important, well-documented, and highly prescient editorial (22-29 December, p 1610). British medical charities are obviously falling behind their international counterparts in the monies which they devote to health education and prevention. The twenty-first century will be the era par excellence in which the practice of medicine must move decisively from cure to prevention and care; the destiny of the profession as a whole will be inextricably linked with its ability to make this metamorphosis. The outlook at present is far from promising and, in spite of relatively massive expenditure, mainly on glamorous feats of technological legerdemain, we remain very far indeed from putting comparable effort into unravelling the complicated web of factors responsible for society's main killers, carcinogenesis and coronary heart disease.

As the decade of the 1980s opens may I offer two suggestions which might assist the foundations in making more effective and rational contributions to disease prevention? The first concerns the type of advice which they seek and particularly their dependence on opinion which, by its very process of moulding over a period of years or decades, tends to be over-specialised and treatment-orientated rather than ecological in character. In an otherwise sombre scene the Spastics Society and the King Edward's Hospital Fund for London stand out as notable exceptions. Here at least the importance of prevention is recognised, as is the idea that in a world pressing ever closer to its resource limits an ecological approach to medicine is mandatory. Both organisations have pioneered imaginative approaches. The Spastics Society conducted a critical but constructive examination of some aspects of antenatal and postnatal care, while the King's Fund was instrumental in establishing the unit for the study of health policy at Guy's Hospital.

The second suggestion which I offer is that it would be very much in the foundations' own interests to be seen to be sponsoring an increasing number of studies in the general field of prevention. To say that the human future is unknowable is, of course, a truism. But we need not be astrologers or soothsayers—merely observers attuned to some degree to the forces of contemporary history—to forecast that for our grandchildren the paramountcy of preventive medicine will be undisputed.

JOHN A LORRAINE

Centre for Human Ecology,
University of Edinburgh,
Edinburgh EH8 9LN

SIR,—In a recent leading article (22-29 December, p 1610) you rightly criticised major British charities such as the British Heart Foundation, the Cancer Research Campaign, and the Imperial Cancer Research Fund for their reluctance to face up to the challenges of prevention. It was perhaps inevitable that the charities should defend themselves (19 January, p 178; 26 January, p 249), although it is regrettable that they should have done so by seeking to cast doubt on the value of preventive activities such as health education. In this depressingly outdated view they are—as your leading article points out—out of step with their highly respected counterparts in several other countries.

The scientific secretary and secretary general of the Cancer Research Campaign, for example, recognise that for lung cancer "action to reduce cigarette smoking is likely to be

more effective in reducing mortality than attempts to find a cure." So far so good; but they continue, "Unfortunately the means of changing people's social habits have yet to be discovered. . . ." It is to be hoped that Dr N H Kemp and Brigadier K D Gribbin will familiarise themselves with the evidence of the past few decades before they next criticise one of your leading articles. The cat seems, however, to have been let out of the fund-raising bag in a further sentence from their letter. They write, "The people who contribute so generously to the Campaign on the basis of an appeal for research into the causes, prevention, and treatment of cancer might reasonably be unhappy were we to allocate large sums to publicity aimed at changing their life habits." This seems almost to suggest that the cancer charities should not campaign on smoking for fear of offending potential donors.

We would suggest that they are wrong on two main counts. Firstly, charities such as the American Cancer Society and—closer to home—the Ulster Cancer Foundation have found that forceful anti-smoking campaigns can coexist with highly successful fund-raising programmes. Secondly, and crucially, cancer and heart charities should make every effort to reduce the mortality and morbidity caused by these diseases even if this means a recognition that time-hallowed policies for allocating funds must be reconsidered, and even if fund raising itself becomes a little more difficult.

We believe that charities such as the Imperial Cancer Research Fund, the Cancer Research Campaign, and the British Heart Foundation should recognise that changed circumstances and knowledge justify the allocation of far more of their resources to prevention. Window dressing—such as the few projects they cite in their responses to your editorial—is not enough. Trusting and generous donors expect those responsible for the running of charities to make decisions in the best interests of the public rather than on the basis of outdated tradition. We ask that the charities involved think again.

