Figure Oral rehydration salts, prepared according to the WHO formula with sodium (upper line) and replacing this buffer salt for sodium acetate (bottom line). The aspect of the two salt mixtures are shown, by 12 hours (left and middle) and by 72 hours (right).

We are sorry to say that the elegant results of this clinical trial, although theoretically interesting, are of no practical use. Ironically, one of the important 'advantages' claimed by the authors, namely stability, is indeed the main disadvantage of sodium acetate as a component of an oral rehydration solution. Sodium citrate, on the other hand, being theoretically three times a better buffer than acetate or bicarbonate, and not being as hygroscopic as acetate, should be investigated in a similar clinical trial.

Reference

- 1 Patra F C, Mahalanabis D, Jalan K N, Sen A, Banerjee P. Can acetate replace bicarbonate in oral rehydration solution for infantile diarrhoea? *Arch Dis Child* 1982; **57**: 625-37.

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Sodium valproate and neutropenia

Sir,

We read with interest the recent report by Barr *et al.*¹ 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 $0.66 \times 10^9/l$. This appeared to be a transient phenomenon and 3 days later the neutrophil count had risen again to $4.8 \times 10^9/l$, 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 trimeprazine 60 mg at night.

She was seen again 2 months later and was noted to have a severe neutropenia of only $0.2 \times 10^9/l$. 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.*² who reported a single case in a 3 month old boy. More recently Coulter *et al.*³ have reported a fall in the neutrophil count in 27 of 100 patients treated with valproic acid, but their minimum count of $2.0 \times 10^9/l$ 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.²

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

References

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- 2 Jaeken J, Van Goethem C, Casaer P, Devlieger H, Eggermont E, Pilet M. Letter: Neutropenia during sodium valproate treatment. *Arch Dis Child* 1979; **54**: 986-7.
- 3 Coulter D L, Wu H, Allen R J. Valproic acid therapy in childhood epilepsy. *JAMA* 1980; **244**: 785-8.

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Nature of complement deficiency in sickle cell disease

Sir,

The work of Larcher and colleagues¹ was of great interest, as it confirmed and expanded our observations,² 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,^{3,4} which they seem to have overlooked. These studies, as well as our more recent work,⁵ 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,³ and C3d levels in plasma.⁵ Mean factor D serum level is depressed in these patients,² but this finding was statistically significant only when we