COMMENT. Biochemical and ultrastructural abnormalities indicative of mitochondrial disease are sufficiently frequent to recommend muscle biopsy as an important diagnostic examination in children with unexplained mental retardation. Both ultrastructural mitochondrial abnormalities and decreased activity of 1 or more respiratory chain enzymes are required for a probable diagnosis of mitochondrial disease. The commonly known mtDNA mutations are a rare cause of childhood encephalomyopathies, in contrast to the adult form that frequently shows the MELAS mutation.

Mitochondrial DNA (mtDNA) defects in neuromuscular disorders are reviewed by Marin-Garcia J. and Goldenthal MJ (Pediatr Neurol February 2000;22:122-129) at the Molecular Cardiology Institute, Highland Park, NJ. Mitochondrial mtDNA deletions were found in 1 child with Kearns-Sayre disease, 1 with stroke/CADASIL, and 1 with progressive external ophthalmoplegia, hypotonia, developmental delay, and lactic acidosis. Reduced mtDNA levels occurred in 2 children with encephalomyopathy, hypotonia, lactic acidosis, and mtDNA depletion. Pathogenic mtDNA point mutations are maternally inherited, and most are located in tRNA and rRNA genes.

CLINICAL APPROACH TO METABOLIC MYOPATHIES

The clinical and laboratory evaluation of the patient with suspected metabolic myopathy is reviewed from the Department of Neurology, Children's Hospital, Boston, MA. Myopathies are classified as *static* characterized by proximal weakness, generalized weakness, and developmental delay; and *dynamic* with recurrent episodes of reversible muscle dysfunction, sometimes myoglobinuria, related to exercise intolerance, fasting, exposure to cold, anesthesia, intercurrent infection, or a low-carbohydrate, high-fat diet. Both forms are common in mitochondrial myopathies. The type or duration of exercise inducing weakness may be specific: Prolonged, low-intensity activity (eg walking) - induced weakness occurs with fatty acid oxidation (FAO) defects; high-intensity exercise (eg weight lifting or sprinting) - glycogen or glucose metabolism defects. Myoglobinuria may be induced by inborn errors of glycogen/glucose metabolism, FA metabolism, and some mitochondrial cytopathies. Laboratory tests include CK, elevated in glycogen defects and lactate dehydrogenase deficiency; blood lactate and pyruvate elevated in mitochondrial myopathies; liver transaminases elevated in FAO defects; and abnormal carnitine, acylcarnitine, free fatty acids, and hypoketotic hypoglycemia in lipid metabolic disorders. EMG, Forearm Ischemic Exercise Test, and muscle biopsy with molecular studies may be required in diagnosis. (Darras BT, Friedman NR. Metabolic myopathies: a clinical approach; Part I. Pediatr Neurol February 2000;22:87-97). (Respond: Dr Darras, Neuromuscular Program, Neurology Department, Fegan 11, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115).

COMMENT. A helpful algorithm for the step-by-step diagnosis of metabolic myopathies is provided by the authors.

SEIZURE DISORDERS

GELASTIC EPILEPSY AND HYPOTHALAMIC HAMARTOMA

Three patients with small hypothalamic hamartomas and a recurrent "pressure to laugh," often without actual laughter, are reported from the University of Melbourne, Australia, and McGill University, Canada. Giggling

attacks began in infancy, at age 4 years, and at 10 years. Complex partial seizures occurred in 2 patients with onset at 14 and 25 years, and focal clonic seizures in 1 beginning at 2 years. EEGs and IQ tests were normal, and pressure-to-laugh sensations were not controlled by anticonvulsants. MRIs revealed the small hypothalamic hamartomas. (Sturm JW, Andermann F, Berkovic SF. "Pressure to laugh": An unusual epileptic symptom associated with small hypothalamic hamartomas. Neurology February 2000;54:971-973). (Reprints: Dr Samuel F Berkovic, Department of Neurology, Austin Medical Center, Studley Road, Heidelberg (Melbourne), Victoria 3084, Australia).

COMMENT. The childhood epileptic syndrome of early-onset gelastic seizures, hypothalamic hamartoma, and precocious puberty is usually associated with a poor prognosis, leading to cognitive deterioration, but in a recent report of 9 cases, 4 were cryptogenic and the outcome was more benign (see Ped Neur Briefs March 1999;13:19-20). The present authors consider their syndrome as a mild form of gelastic epilepsy.

Gelastic seizures with a frontal lobe focus. (Biraben A, Sartori E, Taussig D et al. Epileptic Disorders Dec 1999;1:221-227). A 5-year-old boy had daily episodes of forced laughter, without feelings of mirth, and with loss of contact, automatisms, facial flushing, and right facial jerking. Ictal EEG showed right frontal spikes and slowing that spread to the temporal region. MRI was normal, but interictal SPECT showed hypoperfusion in the right frontal lobe. Seizures were controlled with sodium valproate. Gelastic seizures originating in the frontal lobe are unusual, the more common locus being the diencephalon or temporal lobe.

GENETICS OF CHILDHOOD EPILEPSY

Genetic epilepsies are classified according to the mechanism of inheritance in three major groups: 1) Mendelian idiopathic epilepsies; 2) Non-Mendelian or "complex" epilepsies; and 3) Chromosomal disorders. *Mendelian epilepsies* include the autosomal dominant, benign familial neonatal and infantile convulsions, nocturnal frontal lobe epilepsy, and generalized epilepsy with febrile seizures. *Non-Mendelian "complex" idiopathic epilepsies* include juvenile myoclonic, febrile convulsions, childhood absence, juvenile absence, and benign epilepsy with centrotemporal spikes. Among *symptomatic epilepsies,* progressive myoclonic types account for 1% of childhood epilepsies. These are Mendelian (Unverricht-Lundborg, neuronal ceroid lipofuscinoses, and Lafora disease), and Non-Mendelian "complex" progressive myoclonic, associated with mitochondrial disorders. New classifications based on molecular genetics require identification of common DNA sequence variations between individuals. The authors predict that DNA from a buccal swab will be analyzed for common mutations in ion channel genes, and an antiepilepsy drug designed for the specific electrophysiological dysfunction. With the precise molecular diagnosis of the future, the EEG could become a redundant investigation. (Robinson R, Gardiner M. Genetics of childhood epilepsy. Arch Dis Childhood February 2000;82:121-125). (Respond: Dr Robinson, Department of Paediatrics, Royal Free and University College Medical School, University Street, London WC1E 6JJ, UK. - email: robert.robinson@ucl.ac.uk).

COMMENT. The epilepsies are heterogeneous in manifestations and causes. A genetic etiology may be present in more than 40% of childhood patients.