

(SMA) and lower motor neuron disease. Muscle TK2 activity was reduced compared to controls (28% cf 37%). All 20 patients had COX-negative fibers on muscle biopsies.

In Family 1, Patient 1, a Hispanic boy, had nonconsanguinous parents. Normal until 12 months of age, he developed a progressive ataxic gait impairment, and was unable to walk or stand by 2 years. Muscle weakness and hypotonia involved shoulder and hip girdle muscles, respiratory insufficiency necessitating mechanical ventilation was present by 3 years of age, and he died at 40 months. Laboratory studies had shown an elevated CK level (1.238 U/L,  $n < 200$ ), and nonspecific organic aciduria. An older sister (patient 2) had a slower course, falling frequently at age 16 months, and was unable to walk by 4 years of age. Her CK was 950 U/L and she had lactic acidosis (12 mmol/L,  $n < 2.2$ ). A younger sister was asymptomatic. In Family 2, Patient 4 lost his ability to walk by 2 years, and had severe proximal weakness, muscle wasting, areflexia, and scoliosis at age 3 years. His cognitive function and language were normal for his age. EMG showed chronic partial denervation, fibrillations, and loss of motor unit potentials, compatible with SMA. Serum CK and lactate were mildly increased. He is alive at 48 months of age. His sister, who presented with weakness and hypotonia in early infancy, episodic vomiting, failure to thrive, and metabolic acidosis, had a primary myopathy. She died at 2 years of age, with respiratory infection and insufficiency. The clinical expression of TK2 mutations may be myopathic or neuropathic and the myopathic form is genetically heterogeneous. (Mancuso M, Salvati L, Sacconi S, et al. Mitochondrial DNA depletion. Mutations in thymidine kinase gene with myopathy and SMA. *Neurology* October (2 of 2) 2002;59:1197-1202). (Reprints: Dr Tuan H Vu, Department of Neurology, P&S Building 5-431, Columbia University, New York, NY 10032).

COMMENT. Mitochondrial DNA depletion syndrome (MDS) is an autosomal recessive disorder of early childhood that involves muscle (myopathic form) or liver and brain (hepatocerebral form). The myopathic form is characterized by progressive weakness, hypotonia, areflexia, and respiratory failure before 10 years of age. MDS is a heterogeneous disorder in which mtDNA depletion in affected tissues is generally proportional to the severity of symptoms. Mutations in the thymidine kinase gene (TK2), involved in deoxyribonucleotide metabolism, can be manifested clinically by a pure myopathy or spinal muscular atrophy. Other genes may also be involved in the etiology of myopathic MDS.

## MOVEMENT DISORDERS

### **MYOCLONUS-DYSTONIA SYNDROME**

The clinical phenotypic features of myoclonus-dystonia (M-D), including motor symptoms, psychiatric disorders, and neuropsychological deficits, were evaluated in 50 subjects from three M-D families examined at Mount Sinai School of Medicine, New York, and other centers. Each family had different truncating mutations in the SGCE gene on 7q21 chromosome, and one had an additional missense alteration in the DRD2 gene on 11q23. The families had several motor features in common: symptoms began in the first or second decade and either myoclonus or dystonia or both involved the upper limbs, head, neck, or trunk. Psychiatric disorders, correlating with the motor symptoms, occurred in most patients and included depression, obsessive-compulsive disorder, and substance abuse, especially alcohol dependence. Whether the OCD and other psychiatric problems are specifically related to the M-D gene mutations or are secondary to the stress of the disease remains to be determined. Cognitive tests revealed

impaired verbal learning and memory in one family, impaired memory in a second, and none in a third family. (Doheny DO, Brin MF, Morrison CE, et al. Phenotypic features of myoclonus-dystonia in three kindreds. Neurology October (2 of 2) 2002;59:1187-1196). (Reprints: Dana O Deheny MS, Department of Neurology, Mount Sinai School of Medicine, Annenberg 14-51A, Box 1052, New York, NY 10029).

COMMENT. A plethora of articles on myoclonus-dystonia syndrome (MDS) are published in current literature. The locus for MDS is mapped to 7q21 region and 11q23, and 7 different heterogeneous mutations in the gene for epsilon-sarcoglycan (SGCE) have been identified (see Ped Neur Briefs Oct 2002;16:78-79). The present article identifies 3 families with different mutations in the SGCE on 7q21, and one also with a missense alteration in the DRRD2 gene on 11q23.

A novel locus for inherited myoclonus-dystonia on chromosome 18p11 has been reported in 13 members of a large Canadian family, reported from the Ottawa Hospital, University of Ottawa, Canada (Grimes DA, Han F, Lang AE, et al. Neurology Oct (2 of 2) 2002;59:1183-1186).

Clinical findings of a M-D family with two distinct mutations are reported (Doheny D, Danisi F, Smith C et al. Neurology Oct (2 of 2) 2002;59:1244-1246). A novel deletion in the DYT1 gene on the maternal side and a missense change in the SGCE gene on the paternal side were found. The father of the index case carried the 7q21 missense alteration and had mild intermittent myoclonus beginning in early childhood. The index case and her brother had both mutations and they presented with myoclonus in early childhood. Dystonia developed later, and both patients had psychiatric disorders.

Autosomal dominant GTP-CH deficiency presenting as a dopa-responsive myoclonus-dystonia syndrome is reported from University of Rome, Italy (Leuzzi V, Carducci Ca, Carducci Cl, et al. Neurology Oct (2 of 2) 2002;59:1241-1243). A 17-year-old boy presented with myoclonus and later developed dystonia and bradykinesia. The paternal grandfather and three relatives had M-D and resting or postural tremor. A missense mutation was found in the exon 6 of GCH-1 gene (K224R).

An editorial is provided by Furukawa Y and Rajput AH (Inherited myoclonus-dystonia. How many causative genes and clinical phenotypes? Neurology Oct (2 of 2) 2002;59:1130-1131). Inherited M-D is a new term for "hereditary essential myoclonus" or "hereditary (alcohol-responsive) myoclonic dystonia". Clinical features of inherited M-D are as follows: autosomal-dominant inheritance; onset in childhood or adolescence; myoclonus affecting neck, shoulders, and arms and dystonia manifested by torticollis and writer's cramp; alcohol responsiveness; psychiatric problems; and a benign clinical course with normal life span. Locus heterogeneity includes 7q21 for the SGCE gene (10 families), 18p11 (single family and unknown gene), and possibly, 11q23 for DRD2. Pedigree analysis suggests maternal imprinting in genetically confirmed M-D families; this is responsible for reduced penetrance and non-expression of the trait when the disease is inherited maternally.