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 Tronheim, Norway. (Seidel H et al. <u>Acta Paediatr</u> 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 folinic 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 JIT et al. Obesity and endocrine disorders in women taking valproate for epilepsy. <u>Ann Neurol</u> May 1996;39:579-584). (Respond: Dr Isojarvi, Department of Neurology, University of Oulu, FIN-90220 Oulu, Finland).

COMMEDT. 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 hyperandogenism. 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 (<u>Ann Neurol</u> 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-Universitat Frankfurt, and Universitat Erlanger, FRG. Plasma total carnitine was low (27 mcmol/l cf normal of 40 mcmol/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 hyperammonaemia. <u>Acta Paediatr</u> April 1996;85:446-9). (Respond: Dr H Bohles, Zentrum der Kinderheilkunde, Theodor Stern Kai 7, 60590 Frankfurt/Main, FRG).