More promising were the results obtained by studying the combined creatinine and urea clearances. This method was used in adults by Lavender et al., who demonstrated a good correlation and minimal variability between the clearance of inulin and a value calculated as the sum of the clearance of creatinine and that of urea, divided by 2. We also found a good correlation between these parameters. The best correlation, however, was found between the clearance of inulin and a value calculated as the sum of twice the creatinine clearance and the urea clearance, all divided by three, $2 \times \text{Creat} + \text{Urea}/3$. The regression line ($Y = 14.3 + 0.8 X, r = 0.93$) was statistically indistinguishable from the line of identity. The scatter of points around the regression line was less pronounced but still appreciable.

From this study we concluded that the method of combining the 3 hours clearance of creatinine and urea was the best alternative to the complicated measurements of standard inulin clearance when precise values of GFR are not needed, and that the $Ht/P_c$ ratio could not be taken reliably as an estimate of GFR. This latter conclusion is confirmed by the studies of Davies et al.

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**Figure**  Relationship between standard inulin clearance and the formula $0.55 \times \text{height}/\text{plasma creatinine concentration}$ in 72 children older than one year of age ($Y = 23.6 + 0.7 X$, $r = 0.82$). The slope of the regression line is significantly different from that of the line of identity ($P < 0.001$). The shaded area represents the 95% confidence limits of the regression line.

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**References**


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Oral rehydration salts have a shorter shelf life with sodium acetate than with sodium bicarbonate

Sir,

We have read the interesting report of Patra et al., showing that sodium acetate can successfully replace sodium bicarbonate in the oral rehydration solution currently used for the treatment of infants suffering from diarrhea and acidosis.

Since bicarbonate reacts with glucose to form furfural compounds leading to brown discoloration of the salt packets, the conclusion of the authors is that although there is slight increase in the cost of the packets in which bicarbonate is replaced by acetate, the ‘longer shelf life, ease of packaging, and tablet making should more than compensate for it’. We will not argue about ease of packaging and tablet making, but in connection with shelf life of sodium acetate, the opposite is true: the shelf life of sodium acetate is shorter than that of sodium bicarbonate as it is highly hygroscopic.

We compared in triplicate, two mixtures of salts, identical with those used by the authors. One was prepared according to the formula recommended by the WHO and the other contained acetate instead of bicarbonate in an isosmolar quantity. Both were immediately sealed with heat into plastic bags. After about 72 hours at room temperature, most of the sodium acetate containing package, turned to a jelly or gum like material. At 37°C the change was observed within 12 hours, and was, of course, more apparent by this time, if 0.1 ml of water had been added to the salt mixture. No change was observed in the sodium bicarbonate containing package, however, either in 72 hours at room temperature, or in 12 hours at 37°C. If 0.1 ml water was added at 37°C, the brown discoloration of bicarbonate was observed within 12 hours. The results of a typical experiment, are shown in the Figure.
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 × 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 trimeprazine 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.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 × 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.4

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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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,4 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,4 and C3d levels in plasma.4 Mean factor D serum level is depressed in these patients,2 but this finding was statistically significant only when we