illness, as the optimal prophylactic medication. The benefit demonstrated in this zealously monitored study may not be duplicated in practice when compliance is often less than satisfactory.
In a previous controlled trial, Autret and colleagues in France found the results of intermittent oral diazepam therapy disappointing, a lack of efficacy explained by poor compliance (J Pediatr 1990; 117:490). An approved rectal preparation of diazepam for the home treatment of the acute febrile seizure in high risk patients may offer one alternative to the universal prophylactic intermittent regimen proposed. A survey of pediatric neurologists found only 22% in favor of diazepam (mean dose, 0.46 mg/kg/day at times of fever) in 1990 (see Millichap JG. Progress in Pediatric Neurology, Chicago, PNB Publ, 1991). A more general acceptance of diazepam by pediatricians and parents may be expected following the Boston report, and the results of this wider experience will determine the practical value and safety of this form of treatment.

A clearer understanding of the mechanism of susceptibility to febrile seizures may lead to more specific therapies. Experiments at Ehime Univ School of Medicine, Japan, demonstrate a hyperthermia-induced increase in cortical extracellular glutamate correlating with a decrease in seizure threshold temperature in rats (Morimoto T et al. Pathogenic role of glutamate in hyperthermia-induced seizures. Epilepsia May/June 1993; 34:447-452).

METABOLIC DISORDERS AND SEIZURES

BIOTINIDASE DEFICIENCY AND SEIZURES

The clinical features of 78 symptomatic children with biotinidase deficiency were reviewed and the response to antiepileptic drugs and biotin therapy in 43 (55%) with seizures are reported from the Medical College of Virginia, Richmond, VA. Seizures were the presenting symptom in 30 (38%) patients, with onset between 2 and 24 months (mean, 8 months). Seizure patterns were generalized tonic-clonic or clonic in 56%, infantile spasms or myoclonic in 16%, and partial in only 5%. EEGs were abnormal in 16 (76%) of 21 patients tested; spike or epileptiform discharges were reported in 9. Antiepileptic drugs controlled seizures in 22 (51%) patients, but treatment was withdrawn without relapse after biotin therapy was initiated. Biotin orally, 5 to 10 mg daily, stopped seizures within 24 hours in 12 of 16 (75%) children whose seizures were uncontrolled by AEDs. Five infants died and 3 sustained permanent brain damage before the biotinidase deficiency was diagnosed. (Salbert BA, et al. Characterization of seizures associated with biotinidase deficiency. Neurology July 1993; 43: 1351-1355). (Reprints: Dr Barry Wolf, Dept of Human Genetics, Medical College of Virginia, Box 33, MCV Station, Richmond, VA 23298).

COMMENT. Early diagnosis by newborn screening is recommended by the authors. Biotinidase enzyme deficiency and a trial of biotin should be considered in infants or young children with poorly controlled seizures, especially in those with hypotonia, ataxia, skin rash, alopecia, metabolic ketoacidosis, or organic aciduria. Symptoms resolve rapidly after biotin therapy, but neurologic damage may be irreversible if diagnosis is delayed. (see Ped Neur Briefs, Jan 1990).

MOLYBDENUM-COFACTOR DEFICIENCY AND SEIZURES

The clinical, biochemical, and neuropathological findings in two neonates with molybdenum-cofactor deficiency presenting with convulsions are reported from the Academic Medical Center, Amsterdam, The Netherlands. Patient 1 was admitted at day two with feeding problems, jitteriness, an abnormal cry, apneic spells, and partial and generalized seizures. Head circumference, weight and length were above the 97th percentile. EEGs showed a burst suppression pattern. CT revealed diffuse hypodense ischemic changes. Plasma and urinary cysteine were decreased, and urine sulphite, S-sulphocysteine, taurine, and thiosulphate were increased. Purine analysis showed elevated xanthine and hypoxanthine in the urine, while uric acid was very low. Seizures were refractory, and the infant died on the 10th day. Cultured fibroblasts from a skin biopsy showed absent sulfite oxidase activity. Autopsy findings were meningeal fibrosis, loss of cortical neurons, gliosis and cystic lysis of white matter. Patient 2 was admitted at age 4 days with feeding difficulties, hypertonia, jitteriness, opisthotonus, and high-pitched cry. Generalized and partial tonic-clonic seizures were resistant to treatment. EEG was a multifocal epileptic pattern. An initial diagnosis of postanoxic encephalopathy was changed to molybdenum-cofactor deficiency at 3 years, on reexamination prompted by the revelation of parental consanguinity. Clinically deteriorated, he had spastic tetraplegia, intractable epilepsy, and characteristic metabolic changes. He died 8 months later. Diagnosis was confirmed by liver biopsy and sulfite oxidase and xanthine oxidase analyses. Lens dislocation, a frequent feature of the syndrome, was absent. (Slot HMJ et al. Molybdenum-cofactor deficiency: an easily missed cause of neonatal convulsions. Neuropediatrics June 1993; 24: 139-142). (Respond: Mrs HMJ Slot MD, Dept of Neonatology, Academic Medical Center, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands).

COMMENT. Molybdenum-cofactor deficiency is an inborn error of metabolism that results in characteristic biochemical and clinical symptoms of sulphite oxidase and xanthine dehydrogenase deficiences. Diagnosis can be made simply with a sulphite strip test in fresh urine and by measuring uric acid excretion. Antenatal diagnosis is possible by chorionic villus sampling and sulphite oxidase assay.