DAVID A PLAYER

Scottish Health Education Unit,
Edinburgh EH12 5EH

MIKE DAUBE

University Department of
Community Medicine,
Edinburgh

Follow-up of patients with colorectal cancer after surgery

SIR,—We were very interested to read the paper by Mr J P S Cochrane and others (1 March, p 593) on the follow-up of colorectal cancer patients after surgery.

As the authors state, there are few data to suggest that more detailed follow-up increases the detection rate of curable recurrent carcinoma of the colon. Follow-up must be capable of detecting any new asymptomatic lesions, either polyps or carcinoma, and should include occult blood testing and, as most lesions occur on the left side of the colon,¹ flexible sigmoidoscopy. The association of an adenoma with a rectal or colonic carcinoma when the operative specimen is examined makes such patients a particularly high-risk group.² The detection and treatment of further polyps may even prevent a proportion of these patients developing a second malignancy, and even if this is only in a very small number of patients it is surely a policy worth pursuing.

Improvements in surgical techniques and management have made little impact on the mortality from colorectal cancer in the last 25 years. The hope for the future must rest in the earlier detection of primary colorectal cancer and the better prediction, detection, and management of recurrent carcinoma.

K D VELLACOTT
J D HARDCASTLE
T W BALFOUR

Department of Surgery,
Queen's Medical Centre,
Nottingham NG7 2UH

¹ Gillespie PE, Chambers TJ, Chan KW, *et al.* *Gut* 1979;20:240-5.

² Heald RJ, Lockhart-Murray HE. *Br J Surg* 1972;59:16-9.

Chlormethiazole and temazepam

SIR,—We must criticise the claim of Dr R S Briggs and others (1 March, p 601) to have shown that chlormethiazole and temazepam do not cause detectable hangover effects in young or old, and that these drugs allow sleep to be safely interrupted.

The authors reported negative results. It is difficult to prove a negative. One must always ask first if the tests are sensitive, for if the measuring devices do not work the results are bound to be negative. The results from the sway test underpin the claim about safe interruption of sleep. We are not offered any evidence that this one-minute test is established as sensitive to other hypnotic drugs. One sees that in the sample of old volunteers on placebo the range of scores was 7-59. One would consequently like to know if intra-subject test-retest variability is also very large, for if the variability inherent in measures is large the likelihood of getting a statistically significant difference with only 10 subjects is small.

The psychomotor performance test required the crossing out of the letter e from prose for a mere two minutes. Complex decisions were not required, nor were the subjects required to sustain attention (as, for example, motorway drivers must). The authors have, in our view, used too limited a battery of tests to merit a claim that they have shown that hangover effects may be avoided if these particular drugs are used. One hopes that their statement will not be used to justify intake of these drugs a few hours before skill is required of pilots, drivers, or anyone else.

They state that the order of presentation of placebo, temazepam, and chlormethiazole was balanced. We are unable to see how, when they had three conditions and 10 subjects of each age group. Their subjects slept with catheters in their arms and had blood withdrawn frequently for the first four hours of the night. During the 30-minute electroencephalogram the next morning, any tendency to fall asleep that might have been caused by lingering drug or drug metabolites was therefore presumably confounded by an element of sleep deprivation, so drug effects would be rendered less discriminable. We suggest too that the authors should have first examined their data by analysis of variance, and, where they made so many comparisons and repeatedly used the Wilcoxon test, they should have reminded us to expect a few "statistically significant" differences by chance.

The authors are certainly to be congratulated on combining plasma levels with behavioural tests and for emphasising the

merit of hypnotic drugs of short action; but they are, in our view, too confident in their general conclusions and are not fair, since they imply that they are entitled to say that the two drugs they studied had advantages over other drugs. They could be justified in this only if they had also studied the other drugs with the same subjects and with the same tests.

