METABOLIC DISORDERS

MAPLE SYRUP DISEASE: DIAGNOSIS AND THERAPY

Infants at high risk for maple syrup disease (MSD) were identified by family history and molecular testing for the Y393N mutation of the E1a subunit of the branched chain a-ketoacid dehydrogenase in a study at Johns Hopkins University School of Medicine, Baltimore, MD. Eighteen neonates with MSD were identified in the high-risk group (n=39) between 12 and 24 hours of age using amino acid analysis of blood specimens. Eighteen additional infants, biochemically intoxicated at diagnosis, recovered rapidly with treatment emphasizing enhancement of protein anabolism and dietary correction of amino acid imbalances. Plasma leucine levels decreased to <400 mcmol/L at 2 to 4 days after diagnosis. Infections caused loss of metabolic control, with cerebral edema, hyponatremia and decreased os Morton DH, Strauss KA, Robinson DL et al. Diagnosis and treatment of maple syrup urine disease: a study of 36 patients. <u>Pediatrics</u> June 2002;109:999-1008). (Reprints: D Holmes Morton MD, Clinic for Special Children, Box 128, Strasburg, PA 17579).

COMMENT. The authors describe a treatment program for MSD that provides a benign neonatal course, normal growth and development, and management without hospitalization. Common infection may provoke metabolic intoxication with cerebral edema and hyponatremia. Treatment must inhibit protein catabolism, sustain protein synthesis, prevent amino acid deficiencies, and maintain normal serum osmolarity.

MUSCLE DISEASES

MULTI-MINICORE AND CENTRAL CORE DISEASE

A genome-wide screening was conducted in a consanguinous Algerian family with 3 children with multicore disease at the Groupe Hospitalier Pitie-Salpetriere, Paris, France, and other centers. This recessive disease presented in infancy with moderate predominantly axial weakness, affecting pelvic girdle and hands, joint hyperlaxity, and multiple short-length core lesions (minicores) in both muscle fiber types. The disease was mapped to chromosome 19q13 in this family and in 3 additional families with a similar phenotype. In the Algerian family, a novel homozygous missense mutation (P3527S) was identified in the ryanodine receptor type 1 gene, responsible for autosomal dominant congenital myopathy central core disease. New muscle biopsies performed on reaching adulthood showed typical central core disease with rods. This subgroup of families linked to 19q13 is the first variant of central core disease with genetically proven recessive inheritance and transient early presentation as multi-minicore disease. (Ferreiro A, Monnier N, Romero NB et al. A recessive form of central core disease, transiently presenting as multi-minicore disease, is associated with a homozygous mutation in the ryanodine receptor type 1 gene. Ann Neurol June 2002;51:750-759). (Respond: Dr Ferreiro, INSERM U523, Institut de Myologie, Groupe Hospitalier Pitie-Salpetriere, 47 bd de l'Hopital, 75651 Paris, France),

COMMENT. Multi-minicore disease (MmD) and central core disease (CCD) are congenital myopathies that present with neonatal hypotonia, delayed motor development, and generalized muscle weakness and amyotrophy that are non- or slowly progressive. MmD is autosomal recessive and CCD is autosomal dominant in inheritance. The above study of families provides genetic evidence that MmD is a variant of CCD with autosomal recessive inheritance and transitory expression as MmD.

Congenital myasthenic syndrome (CMS) caused by a newly identified chromosomal microdeletion and N-box mutation of the AChRe gene is reported from Ludwig-Maximilans-University, Munich, Germany. (Abicht A, Stucka R, Schmidt C et al. <u>Brain</u> May 2002;125:1005-1013). CMSs are a heterogeneous group of disorders with impaired neuromuscular transmission due to various inherited defects. This is the first report of a chromosomal microdeletion affecting an AChR gene in skeletal muscle.

Therapies for disorders of the neuromuscular junction are reviewed in an editorial (Pruitt JN II, Swift TR. <u>Arch Neuro</u>] May 2002;59:739-742). These are of 2 types: 1) symptomatic treatment with cholinesterase inhibitors and plasmapheresis; and 2) immunotherapy (immunosuppressant medications), immunomodulating therapy (immunoglobulin (Ig) G), and thymectomy. The most promising approach is the development of more specific and less toxic immunosuppression therapies.

ATTENTION DEFICIT AND COMORBID DISORDERS

ATTENTION DYSFUNCTION AND SUBSTANCE ABUSE

The influence of adolescent attention functioning on the development of substance abuse was studied in 66 high-risk youths over an 8-year period at the University of California San Diego Department of Psychiatry. Substance involvement was assessed by self-report, resource person reports, and randomly sampled toxicology screens at interviews at ages 15 through 23. Lower scores on neuropsychological tests of attention/executive functioning at intake assessment were prospectively (8 years later) associated with greater frequency of substance use and marijuana use in particular. Youths who met one or more substance dependence criteria as adults had significantly poorer attention performance in adolescence. Gender, education, conduct disorder, family history of substance use disorders, and learning disabilities did not influence the relationship between attention functioning and substance involvement. Clinical diagnoses of ADHD were not available in this patient population and study. (Tapert SF, Baratta MV, Abrantes AM, Brown SA. Attention dysfunction predicts substance involvement in community youths. J Am Acad Child Adolesc Psychiatry June 2002;41:680-686). (Respond: Dr Susan F Tapert, Psychology Service (116B), VA San Diego Healthcare System. 3350 La Jolla Village Drive, San Diego, CA 92161).

COMMENT. Adolescents with impaired attention functioning are at increased risk for development of alcohol and drug involvement.

INFANT CRYING AND RISK OF HYPERACTIVITY AND LEARNING DISORDERS

Infants with persistent crying (PC) in the first 6 months (mean age 3.8 months) were reassessed at 8 to 10 years of age and compared with 64 classroom controls for hyperactivity, conduct problems and academic difficulties in a prospective study at the University of Hertfordshire, UK. Ten (19%) of 53 PC infants had pervasive hyperactivity, as reported by child, parent and teacher, compared with 1 of 62 controls, at school age. Parents and children but not