that there is no reason for suspecting bromocriptine to be a teratogen in humans. This statement is based on observations in more than 1100 babies born to mothers who had taken bromocriptine.

WILLIAM P MACLAY

Sandoz Products Limited,
Middlesex TW13 4EP

"Beat Heart Disease"

SIR,—I must protest at the inaccurate and misleading statements which were made about my book *Beat Heart Disease* (Medicine and the Media, 23 February, p 557). Your reviewer states, "The theme of the book is that lack of exercise is the main cause of heart disease and stroke."

In fact at no time in the course of the text do I state that lack of exercise is a cause of heart disease and stroke. On p 38 I say, "... the physically fit person leads a lifestyle which protects from illness such as coronary disease and stroke." On p 39 I state, "Research by The Irish Heart Foundation shows how important exercise is in the prevention of coronary disease and stroke. The Foundation's research is based on a study of more than 15 000 adult males in the community. It shows that physical exercise does not necessarily protect directly against coronary disease and stroke, but the person who is active during his leisure time is less likely to smoke and overeat, has lower blood pressure and blood cholesterol levels. The risk of atherosclerosis is consequently less. This almost certainly accounts for the smaller number of heart attacks amongst physically active people, because exercise reduces high cholesterol and high blood pressure levels, and contributes fundamentally to weight control." The emphasis in my exercise chapters was on the thesis that the quality of life is greatly improved by physical exercise, hobbies, and sport. At no time did I state that lack of exercise was a cause of heart disease. I am sure that many of my epidemiological colleagues will be startled by the statement attributed to me by your reviewer.

Your reviewer also states that I confused physical fitness with health. He cannot have read the text of my book very carefully. I make it quite clear that a life based on regular exercise and physical fitness encourages a low-risk lifestyle and therefore leads to better health. He further makes the point that I assume that because things are risk factors they must be the cause of disease. He then adds the statement, "Oversimplification like this cannot be justified when it distorts the truth"; and he implies that I have deliberately hidden our ignorance on the subject from the public.

I have no hesitation in defending my remarks about cigarette smoking and the various cigarette-related diseases, including coronary heart disease. My views here are based on the numerous and exhaustive publications by the Surgeon General of the United States. In reviewing the evidence of an association between cigarette smoking and coronary heart disease, the Surgeon General in his last report¹ states, "... It can be concluded that smoking is causally related to coronary heart disease in the common sense of that idea and for the purpose of preventive medicine."

In my chapter on hypertension I state that stroke, coronary heart disease, heart failure, and kidney failure are complications of hypertension. Does your reviewer differ with this statement? At no stage do I say that high cholesterol is a cause of coronary heart disease and stroke. The closest I go to such a statement is as follows: "There is now a vast amount of scientific evidence to link the present high incidence of atherosclerosis and its consequences with a high level of blood fats." I give a fair account of uncertainties about the utility of dietary intervention in primary and secondary prevention and I recommend a balanced diet for healthy people, a view which is supported by 20 national and international commissions which have reported on this subject.

I must confess that I find your short review of my book to be inaccurate and misleading. Apart from its reflection on my academic standing in epidemiology and preventive cardiology, it is less than complimentary to the president of the International Society and Federation of Cardiology, who, in your reviewer's words, "aided and abetted" me. Your review is an entire distortion of the message to the public which is contained in my book.

RISTEARD MULCAHY

Department of Preventive
Cardiology,
St Vincent's Hospital,
Dublin 4

¹ US Surgeon General, *DHEW publication No (PHS) 79, 50066*. Washington DC: Department of Health, Education and Welfare, 1979:4-66.

Interaction between lithium and carbamazepine

SIR,—We read with interest the case report by Dr W A G MacCallum (1 March, p 610) of a manic-depressive patient with epilepsy in whom clinical signs of lithium toxicity, particularly thirst, polyuria, and polydipsia, disappeared when carbamazepine was substituted for phenytoin as associated anti-convulsant treatment. Although the case was interpreted as giving unequivocal evidence "that phenytoin was causing the lithium-type toxicity" (presumably by potentiating the toxic effects of lithium on the renal tubules), there is an alternative and more likely explanation for the observed improvement in renal function.

