COMMENT. Young male patients taking AED therapy for seizures are at risk of significant bone loss at the femoral neck. Almost 50% have osteopenia, a 2.5 fold increased prevalence compared to the healthy male population, and the risk of fractures is increased.

LEVETIRACETAM IN PARTIAL SEIZURES

The efficacy and safety of levetiracetam (LEV) as adjunctive therapy were evaluated in 23 children (aged 6-12 years) with monotherapy-resistant partial-onset seizures at Children's Hospital Medical Center, Cincinnati, OH and other major centers. Seizure frequency during an 8-week evaluation period with individualized LEV doses (20-40 mg/kg/day) was compared with the 4-week baseline seizure frequency. Seizure frequency was reduced by >50% in 12 (52%) patients. Plasma concentrations of concomitant AED (carbamazepine or valproic acid) were not affected. Adverse events included headache (33%), anorexia (25%), and somnolence (25%). No alterations in mean clinical laboratory values were observed. A decrease in red blood cell count occurred in 1 patient, and thrombocytopenia in one was attributed to concomitant valproic acid treatment. (Glauser TA, Pellock JM, Bebin EM et al. Efficacy and safety of levetiracetam in children with partial seizures: an open-label trial. Epilepsia May 2002;43:518-524). (Reprints: Dr TA Glauser, Children's Hospital Medical Center, Department of Neurology OSB5, 3333 Burnet Avenue, Cincinnati, OH 45229).

COMMENT. Levetiracetam (Keppra®), an adjunctive therapy for partial seizures in adults, is shown to be effective and relatively safe in children, by open-trial. A randomized, placebo-controlled, double-blind trial is ongoing.

In an editorial (Van Ness PC. Therapy for the epilepsies. Arch Neurol May 2002;59:732-733), Levetiracetam, introduced in 1999, is described as a broad spectrum AED, twice-daily dosing, unique mechanism of action, low toxicity, low protein binding, low risk of rash, and no drug interactions. Sedation is the main disadvantage, occurring in 15% of patients.

DEGENERATIVE DISEASES

MOLECULAR DIAGNOSIS OF ALEXANDER DISEASE

The value of clinical and MRI criteria in the diagnosis of Alexander disease was determined by using GFAP gene sequencing as the confirmatory assay in 13 patients with variable ages of onset in a study at Children's National Medical Center, Washington, DC and other centers. Genomic DNA was screened for mutations in the GFAP gene, and 12 (92%) tested positive. Seven of the 12 presented in infancy (ages 2 to 18 nonths) with megalencephaly, seizures, failure to thrive, and delayed development. Five were juvenile-onset (ages 5 to 9 years) with variable symptoms, 2 being asymptomatic and the remainder with severe symptoms, including growth failure, sleepiness, and vomiting. Both groups showed progression of megalencephaly with increasing age, bulbar signs, spasticity, cognitive deficits, and developmental delay. MRI showed diffuse, symmetrical white matter abnormality in the frontal regions, sparing subcortical U-fibers. GFAP gene mutation analysis should be included in the initial diagnostic evaluation of infants or young children presenting with megalencephaly and predominantly frontal leukoencephalopathy on MRI. Gene analysis may now take the place of brain biopsy histological examination for diagnostic Rosenthal fibers. (Gorospe JR, Naidu S, Johnson AB et al. Molecular findings in symptomatic and pre-symptomatic Alexander disease patients. Neurology May (2 of 2)

and pre-symptomatic Alexander disease patients. Neurology May (2 of 2) 2002;58:1494-1500). (Reprints: Dr Eric Hoffman, Research Center for Genetic Medicine, Children's National Medical Center, 111 Michigan Ave NW, Wasington, DC 20010).

COMMENT. Infantile onset Alexander disease is characterized by megalencephaly, developmental delay, spasticity, and seizures, and juvenile onset cases have brainstem signs, spasticity, with or without megalencephaly or seizures. The diagnosis is strongly suspected when the MRI shows white matter changes predominating in frontal cortical regions. The histological hallmark of Alexander disease is the finding of Rosenthal fibers, astrocytic cytoplasmic inclusions. GFAP gene mutation analysis may preclude the necessity for brain biopsy.

A novel mutation in glial fibrillary acidic protein (GFAP) gene is reported in a 13-year-old boy diagnosed with juvenile Alexander disease. (Sawaishi Y, Yano T, Takaku I, Takada G. Neurology May (2 of 2);58:1541-1543).

GENETICS AND FRIEDREICH ATAXIA

The effects of genetic understanding on clinical evaluation and therapy of Friedreich ataxia (FRDA) are reviewed from the University of Pennsylvania School of Medicine, Philadelphia. The major genetic mutation of FRDA involves a novel gene (X25 or FRDA) encoding the protein *frataxin*. FRDA results from a deficiency of functional frataxin, a protein involved in mitochondrial iron homeostasis. The resultant iron accumulation and mitochondrial abnormalities lead to oxidant damage. Expanded clinical manifestations have resulted from the recognition of broader phenotypic features, including later age of onset and spasticity with hyperreflexia and without ataxia. Diseases that clinically overlap with FRDA include 1) ataxia with vitamin E deficiency; 2) autosomal recessive spastic ataxia of Charlevoix-Saguenay, occurring in Quebec; 3) posterior column ataxia with retinal pigmentary changes; 4) early-onset cerebellar atrophy with retained reflexes; and 5) atypical cases of Charcot-Marie-Tooth disease. In diagnosis, the standard genetic testing measures the GAA repeat length on both alleles, with 95-98% detection rate. Genetic testing also identifies carriers of FRDA. In treatment, observation for progressive cardiomyopathy, arrhythmias, scoliosis, and diabetes mellitus may improve life span, and trials of antioxidants are of potential but unproven value. (Lynch DR, Farmer JM, Balcer Lj, Wilson RB. Friedreich ataxia. Effects of genetic understanding on clinical evaluation and therapy. Arch Neurol May 2002;59:743-747). (Reprints: David R Lynch MD PhD, Division of Neurology, Children' Hospital of Philadelphia, 502 Abramson Bldg, Philadelphia, PA 19104).

COMMENT. Friedreich ataxia is a progressive neurodegenerative disorder affecting 1 in 50,000, the most prevalent early-onset hereditary ataxia. Degeneration involves the dorsal root ganglion neurons, their axons in the dorsal columns, spinocerebellar tracts, and dentate nuclei in the cerebellum. The ataxia is both sensory, due to loss of proprioception, and partially of cerebellar origin. Additional manifestations include cardiomyopathy, scoliosis, and diabetes mellitus. The discovery of the genetic mutation and deficiency of frataxin protein has provided a better understanding of the disease mechanisms and potential therapies.