syndrome, diagnosed by Dr Edward Rabe, now of Maine, USA, had failed to respond to trials of acyclovir, thiamine, carnitine, phenobarbital and diazepam, but showed immediate improvement when biotin was introduced in megadoses, 10-40 x greater than those required in biotin deficiency states. Characteristic signs of the infantile type of biotin encephalopathy, including skin rash, alopecia, ketoacidosis, and organic acidemia, were absent, and presumably, the smaller biotin doses (5-10 mg daily) employed in cases of biotin deficiency were found ineffective. A defect in biotin transport across the blood-brain barrier was postulated, since assays of biotinidase and carboxylase were normal. See Progress in Pediatric Neurology I, II, & III, (PNB Publishers) for reports of neonatal and infantile biotin encephalopathy. This apparent nonspecific effect of biotin in cases of idiopathic familial progressive encephalopathy might prompt trials of megadose biotin in children with chronic refractory encephalopathies.

PYRIDOXINE-DEPENDENT SEIZURES AND MRI CHANGES

Longitudinal brain MRI findings in two patients presenting with neonatal, pyridoxine-dependent seizures and followed for 5 to 9 years are reported from the University of California, Davis, CA. Each patient had three serial MRIs, showing progressive dilation of ventricles and atrophy of cortex and white matter. Patient 1 with AED-resistant seizures was diagnosed at 3.5 months by IV 100 mg pyridoxine administration during EEG monitoring. Seizures characterized by lip smacking, tonic eye deviation, and limb jerking began 2 hours after birth and were initially responsive to phenobarbital. Treatment with 25 mg oral pyridoxine daily controlled seizures, but noncompliance resulted in prolonged seizures and severe developmental disability with hypotonia at 5 year follow-up. Patient 2 developed seizures consisting of eye deviation and facial twitching and responsive to phenobarbital at 4 days after birth. They recurred occasionally up to 8 months of age, when seizures became refractory to anticonvulsants and were found to respond to pyridoxine. During follow-up for 9 years, minor motor seizures, partial and generalized, occurred only during intercurrent illness or noncompliance with pyridoxine, 25 mg daily, treatment. Seizures were preceded by sleepiness and irritability. (Gospe SM Jr, Hecht ST. Longitudinal MRI findings in pyridoxine-dependent seizures. Neurology July 1998;51:74-78). (Reprints: Dr Sidney M Gospe Jr, Child Neurology, UC Davis Medical Center, 2315 Stockton Blvd, Sacramento, CA 95817).

COMMENT. Pyridoxine-dependent seizures of neonatal onset and due to an inborn abnormality of GABA synthesis, if undiagnosed and untreated, can result in progressive cerebral atrophy and severe impairments of psychomotor development. Previous reports have emphasized that the control of seizures alone may not suffice in treating pyridoxine dependency. In order to prevent mental retardation and motor and language delay, it may be necessary to increase the dose of pyridoxine to 10 mg/kg/daily to normalize neurotoxic glutamate levels. Language and cognitive disabilities secondary to pyridoxine-dependency may be partially reversed using optimal pyridoxine dosage. (See Progress in Pediatric Neurology III, PNB Publ, 1997;pp93-98).

GENE LOCATION FOR MOLYBDENUM COFACTOR DEFICIENCY

Linkage of a molybdenum cofactor deficiency (MoCoD) gene to an 8-cM region on chromosome 6p21.3 has been localized by homozygosity mapping in 2 consanguineous affected kindreds of Israeli-Arab origin, including 5 patients, at the Department of Genetics, Tamkin Research Facility, Technion-Israel Institute of Technology, Haifa, Israel. These findings allow prenatal diagnosis with microsatellite markers and carrier detection of this fatal disorder. (Shalata A,

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.