Mandel H, Reiss J, et al. Localization of a gene for molybdenum cofactor deficiency, on the short arm of chromosome 6, by homozygosity mapping. Am J Hum Genet July 1998;63:148-154). (Reprints: Dr Nadine Cohen, Department of Genetics, Tamkin Human Molecular Genetics Research Facility, Technion-Israel Institute of Technology, Bruce Rappaport Faculty of Medicine, POB 9649, Haifa 31096, Israel).

COMMENT. Molybdenum cofactor deficiency (MoCoD) is a fatal inherited, autosomal recessive, disorder manifesting with neonatal seizures unresponsive to therapy, opisthotonus, retardation, craniofacial dysmorphic features, ectopia lentis, and progressive neurologic deterioration. MoCoD is caused by abnormal biosynthesis of the Mo-complexed pterin cofactor for the enzymes: sulfite oxidase, xanthine dehydrogenase, and aldehyde oxidase. Postnatal diagnosis is suggested by hypouricemia and elevated urinary sulfite, and confirmed by sulfite oxidase deficiency in fibroblasts. Microsatellite markers may now be used for prenatal diagnosis, in addition to chorionic villus sampling and sulfite oxidase assay. Dietary therapy with methionine restriction and cysteine supplements has provided short-term clinical improvements (see Progress in Pediatric Neurology II, PNB Publ, 1994;p475).

SEIZURE DISORDERS

INFANTILE EPILEPTIC ENCEPHALOPATHY OF OHTAHARA

A case of infantile epileptic encephalopathy (Ohtahara syndrome) with EEG suppression-bursts at 2 days and associated with diffuse cerebral migrational and maturation disorder, diagnosed at autopsy at 19 months, is reported from Montreal Children's Hospital, McGill University, Montreal, Canada. Seizures of multiple types, usually generalized tonic clonic, began on the first day and persisted until the child died, despite various AEDs, ACTH, and a failed trial of the ketogenic diet. CT at 2 days showed a parietal skull fracture and extradural hemorrhage. MRIs at 1 and 5 months showed delayed myelination, a thin corpus callosum, and increased CSF spaces. EEGs after 5 months of age recorded generalized epileptiform slow spike-and-wave and multifocal abnormalities. CSF exam revealed absence of GABA. Diagnosis of cerebral migration disorder was made only at autopsy by microscopic exam, showing microdysgenesis of cerebral cortex, hippocampal cell loss and astrogliosis, immature neurons, and enlarged dentate and olivary nuclei. (Miller SP, Dilenge M-E, Meagher-Villemure K, O'Gorman AM, Shevell MI. Infantile epileptic encephalopathy (Ohtahara syndrome) and migrational disorder. Pediatr Neurol July 1998;19:50-54). (Respond: Michael I Shevell MD, Department of Neurology, Montreal Children's Hospital, 2300 Tupper Street, Montreal, Quebec H3H 1P3, Canada).

COMMENT. Congenital or acquired structural malformations of cortical development are usually associated with Ohtahara syndrome. Evidence of cortical migration defect may be overlooked on MRI and may be uncovered only at autopsy by microscopic examination.

HIPPOCAMPAL SCLEROSIS IN IDENTICAL TWINS

The genetic and acquired hypotheses of etiology of hippocampal sclerosis (HS) were studied at the University of Melbourne, Australia, using quantitative MRI in three monozygous (MZ) twin pairs, only the index twin having temporal lobe epilepsy and HS. The MZ twin pairs (mean age, 29 years) were compared with 30 age-matched control subjects having no neurologic disorder. All affected twins had HS and a history of prolonged seizures with fever in early childhood.

Temporal lobe epilepsy began at 2 to 6 months after the febrile seizure, at ages 7 mos to 3.5 years. Intracranial volume ipsilateral to the HS was relatively small in 2 of 3 affected twins, when compared to the unaffected twin. HS was not caused by perinatal abnormalities and was unrelated to birth order. The absence of HS in the unaffected twin is evidence against a genetic basis for HS. An acquired lesion secondary to prolonged febrile seizures is the more likely mechanism. (Jackson GD, McIntosh AM, Briellmann RS, Berkovic SF. Hippocampal sclerosis studied in identical twins. Neurology July 1998;51:78-84). (Reprints: Dr Graeme Jackson, Director, Centre for Brain Imaging Research, Austin and Repatriation Medical Centre, Heidelberg (Melbourne), Victoria 3084, Australia).

COMMENT. Monozygotic twin studies support an acquired basis for the hippocampal sclerosis associated with temporal lobe epilepsy, secondary to prolonged febrile seizures in early childhood. All three MZ pairs for which the proband had temporal lobe epilepsy (TLE) and HS were discordant for the clinical diagnosis of TLE. Definitive dysplastic changes were not uncovered by MR, but subtle changes could not be ruled out.

FEBRILE CONVULSIONS AND CONGENITAL HYPOTHYROIDISM

The incidence of febrile convulsions (FCs) among 63 children with congenital hypothyroidism (CH) was compared to that of control children and patient's siblings in a study at Niigata University, Japan. Patients had been treated with L-thyroxine from 1 month of age. FCs had occurred in only one child with CH (1.6%) compared to 8.2% of control children, 9.5% of the patient's siblings, and 6.4% of the patient's parents. (Asami T, Sasagawa F, Kyo S, Asami K, Uchiyama M. Incidence of febrile convulsions in children with congenital hypothyroidism. Acta Paediatr June 1998;87:623-626) (Respond: Dt T Asami, Department of Pediatrics, School of Medicine, Niigata University, Asahimachi-dori 1-757, Niigata, Japan).

COMMENT. Children with congenital hypothyroidism who have been treated regularly with thyroid hormone are less prone to have febrile convulsions. A review of systemic electrolyte and neuroendocrine mechanisms of epilepsy (Millichap JG. In Basic Mechanisms of the Epilepsies. Jasper HH, Ward AA, Pope A (eds), Boston, Little Brown, 1969) found that Timiras PS and Woodbury DM conducted much of the early experimental work on thyroid imbalance and seizures. Timiras showed that thyroxine increased brain excitability in rats, and Woodbury found that an increased seizure threshold in thyroidectomized rats was lowered by giving thyroid hormone. These alterations in brain excitability were correlated with changes in brain electrolytes. Clinical studies have demonstrated that seizures that accompany myxoema coma respond to thyroid treatment. Further studies of the influence of thyroid function on childhood seizures are needed.

KETOGENIC DIET COMPLICATIONS

Serious adverse events are reported in five (10%) of 52 children, aged 1.5-16 years, treated with the ketogenic diet (4:1 ratio/fat: carbohydrate) over a 22-month period at the Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY. The Johns Hopkins KD protocol was followed, and most patients were started at a 4:1 ratio. All patients had intractable epilepsy and had received at least 3 antiepileptic drugs. At diet initiation, 29 were receiving valproate (VPA), of whom 4 developed complications within one month. These included hypoproteinemia, lipemia, hemolytic anemia, and Fanconi's renal tubular acidosis. Two had severe abnormalities of liver function tests, one with a