clinical, and therapeutic aspects. If the disease is shown to be an irreversible one, then ancillary workers are most helpful in assisting with the difficult and important skills of subsequent psychosocial adjustment and management.

But please, Sir, when we are discussing illness (as opposed to the more vague, pure social maladjustments of contemporary society) let us not be falsely persuaded by the fashionable soft sciences into abrogating our inalienable role as leader of the clinical team.

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¹ Anderson, W F. and Carlton-Ashton, J R, eds, *Age and Ageing*, 1977, suppl.

² Harrison, M J G, and Marsden, C D, *Archives of Neurology*, 1977, **34**, 199.

³ Pearce, J, and Miller, E, *Clinical Aspects of Dementia*. London, Baillière Tindall, 1973.

Cholestyramine in uraemic pruritus

SIR,—Most renal physicians find uraemic pruritus difficult to treat, so the report of Dr D S Silverberg and his colleagues (19 March, p 752) of a favourable response to cholestyramine will excite interest and encourage others to try this treatment.

The authors realise that cholestyramine has the potential to cause acidosis but found no evidence of this in their patients. The absence of acidosis was probably the result of haemodialysis three times a week, which would return the acid-base state to normal and prevent cumulative hydrogen ion retention. But dialysed patients are less liable to this complication than uraemic non-dialysed patients, and the latter would be particularly at risk from the acidifying effect of cholestyramine, as the following argument makes clear.

Cholestyramine is a strongly basic anion-exchange resin in the chloride form, with an exchange capacity of 4.1 mEq/g. A study of several similar anion-exchange resins some years ago found that after oral ingestion the resin was excreted in the stool predominantly with organic anion and bicarbonate, and only 15% in the chloride form.¹ By extension of this finding to cholestyramine, every gram of resin taken would contribute 3.5 mEq of chloride to body fluids and remove in exchange 3.5 mEq of bicarbonate or bicarbonate-precursor from the body. Loss of bicarbonate from the body is equivalent to a gain in hydrogen ion, so the 10 g dose of cholestyramine used daily by Dr Silverberg would donate 35 mEq of hydrogen ion to body fluids, an amount which is only a little less than the daily excretion of hydrogen ion by healthy kidneys. It might be argued that this would not occur in a uraemic subject because of a change in the ionic pattern of intestinal juices; however, a study of this point has been made and showed no significant difference in the anion pattern of faeces from uraemic and normal subjects.² There are therefore strong a priori grounds for predicting progressive hydrogen ion retention in non-dialysed uraemic subjects given cholestyramine. Although Silverberg referred to *hyperchloraemic* acidosis, the resultant acidosis might not be accompanied by hyperchloraemia because of the retention of unmeasured anion, which is usual in renal failure.

This problem would not arise if the manufacturers marketed cholestyramine in acetate or lactate form rather than as chloride. The necessary conversion can easily be carried out

in a laboratory with the simplest equipment, such as exists in hospital pharmacies, but this would remove the added flavouring which is important for palatability, and the conversion would therefore be best incorporated during manufacture. Cholestyramine modified in this way would be just as effective as the present chloride form for the other therapeutic purposes for which it is used.

Incidentally, the name "cholestyramine" is misleading, as it implies a particular mode of action (binding of bile anions), whereas the approved names of most modern drugs are derived from the chemical structure of the drug alone. Anion exchange resins remove much more from the body than bile anions, which are not retained in renal failure, and any effect they may have in relieving uraemic pruritus is likely to be mediated by some other action.

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¹ Hurst, P E, *et al*, *Clinical Science*, 1963, **24**, 187.

² Wilson, D R, *et al*, *Clinical Science*, 1968, **35**, 197.

Aerosols containing neomycin

SIR,—I refer to your "Warning on Aerosols containing Neomycin" (21 May, p 1360). May I draw your attention to two illustrations, 19.1 and 19.2 (pp 454 and 455), in my textbook,¹ which show the extensive damage to Corti's organ and its innervation caused by neomycin aerosols in two children with cystic fibrosis treated in a neomycin atmosphere for several months.

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¹ Friedmann, I, *The Pathology of the Ear*. Oxford, Blackwell, 1974.

Side effects of sodium valproate

SIR,—While we agree that sodium valproate (Epilim) is a most useful anticonvulsant in childhood, we should like to report an apparent side effect not mentioned in your leading article (16 April, p 986).

A 14-year-old Asian boy was born in hospital in Kenya. Delivery was apparently normal, birth weight 3 kg. From the age of 6 months he started attacks of eye rolling, rigidity, and shaking, which lasted about three minutes and occurred about every two weeks until he was 5 years old, when they became less frequent. He came to the UK in 1969 and now attends a boarding school for educationally backward children. Clinical assessment revealed bilateral optic atrophy, clumsy gait, but no obvious syndrome. Head circumference was at the 10th centile and skull x-ray was normal.

Since 1973 he has had occasional brief episodes of loss of vision and jerking of the head followed by intermittent "blackouts." Electroencephalography showed epileptic features, and he was prescribed phenobarbitone. The convulsions became more frequent, occurring two or three times a week, and treatment has included various combinations of anticonvulsant drugs, including sodium valproate, with no definite success. The regimen was changed recently to sodium valproate alone at a dose of 42 mg/kg (1600 mg) per day. After 14 days free from convul-

sions he became confused and had recurrent episodes of bizarre behaviour in which he stared vacantly, shouted gibberish, and had frightening hallucinations. He was visited by a general practitioner deputy, who stopped the drug. Two days later he was seen at hospital, when he was still moderately confused and appeared frightened though apparently had steadily improved since the sodium valproate had been stopped. Plasma valproate level at that time was 13 µg/ml. The drug was recommenced at half the previous dose (800 mg per day). Ten days later his behaviour had returned to normal and he remained free from convulsions.

The clinical course of this patient's acute episode of psychotic behaviour in relation to his medication is suggestive of a drug reaction. The plasma level two days after discontinuing sodium valproate is surprisingly high. Considering the average half life of the drug in epileptic patients to be about six hours, the level at the time of the reaction would have been far above the expected therapeutic range. Careful questioning did not suggest that an overdose had been taken (this would have been unlikely as the patient had been on anticonvulsant drugs for many years under the supervision of the excellent nursing sister and medical officer at his special school). We have found no other reports of similar side effects of sodium valproate when given on its own and suggest that a watch should be kept for psychotic changes in patients on this drug.

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Basal body temperature

SIR,—In their paper "Problems in using basal body temperature recordings in an infertility clinic" (26 March, p 803) Dr Elizabeth A Lenton and others are trying to achieve the impossible. They asked "experts" and "non-experts" to diagnose a small mixed sample of BBT curves from healthy volunteers (8), infertility patients with ovulatory cycles (14), with anovulatory cycles (24), and pregnant cycles (4). Such a hodgepodge of variables cannot be analysed statistically and meaningfully. Further, the authors did not provide definitions according to which the BBT curves should be examined, nor were the experts and non-experts asked to spell out their own diagnostic criteria. Thus, the results reflect the participants' guesses but not the diagnostic value of the BBT curve.

The elevated phase of the biphasic BBT curve indicates corpus luteum activity, and consequently an ovulatory menstrual cycle. However, the BBT curve does not allow us to time precisely the day of ovulation.

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Guillain-Barré syndrome and influenza vaccine

SIR,—Your leading article on Guillain-Barré syndrome and influenza vaccine (28 May, p 1373) stimulates me to consider the various possibilities of neural disturbances after influenza immunisation. We differentiate the