It is now widely recognised that carbamazepine has potent antidiuretic properties,¹ possibly related to a direct action of the drug on the renal tubules in the presence of abnormal resetting of the hypothalamic osmoreceptors.² These properties can cause excessive water retention in patients with epilepsy³ and trigeminal neuralgia,⁴ and can be exploited therapeutically to reduce the polyuria associated with diabetes insipidus.⁴ Therefore it is reasonable to assume that in the case described by Dr MacCallum the disappearance of polyuria, thirst, and polydipsia resulted from the additional pharmacological action of carbamazepine rather than from the withdrawal of phenytoin. Such an explanation would not require postulating an interaction between phenytoin and lithium at the receptor site. The potential ability of carbamazepine to inhibit lithium-induced polyuria may have important clinical implications and deserves, in our opinion, formal evaluation.

EMILIO PERUCCA
ALAN RICHENS

Clinical Pharmacology Unit,
Institute of Neurology,
London WC1N 3BG

¹ Perucca E, Garratt A, Hebidge S, Richens A. *J Neurol Neurosurg Psychiatry* 1978;41:713-8.

² Stephens WP, Coe JY, Baylis PH. *Br Med J* 1978;ii:1445-7.

³ Stephens WP, Espir MLE, Tattersall RB, et al. *Br Med J* 1977;i:754-5.

⁴ Wales JK. *Lancet* 1975;ii:948-51.

Prophylaxis against febrile convulsions

SIR,—I agree with Dr J B P Stephenson (1 March, p 643) that continuous therapy with antiepileptic drugs may not be needed in children with febrile convulsions. There is evidence of the efficacy of intermittent therapy

with rectal diazepam,¹ especially when combined with adequate parental education,² the need for which has been clearly shown.³ Oral administration of 600 mg of sodium valproate syrup immediately after the convulsion, with subsequent administration of 200 mg thrice daily during the febrile illness, has proved effective in my patients.

There is little evidence, however, that the so-called "optimal" levels of sodium valproate are of value in assessing the dose of sodium valproate which will control seizures, and it is common knowledge that with most anti-convulsants control of seizures can be obtained with serum levels which are below the "optimum" or "therapeutic" levels.

Dr Stephenson quotes a number of North American reports relating to the toxic effects of valproic acid. It may be important that the North American form of the drug is valproic acid and not sodium valproate, since the former appears to cause more gastrointestinal symptoms and is not available in an enteric-coated form. Furthermore, in most cases the drug can only be added to previous medication, except in children with absences, and polypharmacy makes evaluation of side effects difficult.

Sodium valproate has been used extensively in Germany and The Netherlands since 1968 and in the UK since 1974, and there have been very few European reports of serious side effects. The pancreatitis reported by Dr Stephenson occurred in three cases from North America. The paper by Gerber *et al*⁴ has an addendum which notes that there had been 14 deaths from hepatic disease—six in the United States and eight in Europe—but no details were given. To my knowledge there are five European cases in which sodium valproate may be implicated, all of them in patients who had received other drugs. The information available suggests that hepatic failure, if due to sodium valproate, is an idiosyncratic response and must be very rare.

I have used sodium valproate for seven years and have treated over 500 patients, none of whom have shown any serious side effects. Sodium valproate is not a drug of "unproved benefit" as suggested by Dr Stephenson, nor is there much evidence of its toxicity, at least in European experience over the past 12 years. It is one of the most effective anti-epileptic drugs in the generalised epilepsies of childhood and it would be regrettable if its use was restricted on the basis of the references quoted by Dr Stephenson.

P M JEAVONS

Dudley Road Hospital,
Birmingham B18 7QH

¹ Agurell S, Berlin A, Ferngren H, Hellström B. *Epilepsia* 1975;16:277-83.

² Bower BD. *Br J Hosp Med* 1978;19:8-19.

³ Rutter N, Metcalfe DH. *Br Med J* 1978;ii:1345-6.

⁴ Gerber N, Dickinson RG, Harland RC, et al. *J Pediatr* 1979;95:142-4.

