

co-factor in methionine synthetase and methylmalonyl-CoA-mutase, a deficiency leading to the accumulation of homocysteine and methylmalonate in the plasma.

CSF NEOPTERIN LEVELS IN FEBRILE CONVULSIONS

Neopterin, a marker for activation of the cellular immune system, and interferon-gamma were measured in the cerebrospinal fluid of 40 infants and young children (ages 0.75 to 4.6 years) admitted with fever and/or convulsions to Nippon Medical School 2nd Hospital or Tama Nagayama Hospital, Japan.

CSF neopterin levels were significantly higher in 11 patients with febrile convulsions than in 22 with fever without convulsions or in 7 with convulsions without fever, 4 with status epilepticus. The CSF neopterin/serum neopterin ratio was also higher in patients with typical febrile convulsions, and those with prolonged febrile convulsions had higher CSF neopterin levels than patients with typical febrile convulsions. CSF interferon-gamma showed a tendency to higher levels in patients with febrile convulsions. (Kawakami Y, Fukunaga Y, Kuwabara K et al. Clinical and immunological significance of neopterin measurement in cerebrospinal fluid in patients with febrile convulsions. Brain Dev Oct 1999;21:458-460). (Respond: Dr Y Kawakami, Nippon Medical School Second Hospital, Department of Pediatrics, 1-396, Kosugi, Nakahar-ward, Kawasaki, Kanagawa 211-8533, Japan).

COMMENT. Neopterin CSF levels are elevated in children with febrile convulsions, pointing to a mechanism involving an immune activation in the central nervous system. None had pleocytosis of the CSF, and the cause of the elevated neopterin levels is undetermined.

LOW-DOSE ACTH THERAPY FOR INFANTILE SPASMS

The lowest effective ACTH dose, with fewest adverse effects, for the treatment of West syndrome (WS) was determined in a comparative, randomly assigned, controlled study involving 25 patients with cryptogenic (CWS, n=9) or symptomatic (SWS, n=16) WS, at the Department of Pediatrics, Tokyo Women's Medical University, Tokyo, Japan.

Either low dose (0.005 mg/kg per day = 0.2 IU/kg per day) or high dose (0.025 mg/kg per day = 1 IU/kg per day) synthetic ACTH, was administered every morning for 2 weeks and tapered to zero over the subsequent 2 weeks. In the CPS group, infantile spasms and hypsarrhythmia were completely controlled in 3/4 given low-dose and 5/5 on high-dose ACTH. In the SWS group, spasms and hypsarrhythmia were controlled in 6/8 at each dose level. No significant differences were observed between low and high-dose ACTH for either type of WS. Long-term responses in the 17 responders followed for more than 1 year showed no significant differences among groups. Sleepiness and brain shrinkage estimated by CT scan were significantly milder in the low-dose group. Low-dose ACTH therapy may be equally effective as high-dose and is recommended in CWS and in SWS with cerebral atrophy. (Yanagaki S, Oguni H, Hayashi K et al. A comparative study of high-dose and low-dose ACTH therapy for West syndrome. Brain Dev Oct 1999;21:461-467). (Respond: Dr Shigeru Yanagaki, Department of Pediatrics, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162, Japan).

COMMENT. The controversy regarding the optimum dosage of ACTH for treatment of infantile spasms continues, the low-dose, short-duration regimen favored in Japan, the high-dose, extended treatment advocated by the majority in the United States and the UK. My own preference has been for smaller doses (10-20 units Acthar gel daily IM for 3 weeks), with relative avoidance of serious side-

effects. The present report involving the use of synthetic ACTH confirms previous studies in Japan, using natural ACTH (Hrachovy RA et al. High-dose, long-duration versus low-dose, short-duration corticotropin therapy for infantile spasms. J Pediatr 1994;124:803-806; Fois A et al. Brain Dev 1987;9:82-84; and Ito M et al. Pediatr Neurol 1990;6:240-244). Proponents of high-dose ACTH include Snead OC et al. Neurology 1989;39:1027-1031; and Bobele GB, Bodensteiner JB. Neurologic Clinics Aug 1990, Philadelphia, WB Saunders. See Progress in Pediatric Neurology I, PNB Publ, 1991;pp30-34, for further discussion of ACTH in treatment of infantile spasms.

SHORT-TERM MORTALITY AFTER FIRST EPILEPTIC SEIZURE

The short-term mortality in a prospective study of a cohort of 804 patients, aged 2 months to 94 years, with a first seizure was determined at the University Hospitals of Bordeaux and Montpellier, France. At 1-year follow-up, 149 patients had died as compared to 16 expected deaths. None who died had idiopathic seizures. Mortality was increased in patients with remote symptomatic seizures, provoked seizures, and seizures due to progressive neurologic disease. Only 6% of deaths were seizure-related. The majority (64%) were caused by the underlying pathology, 20% an unrelated condition, and 9% unknown factors. (Loiseau J, Picot M-C, Loiseau P. Short-term mortality after a first epileptic seizure: a population-based study. Epilepsia Oct 1999;40:1388-1392). (Reprints: Dr P Loiseau, 4 allée de Carabin, 33460 Arsac, Bordeaux, France).

COMMENT. Early mortality following a first epileptic seizure is rarely related to the seizure per se and is determined by the underlying etiology, especially those with underlying pathology and with seizures caused by progressive neurologic disease, or by unrelated conditions. Provoked seizures must be distinguished from unprovoked seizures, when determining risk factors for a poor prognosis in epilepsy.

ANTICONVULSANT DRUGS

ADVERSE EFFECTS OF TOPIRAMATE

The effectiveness and safety of topiramate in 87 children with intractable epilepsy treated at three Canadian Centers were evaluated at the IWK-Grace Health Centre, Halifax, NS, Canada. Seizure reduction was >90% in 8 (9%), 50-90% in 21 (24%), and <50% in 54 (62%) of patients. Treatment was discontinued in 36 (41%) because of adverse events, especially cognitive dulling, in 27 (31%). The occurrence of cognitive dulling was not related to the rate of dose escalation and final dose level. (Dooley JM, Camfield PR, Smith E, Langevin P, Ronen G. Topiramate in intractable childhood onset epilepsy - a cautionary note. Can J Neurol Sci Nov 1999;26:271-273). (Reprints: Dr JM Dooley, Neurology Division, IWK-Grace Health Centre, 5850 University Ave, Halifax, Nova Scotia, Canada B3J 3G9).

COMMENT. Cognitive dysfunction can be a serious and frequent side effect of topiramate treatment of intractable epilepsy in children.

AED-ASSOCIATED MAJOR CONGENITAL ABNORMALITIES

The risk of major congenital abnormalities associated with maternal antiepileptic drug (AED) therapy during the first trimester of pregnancy was determined in 1,411 children born between 1972 and 1992 in four provinces in the Netherlands, and compared to 2000 nonepileptic matched controls. The risk