

## MOVEMENT DISORDERS

### **PAROXYSMAL NONKINESIGENIC DYSKINESIA**

A Canadian family of European descent with paroxysmal nonkinesigenic dyskinesia (PNKD), and a gene locus that links to a distinct region on chromosome 2q31, is reported by researchers at University of British Columbia, Canada. The age at onset in 10 affected members of the 14-member family was childhood in 2, teens in 2, and 30 to 50s in the remainder. They presented with episodes of dystonia, primarily affecting hands and feet symmetrically, and not triggered by movement, exercise, alcohol, caffeine or excitement. Attacks lasted 2-5 minutes and occurred daily. Treatment with various anticonvulsants, including acetazolamide, in one patient was ineffective. Mutation analysis of the MR-1 and GAD67 genes showed no linkage in affected family members. A genome-wide screen generated positive LOD scores at chromosome 2q31. (Spacey SD, Adams PJ, Lam PCP et al. Genetic heterogeneity in paroxysmal nonkinesigenic dyskinesia. **Neurology** May (2 of 2) 2006;66:1585-1590). (Reprints: Dr Sean Spacey, Neurology and Neurogenetics, Room S-127, 2211 Wesbrook Mall, UBC Hospital, Vancouver, BC V6T 2B5, Canada).

COMMENT. This family is distinguished from 10 previously reported PNKD families in not having a linkage to the myofibrillogenesis regulator 1 gene (MR-1), on chromosome 2q32-36, but instead, having a novel gene locus at chromosome 2q31. Also, caffeine and alcohol, which act as consistent triggers in other PNKD pedigrees with MR-1 gene mutations, failed to stimulate attacks. Two different genes appear to be responsible for PNKD, indicative of genetic heterogeneity.

### **ACTION DYSTONIA IN LESCH-NYHAN DISEASE**

The motor disorder associated with Lesch-Nyhan disease (LND) was studied in a total of 44 patients (ages 2 to 38 years) seen at Johns Hopkins Hospital, Baltimore, MD, and other US and international centers. A characteristic motor syndrome begins with hypotonia and/or delayed motor development in the first 3-6 months of age, and is followed by involuntary movements between 6 and 24 months. The course is then relatively static with severe action dystonia, sometimes associated with choreoathetosis or ballismus, and less frequently, pyramidal signs affecting the lower extremities. The evolution of the motor syndrome of LND parallels the cognitive disability and behavioral syndrome that includes mental retardation and self-injurious behavior. Brain MRI in 25 patients showed cerebral atrophy or maldevelopment in 3, and 34% reduction in basal ganglia volume in 7 compared to normal controls. The results of this large multi-centre prospective study are compared with a review of 122 previous reports, including 254 patients. (Jinnah HA, Visser JE, Harris JC et al. Delineation of the motor disorder of Lesch-Nyhan disease. **Brain** May 2006;129:1201-1207). (Respond: HA Jinnah MD PhD, Meyer Room 6-181, Department of Neurology, Johns Hopkins Hospital, Baltimore, MD 21287).

COMMENT. LND is an X-linked recessive neurobehavioral disorder of purine metabolism caused by deficiency of the purine salvage enzyme hypoxanthine-guanine phosphoribosyltransferase (HPRT). The triad of clinical manifestations, mental retardation, self-injurious behavior, and motor disability, develops after birth, and the extrapyramidal movements are evident in the second year of life. In the present report, hypotonia and dystonia were more frequent than spasticity, noted in earlier descriptions of the syndrome. The authors attribute these discrepancies in neurological findings to a possible misinterpretation of a "striatal toe" as a Babinski reflex, and changes in signs with age, not observed in retrospective studies. In laboratory tests, serum uric acid is elevated, and diagnosis is confirmed by a urinary uric acid-creatinine ratio of 2:1 or higher, and enzymatic analysis of blood, cultured skin fibroblasts, or prenatal, amniotic fluid (Menkes JH, 1985).

## SEIZURE DISORDERS

### LONG-TERM FOLLOW-UP OF JUVENILE MYOCLONIC EPILEPSY

A population of 257 juvenile myoclonic epilepsy (JME) patients and family members was prospectively evaluated in a study at UCLA School of Medicine and international centers. Patients were subdivided into four groups: 1) classic JME [186 patients]; 2) childhood absence epilepsy (CAE) evolving as JME with GM, myoclonic and absence seizures [45]; 3) JME mixed with adolescent onset pyknolepsy [18]; and 4) JME plus astatic seizures [8]. JME was the sole clinical phenotype in 40% of JME family members, followed over a mean of 11+/-6 years (max 52 years); grand mal (GM) occurred in 35%. Absence seizures were more common in family members of CAE evolving to JME than in those of classic JME families; 66% of CAE families evolving to JME had various phenotypes of idiopathic generalized epilepsy (IGE). Patients with CAE evolving to JME showed female preponderance, maternal transmission and poor response to treatment; 7% were seizure free of 58% of those with classic JME ( $P<0.001$ ), 56% with JME and pyknolepsy, and 62% with JME plus astatic seizures. The various epilepsy syndromes persisted in to adulthood; as long as 11-50 years in 25 patients ages 21 to 52 years. JME is genetically heterogeneous, with 7 known chromosome loci, 3 epilepsy-causing mutations and 2 genes with single nucleotide polymorphisms. (Martinez-Juarez IE, Alonso ME, Medina MT et al. Juvenile myoclonic epilepsy subsyndromes: family studies and long-term follow-up. *Brain* May 2006;129:1269-1280). (Respond: Dr Antonia V Delgado-Escueta, Epilepsy/Genomics Laboratories, Comprehensive Epilepsy Program, David Geffen School of Medicine at UCLA and VA GLAHS-West Los Angeles, Room 3405 (127B), Bldg 500, West Los Angeles VA Medical Center, 11301 Wilshire Bldg, Los Angeles, CA 90073).

COMMENT. The authors suggest the inclusion of 4 syndromes under IGE in the ILAE Classification, based on the above study: (1) classic JME; (2) pyknoleptic CAE evolving to JME; (3) JME with adolescent onset pyknoleptic absences; and (4) JME with astatic seizures. CAE that evolves into JME should be separated from CAE that remits in adolescence and does not develop myoclonic seizures.

**Perioral reflex myoclonias**, the leading seizure type in reading epilepsy, is more frequent in JME compared to focal epilepsies, according to Mayer TA et al. (*Epilepsia* June 2006;47:1059-1067). PRM may be induced by reading, writing or talking.