SIR,—Dr A Herxheimer (1 March, p 642) succinctly highlights some of the difficulties common to clinical field studies. Our investigation (9 February, p 353) is no exception. To directly monitor frequency and time of day of medication would, even if practicable, necessarily seriously confound compliance data. What we can say is that (a) medication was prescribed to be taken two or three times a day and (b) blood was sampled routinely every six months at three clinics run particularly for our study group. Two of the

clinics were held in the morning and one in the afternoon. The majority of the children were seen on the same day of the week at about the same time of day. Further blood samples were taken if a child was admitted to hospital febrile, with or without a fit. Our report examining the factors involved in compliance has yet to be accepted for publication. We welcome the confirmation that the investigation of such factors should not be regarded as "a minor footnote" to our main study.

Our use of χ^2 is on the basis of the independence of the six-month periods and the importance of age-dependence in vulnerability to febrile convulsions. We should have preferred the more direct calculation using numbers of children, but with a sample size of 108 children such an approach would require consistent medication in all children over 24 months. This methodological criterion was clearly clinically unattainable.

Dr J B P Stephenson (1 March, p 643) ignores the possibility that a recurrence of a febrile convulsion may be long and damaging^{1,2}; that repeated fits with fever predispose, in at least some children, to later epilepsy³; that the longer the duration of a seizure disorder the greater is the difficulty in controlling fits⁴; and that continuance of seizures may produce severe educational and employment problems in the future.⁵ Although most series report very low mortality rates, up to 11% of children with fits may convulse to death.⁶ Dr Stephenson notes that the incidence of reported fever per se is less in children receiving either phenobarbitone or sodium valproate, and comments on our indication that this may reflect a greater use of additional non-drug management procedures by this group. However, in his arguments against anticonvulsant medication he fails to note that one implication of the lack of difference between theoretically "optimal" and "sub-optimal" blood levels could be that "optimality" needs reconsideration.

SHEILA J WALLACE
JAN ALDRIDGE SMITH

Department of Child Health,
Welsh National School of Medicine,
Cardiff CF4 4XN

¹ Aicardi J, Chevrie JJ. In: Brazier MAB, Coceani F, eds. *Brain dysfunction in infantile febrile convulsions*. New York: Raven Press, 1976:247-57.

² Lennox-Buchthal MA. *Febrile convulsions: a reappraisal*. Amsterdam: Elsevier, 1973:59.

³ Nelson KB, Ellenberg JH. *New Eng J Med* 1976; **295**:1029-33.

⁴ Rodin EA. *The prognosis of patients with epilepsy*. Springfield: Charles Thomas, 1968.

⁵ Harrison RM, Taylor DC. *Lancet* 1976;ii:948-51.

⁶ Ekholm E, Niemineva K. *Acta Paediatr* 1950;**39**: 481-501.

Compliance and epilepsy

SIR,—We must take issue with the comments of Dr S D Shorvon and others (16 February, p 484).

In support of their statement "... poor compliance is the major cause of recurrence of seizures, the apparent failure of the first drug, and the subsequent escalation of polytherapy" they quote their own work.^{1,2} However, there is no evidence, even in their own published work, to support this. We can find no research published of the actual drug compliance in epilepsy.

Our own study among 64 epileptics taking anticonvulsants suggests that compliance with therapy is high. Eighty-five per cent of the

predicted number of prescriptions for 12 months were actually recorded as issued. This does not take into account prescriptions issued but not recorded (on home visits, etc.). In only three cases was failure to take tablets identified as the cause of the occurrence of fits.

Shorvon *et al* in their work¹⁻³ have demonstrated that the responsibility for failure in the treatment of epilepsy usually lies neither with the disease itself nor with the patient, but with the doctor. Our audit, which is soon to be completed, strongly supports this. While compliance is important, it has not been shown to be anything but a minor cause in the failure of treatment in epilepsy.

We do strongly support Dr Shorvon and colleagues in their advocacy of single-drug prescribing for epilepsy and the need to monitor serum anticonvulsant levels.

P T WHITE
E G BUCKLEY

Howden Health Centre,
Howden Livingston,
West Lothian EH54 6BX

¹ Shorvon SD, Chadwick D, Galbraith AW, Reynolds EH. *Br Med J* 1978;ii:474-6.

² Reynolds EH. *Lancet* 1978;ii:721-5.

³ Shorvon SD, Reynolds EH. *Br Med J* 1979;iii:1023-5.

