Correspondence

235

Sodium valproate and neutropenia

Sir,

We read with interest the recent report by Barr et al. in which they noted that 12 of 45 patients receiving valproic acid developed absolute neutropenia, but that in all cases this phenomenon was transient and self limiting.

Recently we saw a more severe manifestation of this problem. A 9 year old girl suffered from mental retardation and severe fits after hypoglycaemia in the neonatal period. She had previously been treated with a number of different anticonvulsant drugs. Because of continuing fits and her mother’s concern about behaviour problems her anticonvulsant therapy was changed to sodium valproate. With monitoring of valproate blood levels her dose of sodium valproate was gradually increased to 600 mg four times a day. Twenty-five days after starting valproate her neutrophil count, which had previously been normal fell to 0.66 × 10⁹/l. This appeared to be a transient phenomenon and 3 days later the neutrophil count had risen again to 4.8 × 10⁹/l, without alteration of the valproate dose. At this point she was discharged from hospital. Her other treatment at this time was diazoxide, 50 mg in the morning and 100 mg at night, and trimetrazine 60 mg at night.

She was seen again 2 months later and was noted to have a severe neutropenia of only 0.2 × 10⁹/l. This persisted for 3 weeks despite reducing her dose of sodium valproate and the drug was therefore stopped. Within 3 days her neutrophil count had returned to normal and has remained normal for 5 months. No alteration was made to her other drug therapy. There was never any evidence of viral infection as a possible cause of the neutropenia.

Neutropenia was first described during sodium valproate treatment by Jaeken et al. who reported a single case in a 3 month old boy. More recently Coulter et al. have reported a fall in the neutrophil count in 27 of 100 patients treated with valproic acid, but their minimum count of 2.0 × 10⁹/l is of little clinical significance. Although the thrombocytopenia found with valproate therapy may be due to immune platelet destruction immunofluorescence studies have failed to show antibodies against granulocytes.

We would suggest that neutrophil counts as well as the customary platelet count should be performed on all patients treated with sodium valproate.

References


David N K Symon and George Russell
Department of Child Health, University of Aberdeen, Foresterhill, Aberdeen AB9 2ZD

Nature of complement deficiency in sickle cell disease

Sir,

The work of Larcher and colleagues was of great interest, as it confirmed and expanded our observations, cited by Dr Larcher et al., on the nature of complement deficiency in sickle cell disease. We feel, however, that in discussing their findings, Dr Larcher et al. could have taken account of our further studies of this problem, which they seem to have overlooked. These studies, as well as our more recent work, indicate that about half of ‘steady state’ (intercritical) subjects with homozygous sickle cell disease have hypercatabolism of the alternative complement pathway, as judged by the in vivo factor B metabolic turnover rate, and C3d levels in plasma. Mean factor D serum level is depressed in these patients, but this finding was statistically significant only when we...