IAN OSWALD
KIRSTINE ADAM

University Department of
Psychiatry,
Royal Edinburgh Hospital,
Edinburgh EH10 5HF

SIR,—We read with interest the article "Improved hypnotic treatment using chlor-methiazole and temazepam" (1 March, p 601). This is an important area of research—particularly in relation to elderly people, for it is this group who constitute the most frequent users of hypnotics and who are most at risk of morbidity from such use. We feel that the conclusions drawn by the authors require substantial qualification and merit further discussion.

The concluding statement of the summary that these drugs may not cause hangover and allow sleep to be interrupted safely are valid only under the conditions described—that is, following a single dose—whereas the vast majority of prescriptions for hypnotics are given for regular nightly consumption. The authors further suggest that the plasma half life of temazepam in the elderly is approximately 14 hours. However, they have sampled over an inadequate period of time and plotting the data on a logarithmic scale suggests a terminal half life of the order of 26 hours. Thus accumulation would seem inevitable and, unless tolerance develops, adverse side effects will develop.

It is unfortunate that the authors' summary and conclusions may suggest that these hypnotics are safe for all old people, which is not in fact proved.

A F MACKLON
E H JARVIS
J GRIMLEY EVANS

Department of Medicine
(Geriatrics),
Newcastle General Hospital,
Newcastle upon Tyne NE4 6BE

M D RAWLINS

University Department of
Clinical Pharmacology,
Wolfson Unit,
Newcastle upon Tyne NE1 7RU

Nocturnal polyuria and saluresis in renal allograft recipients

SIR,—Dr M K Chan and others at the Royal Free Hospital (19 January, p 150) contrasted ratios of urine excretion by night and by day in healthy controls with those in patients with chronic renal failure and in patients who had received a renal transplant. Our studies relevant to these observations now extend over more than 100 patients and controls, many studied over long periods; and we were therefore very interested in their findings.

Most of our patients after transplantation also show the abnormal day:night ratios of urinary volume, sodium, and potassium¹ reported by Dr Chan and his colleagues and we also observe that the increased nocturnal excretion becomes less marked the longer the period since transplantation. We have found, like some of the others who have studied this phenomena,^{2,3} individual patients with

more normal patterns even in the first few months. Dr Chan and his colleagues in one patient and Lines and others³ in four patients showed that the urinary patterns of excretion were more normal when patients with renal transplants were kept recumbent. We have demonstrated in chronic renal failure^{4,5} and after renal transplantation a close relationship between the time of getting up and the onset of reduced urine flow. These observations support the suggestion that posture is an important influence on the abnormal distribution of urine flow in the 24 hours. More studies after transplantation, in chronic renal failure, and in other situations are needed to determine whether it is the only one.

Patients with Cushing's syndrome, and also those on prednisolone therapy,⁵ often have an abnormal distribution of urine excretion, and the contribution of steroid treatment in the patients after transplantation may have been underestimated. When patients with rheumatoid arthritis took 5 or 10 mg of prednisolone at 0800 hours the calculation of a ratio of daytime excretion to night-time excretion showed higher day:night ratios for sodium ($P < 0.01$), potassium ($P < 0.05$), total solute ($P < 0.001$), and creatinine ($P < 0.01$) than did the same patients taking the same dose at 2300 hours. With treatment at 0800 hours most of the patients had rhythms of excretion that could be analysed as sine waves and were not different to healthy age-matched controls, in contrast to treatment at 2300 hours, when few patients showed statistically significant rhythmicity in renal excretion.⁶ We have not yet completed our studies at higher doses but some of the differences between patients soon after transplantation and those studied later may relate to differences in the magnitude or timing of steroid doses. A contribution of therapy to the abnormalities described should not be dismissed on account of a presumed antinatriuretic effect of prednisolone; the renal responses to this drug are very variable under different circumstances.

