

High-dose methotrexate for acute lymphocytic leukemia in young children did not cause neurological abnormalities or MRI changes in a study of 12 children treated at the University Hospital of Trondheim, Norway. (Seidel H et al. Acta Paediatr April 1996;85:450-3). Some previous studies have demonstrated reversible acute and subacute neurotoxicity following methotrexate (MTX) therapy for ALL. The possible role of folic acid rescue in avoiding MTX toxicity needs further study.

ANTICONVULSANT DRUG TOXICITY

VALPROATE INDUCED OBESITY AND POLYCYSTIC OVARIES

Fourteen (64%) of 22 women receiving valproate monotherapy for epilepsy had polycystic ovaries, hyperandrogenism, or both, in a study at the Departments of Neurology, Obstetrics and Gynecology, and Pediatrics, University of Oulu, Finland. They had a progressive obesity associated with hyperinsulinemia and low serum insulin-like growth factor-binding protein 1, leading to hyperandrogenism and polycystic ovaries. The mean duration of treatment was 7 years, and the mean daily dose of valproate was 1070 mg. In contrast, polycystic ovaries/hyperandrogenism occurred in 9 (21%) of 43 women receiving carbamazepine monotherapy and 8 (19%) of 43 in a control group. (Isojarvi JT et al. Obesity and endocrine disorders in women taking valproate for epilepsy. Ann Neurol May 1996;39:579-584). (Respond: Dr Isojarvi, Department of Neurology, University of Oulu, FIN-90220 Oulu, Finland).

COMMENT. Polycystic ovarian syndrome (PCOS), hyperandrogenic chronic anovulation, is characterized clinically by hirsutism and menstrual disorders. Obesity occurs in 30 to 50% of patients affected. It may have multiple etiologies, including genetic, endocrine, metabolic, and neurologic. PCOS induced by valproate medication for epilepsy has been attributed to the coincidental obesity and resultant endocrine abnormalities. An increased incidence of PCOS among untreated epileptic women is greater with left than with right-sided temporal lobe foci. Antiseizure medications other than valproate induce hepatic enzymes that reduce testosterone levels and tend to moderate hyperandrogenism. Hertzog AG, at the Harvard Neuroendocrine Unit, Beth Israel Hospital, Boston, MA, suggests that valproate may not be the primary cause of PCOS, citing epileptic and neurologic factors (Ann Neurol May 1996;39:559-560).

CARNITINE IN VALPROATE-INDUCED HYPERAMMONEMIA

The effect of carnitine supplementation in valproic acid (VPA) treated patients presenting with hyperammonemia was investigated in 69 children and young adults seen at the Zentrum der Kinderheilkunde, Goethe-Universität Frankfurt, and Universität Erlanger, FRG. Plasma total carnitine was low (27 $\mu\text{mol/l}$ cf normal of 40 $\mu\text{mol/l}$) in 48 tested. After supplements of carnitine (1 gm/m² per day) in 15 patients, the plasma ammonia decreased by 25% after 9 days and 46% after 80 days. The plasma free carnitine was increased by 12%. Plasma ammonia concentrations were significantly correlated with free plasma carnitine %. (Bohles H, Sewell AC, Wenzel D. The effect of carnitine supplementation in valproate-induced hyperammonemia. Acta Paediatr April 1996;85:446-9). (Respond: Dr H Bohles, Zentrum der Kinderheilkunde, Theodor Stern Kai 7, 60590 Frankfurt/Main, FRG).

COMMENT. Carnitine supplementation was recommended in VPA-treated patients with hyperammonemia. The risk of VPA-induced Reye's-like syndrome could not be determined from this study.

VALPROATE-INDUCED LUPUS ERYTHEMATOSUS

A mentally retarded 30-year-old woman with partial trisomy of chromosome 9, suffering from epilepsy since age 11 months, developed systemic lupus erythematosus after one year of treatment with valproate (VPA) and ethosuximide (ESM) at the Clinica Neurologica, Università di Roma Tor Vergata, Italy. When prednisone 1 mg/kg/day was administered and VPA gradually discontinued, clinical remission occurred within 10 days. The patient was maintained on ESM without relapse. (Gigli GL et al. Valproate-induced systemic lupus erythematosus in a patient with partial trisomy of chromosome 9 and epilepsy. Epilepsia June 1996;37:587-588). (Reprints: Dr GL Gigli, Clinica Neurologica, Università di Roma Tor Vergata, Ospedale S Eugenio, Piazzale Umanesimo 10, 00144, Rome, Italy).

COMMENT. This was the fourth reported case of VPA-induced systemic lupus erythematosus. It presented with arthralgia, fever, and fatigue, after prolonged treatment. It resolved rapidly after discontinuing the drug.

SEIZURE DISORDERS

PET BITEMPORAL HYPOMETABOLISM IN INFANTILE SPASMS

A group of 18 infants (age range, 10 mo to 5 yr) with infantile spasms and a common metabolic pattern on positron emission tomography (PET) is reported from the Children's Hospital of Michigan, Wayne State University School of Medicine, Detroit, MI. CT and MRI scans were negative for focal abnormalities. EEGs showed bilateral or multifocal epileptogenicity. All had bilateral hypometabolism in the temporal lobes on PET. Analysis of outcome of 14 of the subjects at a mean follow-up of 4 years revealed 1) severe developmental delay; 2) absent language development; and 3) an autistic disorder in 10. The hypometabolic areas were thought to represent cortical dysplasias, but the patients were not considered candidates for cortical resection. (Chugani HT, Da Silva E, Chugani DC. Infantile spasms III. Prognostic implications of bitemporal hypometabolism on positron emission tomography. Ann Neurol May 1996;39:643-649). (Respond: Dr HT Chugani, Division of Pediatric Neurology and the PET Center, Children's Hospital of Michigan, 3901 Beaubien Blvd, Detroit, MI 48201).

COMMENT. Children with infantile spasms associated with bitemporal glucose hypometabolism on PET appear to comprise a homogeneous group having a poor prognosis, delayed development and severe dysphasia, and autism. They are not candidates for cortical resection. About 10% of children with infantile spasms are autistic.

PET in epilepsy is reviewed from the University Hospital Center of Liege, Belgium (Sadzot B. Epilepsia June 1996;37:511-514). The effect of valproate on cerebral metabolism and blood flow was investigated by deoxyglucose and ¹⁵O water PET at the NIH, Bethesda, MD (Gaillard WD et al. Epilepsia June 1996;37:515-521). VPA reduced regional cerebral blood flow but not cerebral metabolic rate for glucose in the thalamus, an effect associated with VPA's mechanism of action in generalized seizures.