosis is often made clinically as the clinical course progresses. Verification requires molecular examination of muscle tissue. Because seizures are one of the presenting signs of this disorder, VPA could be prescribed prior to diagnosis.3