METABOLIC AND DEGENERATIVE DISORDERS

MOLECULAR BASIS OF METACHROMATIC LEUKODYSTROPHIES

Arylsulfatase A alleles were analyzed in 68 patients with metachromatic leukodystrophy in the Department of Biochemistry II, Georg-August-Universitat Gottingen, Gosslerstr, Gottingen, Germany. Of the 68 patients 50 carried at least one of the two metachromatic leukodystrophy alleles (I or A). Twenty-three patients were homozygous for either allele I or allele A or heterozygous for both alleles. In 18 patients neither allele I nor allele A was found. These two alleles accounted for about half of all arylsulfatase A alleles in this selection of patients. Patients were classified clinically as late infantile, juvenile, or adult forms. All six patients with MCL homozygous for allele I had the late infantile form. Five who were homozygous for allele A had the adult form and three had the juvenile form. Seven with both allele I and allele A had the juvenile onset MCL. The authors conclude that like many lysosomal storage disorders MCL shows clinical heterogeneity that reflects genetic heterogeneity. Allele I is associated with late infantile and more severe disease and allele A occurs with the adult form and juvenile forms of MCL. (Polten A, Gieselmann V et al. Molecular basis of different forms of metachromatic leukodystrophy. N Engl J Med Jan 3, 1991; 324:18-22).

COMMENT. Three forms of metachromatic leukodystrophy are distinguished according to the age of onset: late infantile (1-2 years), juvenile (3-16), and adult (more than 16 years). The incidence is estimated at 1:40,000. These authors describe four genotypes as combinations of two arylsulfatase A alleles that cause MCL and a pseudo deficiency allele. These genotypes are associated with levels of residual arylsulfatase A activity from 0 to 10% and represent the infants and children affected most severely to adults who may be asymptomatic or suffer from a slowly progressive form of MCL. The authors had identified two persons with compound heterozygosity for the pseudo deficiency allele and the MCL allele I. This combination reduces arylsulfatase A to about 10% of normal activity. Both persons were in their third decade of life and were asymptomatic. The most severe type of MCL is associated with homozygosity for allele I. One copy of allele A lessens the severity and produces the juvenile form, and two copies of allele A results in the mildest or adult form of MCL. One copy of arylsulfatase A pseudo deficiency allele permits a normal phenotype. Patients with the juvenile or adult form of MCL were thought to be better candidates for bone marrow transplantation than those with the late infantile form since less enzyme needed to be replaced.

MENKES MAPLE SYRUP URINE DISEASE: TREATMENT

Five patients with maple syrup urine disease were treated intravenously with branched-chain amino acid-free solution of amino acids during nine episodes of acute illness and are reported from the Children's Hospital of Philadelphia, PA. In a regimen of total parenteral