Phenobarbitone and epilepsy

SIR,—Dr R H E Grant's comment in his letter (23 February, p 560) with regard to absence of side effects of phenobarbitone therapy in epileptics prompted me to write this note. Undoubtedly, phenobarbitone adequately controls epilepsy; but in long-term therapy biochemical osteomalacia,¹ evidenced by low calcium and phosphorus and raised alkaline phosphatase, associated with proximal myopathy and folate-deficient megaloblastic anaemia may occur. These side effects should be looked for as they can be adequately treated if not prevented.

ABU NASAR

St John's Hospital,
London SW11 1SP

¹ Davies-Jones GAB. In: Dukes MNG, ed. *Side effects of drugs annual 2*. Amsterdam: *Excerpta Medica* 1978:62.

Retroperitoneal fibrosis associated with atenolol

SIR,—We wish to report a second case of retroperitoneal fibrosis in a patient receiving the beta-blocker atenolol (Tenormin). The patient had taken no other drugs in the six months prior to his presentation with abdominal pain.

A 48-year-old man suffered coronary thromboses in 1969 and 1974. After the second he became hypertensive and was treated with atenolol 100 mg daily. In June 1979 he was referred to hospital with right-sided abdominal pain and an intravenous pyelogram (1.6 mg/100 ml) revealed a non-functioning right kidney. Retrograde pyelography suggested a diagnosis of retroperitoneal fibrosis. Serum creatinine was 145 μ mol/l and the erythrocyte sedimentation rate was raised at 106 mm in one hour. The right ureter was explored by an extraperitoneal approach and freed from dense retroperitoneal fibrous tissue. A biopsy of this tissue showed infiltration with large numbers of chronic inflammatory cells and lymphoid follicles suggesting idiopathic retroperitoneal fibrosis. A postoperative intravenous pyelogram revealed a return of function to the right kidney.

The relationship between the beta-blocker practolol and intraperitoneal sclerosing fibrous

reactions is well known, and this drug has now been withdrawn. We report this case because of its similarity to an earlier case of retroperitoneal fibrosis in a patient receiving the more recently developed beta-blocker atenolol.¹

JAMES N JOHNSON
JOHN MCFARLAND

Royal Liverpool Hospital,
Liverpool L7 8XP

¹ Doherty CC, McGeown MG, and Donaldson RA. *Br Med J* 1978;ii:1786.

Vomiting in the first year of life

SIR,—Dr H B Valman's excellent article (1 March, p 620) on Vomiting in the first year of life is, unfortunately, written from the experience of a hospital consultant. During my days in hospital I saw numerous cases of oesophageal atresia, but I have not seen one in over 25 years of general practice.

Dr Valman fails to mention that the commonest cause of anorexia or vomiting in infants between the ages of 1 week and 2 years seen in general practice is otitis media, which accounts for about 80% of cases. Ten per cent are probably due to virus infections and the remainder to other causes. I have been surprised that not one of the medical students who have come to me has been taught this, and they have been equally surprised to discover how common and how easily missed is otitis media, whether complicated by vomiting or not.

R T D FITZGERALD

Sheerness, Kent ME12 1TR

Antibiotics for whooping cough

SIR,—Your otherwise excellent article on vomiting, in the "First Year of Life" series (1 March, p 620), suggests that erythromycin and ampicillin are equal alternatives for the reduction of infectivity in cases of whooping cough. This is not so. Erythromycin has been shown to be highly effective and ampicillin ineffective *in vivo* using culture and fluorescent antibody techniques.¹ This is supported by my own experience in a previously reported outbreak of whooping cough,² during which I isolated *Bordetella pertussis* from one child after a five-day course of ampicillin and from five children after seven-day courses of amoxycillin. The best available evidence suggests that either erythromycin or cotrimoxazole should be used for this purpose.³

D JENKINSON

Keyworth Health Centre,
Keyworth, Notts NG12 5JU

¹ Bass JW, Klenk EL, Kotheimer JB, Linneman CC, Smith MHD. *J Pediatr* 1969;**75**:768-81.

² Jenkinson D. *Br Med J* 1978;ii:577-8.

³ Arneil GC, McAllister TA. *Practitioner* 1977;**219**: 855-8.

The coefficient of static friction for infants

SIR,—We were interested to read Dr H B Valman's article (1 March, p 620) concerning the management of vomiting in the newborn. We would, however, like to question the mechanics of nursing a baby prone with the mattress at an angle of 30-45°.

The photograph accompanying the article shows a baby tilted at slightly less than 10°.