There has been intermittent interest in the abnormal patterns of urine flow after transplantation, and we have demonstrated that a study of these contributes to the diagnosis of rejection. The study into changes in the day:night differences in urine flow and excretion during allograft rejection¹ has now been extended, and we still consider that a sudden change in the ratio is a guide to rejection. We anticipate that patients will be trained to suspect rejection by making simple observations on the pattern of their urine excretion. Our results in 20 rejection episodes in patients studied over 567 patient days are still preliminary, but if confirmed with further experience may provide another example of how a study of circadian changes may allow improvement in diagnosis or treatment.

MARK S KNAPP
R POWNALL
M J HEATH
I TRIMBLE
I C KOWANKO

City Hospital,
Nottingham NG5 1PB

- ¹ Knapp MS, et al. *Kidney International* 1978;14:794.
- ² Gunn HE, et al. *J Lab Clin Med* 1960;56:1-13.
- ³ Lines JG, et al. *J Med (Basel)* 1970;1:345-57.
- ⁴ Hillier P, Knapp MS. *J Physiol* 1974;242:83.
- ⁵ Hillier P, Knapp MS. *Quart J Med* (in press).
- ⁶ Kowanko I, et al. *Chronobiologia* 1979;6:121.

Sulphasalazine in rheumatoid arthritis

SIR,—Any study which establishes "disease-modifying" efficacy in rheumatoid arthritis for a drug less hazardous than gold and penicillamine, etc, would have important implications. Experience suggests that nothing short of rigorously controlled trials give

reliable information about such "slow-acting" drugs in this disease. We presume therefore that you must have been particularly cautious about deciding to publish the report by Dr B McConkey and others (16 February, p 442) of their uncontrolled trial of sulphasalazine.

We find this report misleading, incomplete, and difficult to follow. The authors rightly stress the importance in an uncontrolled study of objective measures of disease activity (erythrocyte sedimentation rate (ESR) and C-reactive protein). However, a careful study of the text and table as published suggests that the mean values among those available for analysis at each stage have been compared with the means for the group as a whole at the start (although elsewhere there is mention of a paired *t* test, but no details are given). Thus for the ESR the initial mean value among 74 patients (58.4 mm) is used for comparison with the mean value at week 50, even though this latter value represents the mean of only 28 patients (38%) available at that stage. The authors state that the principal reasons for these numbers falling were "failure to respond and adverse effects." In these circumstances (and in a disease in which activity anyhow tends to fluctuate) conclusions based on such differences are clearly unacceptable. The same argument applies to the C-reactive protein values and to the clinical score. There are other points to criticise (dropouts not all accounted for, 14 patients apparently not included in the six-week run-in, etc); but the falling numbers issue is central.

Reports making claims for effective treatments for rheumatoid arthritis demand particularly careful editorial scrutiny before publication. As published, this report appears either to contain important errors or to be statistically completely unacceptable. It may be that the authors have answers to these questions, but this does not explain how you, Sir, came to allow this report to appear as it does in your journal.

H L F CURREY
D M CHAPUT DE SAINTONGE

The London Hospital,
London E1 1BB

SIR,—Dr B McConkey and others (16 February, p 422) have failed to submit either sulphasalazine or dapsone¹ to a controlled clinical trial. We do not therefore know from their papers whether either dapsone or sulphasalazine is more effective than placebo in the treatment of rheumatoid arthritis (rheumatoid arthritis). Other conventions have also been ignored—for example, clinical assessment has not been carried out by a blind observer. Additionally, the only clinical assessment has been a subjective one by the patient, and this arbitrary clinical score has then been subjected to statistical analysis. There do exist various well-tried clinical measurements that can be used to assess progress in rheumatoid arthritis, and the rationale for formal clinical trials has been well expounded.²

It is important to remember that rheumatoid arthritis is a disease of remission and exacerbation. In this group of 74 patients only 31 remained at 50 weeks, 18 of the withdrawals having failed to respond. Therefore by the nature of the disease some of those remaining would have been expected to improve, so it is not surprising that they appeared to do so.