NON-DEPOT ACTH FOR INFANTILE SPASMS

The effects and side-effects of non-depot ACTH therapy in 18 children with infantile spasms are reported from the Wilhelmina Children's Hospital, University of Utrecht, The Netherlands. In i.m. doses of 0.4 mg bid for 4 weeks, followed by gradual withdrawal over 2 weeks, non-depot ACTH resulted in complete control of spasms and normalization of the EEG in 6 (33%) patients, and a partial control in 5. Those with cryptogenic seizures responded whereas infants with congenital defects, excepting 2 with tuberous sclerosis, were refractory to treatment. Response to non-depot ACTH was comparable to that reported for depot ACTH, the incidence of side-effects was lower, and a persistent hypercortisolism was not induced. (Kusse MN et al. The effect of non-depot ACTH(1-24) on infantile spasms. Dev Med Child Neurol Dec 1993;35:1067-1073). (Respond: O van Nieuwenhuizen MD, PhD,Dept Child Neurology WKZ, Academisch Ziekenhuis Utecht, PO 85500, 3508 GA Utecht, The Netherlands).

> COMMENT. Non-depot ACTH appears worthy of further trial in patients with West syndrome. As with depot ACTH, the dosage schedule may require controlled studies to establish optimal efficacy. Dosage based on surface area or body weight would seem more appropriate, if the mechanism of action is related to a direct effect on the brain, as suggested by these authors and by others. The relatively high frequency of serious side-effects sometimes reported with depot ACTH (eg. Riikonen R, Simell O. Dev Med Child Neurol 1990;32:203) was associated with a high dose regimen(80-140 IU daily for 6 weeks). I have favored the more conservative regimen with smaller, less toxic doses (10-20 IU daily for 2-3 weeks), a treatment schedule also followed in Japan. (see Millichap JG. Progress in Pediatric Neurology , Chicago, PNB Publ, 1991, pp 25-26, 30-34).

ACTH EFFICACY IN SYMPTOMATIC INFANTILE SPASMS

A retrospective evaluation of 26 case records of patients with diagnoses of symptomatic infantile spasms and classic hypsarrhythmia is reported from the Division of Pediatric Neurology, University of Minnesota Medical School, Minneapolis, MN. Seventeen (65%) had complete control of spasms and 9 did not respond. Both responders and nonresponders received similar ACTH dosages (87.4 and 84.5 U/m^2, respectively). High-dose ACTH (>100 U/m^2) was not more effective than lower dose regimens. Favorable outcome was associated with late onset (>8 months of age) and prompt treatment (1 month of onset). Responders either improved or did not deteriorate in development, whereas nonresponders were more impaired neurologically. (Sher PK, Sheikh MR. Therapeutic efficacy of ACTH in symptomatic infantile spasms with hypsarrhythmia. Pediatr Neurol Nov/Dec 1993;9:451-6). (Respond: Dr Sher, Division of Pediatric Neurology, Box 486 Mayo Building, Minneapolis, MN 55455).

> COMMENT. The control of seizures in responders occurred in 1.6 weeks (0.5-6), and hypsarrhythmia disappeared in all. Despite the symptomatic nature of the infantile spasms and pre-treatment neurologic abnormalities, the results of moderate and relatively short duration ACTH dosage can be satisfactory provided seizure onset is delayed until after 4 months of age and treatment is initiated promptly. High dose regimens with increased risk of serious toxicity are

apparently not justified. The need for early diagnosis and treatment has been emphasized previously (Millichap JG et al. JAMA 1962;182:125).

ANTICONVULSANT TOXICITY

LONG-TERM VALPROATE HEMATOLOGIC SIDE EFFECTS

Hematologic side effects in 60 patients, aged 2-29 years (mean 14 years), receiving valproate (VPA) monotherapy for >4 years in a long-term care facility, are reported from the Department of Pediatrics, East Carolina University School of Medicine, Greenville, North Carolina. Hematologic abnormalities, especially thrombocytopenia, <130,000/mcl (12 patients) and macrocytosis (11), were demonstrated in 20 (33%) patients. With VPA levels >100 mcg/ml in 22 patients, the incidence increased to 55%. Platelet counts were inversely related to VPA levels; thrombocytopenia was corrected when VPA dosage was reduced. Three had anemia, and 3 had leukopenia. Serum B_{12} levels were increased (>1000 mcg/ml) in 51 (86%); folate levels were normal. Blood smears showed increased numbers of bilobed polymorphonucleic cells (Pelger-Huet-like cells), an anomaly commonly associated with VPA-induced macrocytosis. (May RB, Sunder TR. Hematologic manifestations of long-term valproate therapy. Epilepsia Nov/Dec 1993;34:1098-1101). (Reprints: Dr RB May, Craven County Health Department, PO Drawer 12610, New Bern, NC 28561).

> COMMENT. The authors recommend close regular surveillance of patients receiving valproate, with continuous attention to blood counts, especially platelets and mean corpuscular volumes. The early recognition of these relatively frequent blood count anomalies may lead to reduction in VPA dosage or drug withdrawal and avoidance of major hematologic toxicity.

CARBAMAZEPINE, AUDITORY ERPs, AND BCECT

The effects of carbamazepine (CBZ) on cognitive function were evaluated by using measurements of auditory event-related potentials (ERPs) and P300 latencies in 23 patients, aged 7 to 16 years, with benign childhood epilepsy and centrotemporal spikes (BCECT), at the Department of Pediatrics, Toyama Medical and Pharmaceutical University, Toyama, Japan. As the epilepsy was controlled at the initiation of therapy, and with increasing age, the P300 latency was at first shortened. During the course of therapy with CBZ, P300 latency was prolonged, and the age-corrected P300 latency showed a significant correlation with the serum CBZ level. The dose of CBZ ranged from 10-23 mg/kg/day (mean 15.8). The latency became shorter when CBZ was discontinued. (Naganuma Y et al. Auditory event-related potentials in benign childhood epilepsy with centrotemporal spike: The effects of carbamazepine. Clin Electroencephalogr Jan 1994;25:8-12). (Reprints: Yoshihiro Naganuma MD, Department of Pediatrics, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-01, Japan).

> COMMENT. The major positive component of auditory event-related potentials, at a latency of 300 msec (P300) for rare tones (2000 Hz), has been correlated with cognitive function. Abnormalities in ERPs in patients with epilepsy, and particularly prolongation of P300 latency, have been ascribed to the effects of the seizures and to antiepileptic drug therapy. Various epileptic syndromes have shown different