

GLUT1 deficiency, a non-invasive initial test, may be preferred to lumbar puncture in children with early-onset absence epilepsy suspected of having GLUT1 deficiency syndrome. (Suls A et al. *Ann Neurol* 2009;66:415-419). GLUT1 deficiency may underlie a significant proportion (>10%) of early-onset absence epilepsies. The ketogenic diet, supplying an alternative fuel to glucose for brain energy metabolism, is an effective treatment for drug refractory seizures associated with GLUT1 deficiency. The transient improvement in attention and occipital alpha rhythm following glucose loading demonstrates the critical dependence of cerebral function and alpha EEG activity on glucose as brain fuel. Of interest, a trial of a chronic hyperglycemic diet failed to provide a protracted improvement in seizure control (Akman CI, De Vivo DC et al. Preliminary observation).

EXPANDING GENETIC AND CLINICAL SPECTRUM OF GLUT1D

A multicenter international genetic and clinical study of GLUT1 deficiency received 132 requests for mutational analysis of *SLC2A1* gene from 2004-8. Mutations identified in 57 patients (43%) were novel in 37, known in 6, and multiple exon deletions in 6. Clinical data retrospectively collected by questionnaire revealed three different phenotypes: 1) classical (84%), early onset (<2 years) (65%) and late-onset (18%); 2) non-classical with mental retardation and movement disorder, without epilepsy (15%); and 3) one adult case with minimal symptoms. The ketogenic diet controlled epilepsy in 86% and reduced movement disorders in 48% patients with classical phenotype and in 71% of non-classical. Delay in diagnosis of classical cases was 6.6 years (range, 1 month-16 years). CSF glucose was <2.5 mmol/l (range 0.9-2.4 mmol/l), and CSF:blood glucose ratio was <0.5 in all but one (range 0.19-0.52). CSF lactate was low to normal. Type of mutation was related to severity of phenotype. CSF:blood glucose ratio was related to type of mutation and phenotype. (Leen WG, Klepper J, Verbeek MM, et al. Glucose transporter-1 deficiency syndrome: the expanding clinical and genetic spectrum of a treatable disorder. *Brain* March 2010;133(3):655-670). (Respond: WG Leen MD, Nijmegen Medical Centre 935 Neurology, PO Box 9101 6500 HB Nijmegen, The Netherlands. E-mail: w.leen@neuro.umcn.nl).

COMMENT. Lumbar puncture with CSF glucose determination was the key to diagnosis of GLUT1 deficiency and prompt treatment with the ketogenic diet. Seizures were not a symptom in 15% of patients.

NEUROLOGICAL VARIANTS OF LESCH-NYHAN DISEASE

A prospective, multicenter international study of neurological manifestations of Lesch-Nyhan disease variants is reported from Emory University School of Medicine, Atlanta, GA. Of 46 patients (age range 3 to 65 years) from 34 families, 43 (93%) had neurological dysfunction. Classic cases with self-injurious behavior were excluded. Variant cases were male and had overproduction of uric acid and deficiency of the enzyme hypoxanthine-guanine phosphoribosyl-transferase or evidence for an HPRT gene mutation. Eight had gout, 6 had kidney problems, and 1 had a tophus. Delay in motor and speech development was common. Motor abnormalities in 42 (91%) ranged from subtle

clumsiness to severely disabling generalized dystonia. Mild to moderate cognitive dysfunction was present in 31 (67%). Maladaptive behaviors included onychophagia in 6 patients, and impulsivity, OCD, aggression, OCD and anxiety in isolated cases. Together with 78 prior reports of 127 Lesch-Nyhan disease variants, a spectrum of clinical features includes patients with a full phenotype of classical L-N disease and patients with uric acid overproduction but no neurological or behavioral deficits. Between classical and asymptomatic variants are patients with varying degrees of motor, cognitive, or behavioral abnormalities. Of 47 previously reported cases of L-N variants, 18 (38%) had extrapyramidal features, 19 (40%) hyperreflexia and spasticity, 19 (40%) dysarthria, and 7 (15%) seizures. (Jinnah HA, Ceballos-Picot I, Torres RJ, et al. Attenuated variants of Lesch-Nyhan disease. **Brain** March 2010;133(3):671-689). (Respond: Dr HA Jinnah, Department of Neurology, Emory University School of Medicine, Atlanta, GA 30322. E-mail: hjinnah@emory.edu).

COMMENT. The diagnosis of classical Lesch-Nyhan disease is not difficult when a young child presents with self-injurious behavior, symptoms of hyperuricemia, and early-onset dystonia or clumsiness. In patients with attenuated variants of L-N disease, diagnosis should be suspected when a child has nephrolithiasis, gout, and motor or cognitive abnormalities. Serum uric acid may be normal or mildly elevated initially, and molecular testing for mutations of *HPRT* gene sometimes unavailable. A knowledge of the spectrum of neurological variants of L-N disease should lead to more prompt diagnosis, treatment, and carrier identification for family counseling.

ACUTE ENCEPHALITIS

ACUTE ENCEPHALITIS WITH REFRACTORY, REPETITIVE PARTIAL SEIZURES

Clinical characteristics and outcome of 29 children (19 male; 10 female) with acute encephalitis with refractory, repetitive partial seizures (AERRPS) were analyzed in a retrospective, multicenter nationwide questionnaire-based study in Japan. Age of disease onset ranged from 1 to 14 years (6.8 +/- 4.0). Four had a history of febrile seizures but none had preceding neurologic abnormalities. The acute phase characterized by persistent fever (>39°C) and persistent seizures ranged from 15 to 312 days. Seizures were partial and repetitive, and consisted of eye deviation or facial twitching. They were refractory to conventional anticonvulsants and were suppressed by high-dose IV barbiturate. Impairment of consciousness was common. Pre-treatment EEGs in the first 14 days of illness showed high voltage slowing and in later stages, interictal epileptiform discharges. Ictal discharges were periodically repeated every 5-10 min. Early MRI, within 7 days of onset, showed mild brain edema in 2 of 14 cases, and later, 6 showed hippocampal or amygdaloid hyperintensities on FLAIR, without development of epileptic foci. Serial MRI revealed diffuse brain atrophy after a month or more. Laboratory studies showed high serum ferritin (221-2370 mg/dl) in 4/4 and positive anti-GluRe2 antibodies in 6/9 blood and CSF specimens. Other CSF abnormalities included pleocytosis in 19/29, high protein in 5/29, and high neopterin in 4/4. IV methylprednisolone in 12 was