in May 1977. She was receiving no other medication. At the end of 1977 she complained of pain and swelling in both wrists, which subsequently spread to involve the knees, ankles, hands, and elbows. In July 1978 there was clinically detectable synovitis of the proximal interphalangeal, metacarpophalangeal, and wrist joints. Her blood pressure was 150/80 mm Hg and her general examination was otherwise normal. There was no history suggestive of pleuropericardial disease or skin involvement. Investigations showed haemoglobin 9.6 g/dl, white blood cells $3.7 \times 10^9/l$, erythrocyte sedimentation rate 50 mm in the first hour, Coombs test negative, antinuclear antibody (ANA) test positive (titre 1/320), urea and electrolytes normal; the urine contained no protein, the Rose-Waaler test was negative, C3 and C4 levels were normal, DNA binding activity was <25 units/ml (normal), and the test for extractable nuclear antibodies was negative. Radiographs of the hands, feet, and chest were normal.

She continued to have evidence of a low-grade synovitis and in December 1978 she developed painful, pitting oedema of the right hand and left foot. The ANA titre remained at 1/320, the DNA binding was normal, and the leucopenia persisted. Labetalol was stopped in January 1979 and the patient was started on propranolol long-acting 160 mg daily. By February 1979 the symptoms had resolved; there was no evidence of synovitis and the ESR had fallen to 16 mm in the first hour. The ANA titre had then fallen to 1/80 and by April 1979 it was 1/20; and the patient remained asymptomatic.

We feel that this patient developed a lupus diathesis with synovitis, leucopenia, possible vasculitic oedema, and antinuclear antibodies during treatment with labetalol. There was resolution of the clinical signs and improvement of serological abnormalities on withdrawal of the drug. Our patient differs from the one described by Dr Bensaid and his colleagues in that pleuropericardial involvement was not present and at no stage was our patient's illness sufficiently severe to require corticosteroid therapy. Antibodies to double-stranded DNA were absent in both cases, as is usual in drug-induced lupus disorders. Although labetalol proved effective in controlling this patient's hypertension, it is probable that it induced a lupus syndrome and, as such, should be added to the list of drugs capable of provoking lupus-like illnesses.

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Sulphinpyrazone and warfarin after myocardial infarction

SIR,—Drs J A Tulloch and T C K Marr (14 July, p 133) ask for comments on their report of their experience with sulphinpyrazone (Anturan) and warfarin used early after myocardial infarction. I hope that the following remarks may be of some help.

At the present time evidence from controlled clinical trials of sulphinpyrazone following myocardial infarction is available only with respect to treatment being started approximately one month after the acute event and with a daily dose of 800 mg given in four divided doses. Indeed, the relevant current product licence for this product specifies both these conditions for its use.

The final results of the sulphinpyrazone reinfarction trial were presented at the recent

VIIth Congress on Thrombosis and Haemostasis in London and indicate a statistically significant reduction in "sudden death" in the sulphinpyrazone-treated group over the whole period of the trial (mean exposure time 16.1 months). No significant effect on reinfarction was noted. However, the benefit seemed to be due to an early effect which was maintained through the study, and it was therefore suggested that further controlled studies should be performed with earlier use of sulphinpyrazone following myocardial infarction.

At the present moment, however, little or no information is available on the use of this agent on admission of patients to the coronary care unit. Interpretation of results of therapeutic intervention in such patients is extremely difficult in view of the very labile natural history of the disease. For this reason, a comparative control group is essential in any trial attempting to assess new measures in this clinical setting. Preferably this comparison should be made on a double-blind basis. Unfortunately, it would seem that Drs Tulloch and Marr do not have such a comparative group and therefore an assessment of whether a particular event has occurred exceptionally frequently must have been made subjectively. Does "six recurrences . . . within a short period among 41 patients" represent a significant variation from the norm?

Even disregarding these methodological considerations, there are certain questions about this report which need to be answered before any attempt can be made to interpret the results. Did all patients admitted to the coronary care unit during the relevant period receive sulphinpyrazone? If not, how was the selection made? Similarly, were all patients admitted to the coronary care unit anticoagulated? What determined whether a patient received warfarin rather than heparin? Is any information available on the "coagulation status" of the patients following the withdrawal of warfarin? Were the recurrent episodes "fresh ischaemic episodes" or conventionally diagnosed myocardial infarctions?

We are not given any information as to the clinical course of patients during the hospital admission period, but it appears that there may have been only one death among the 78 patients following discharge from hospital. Subjectively, this figure would seem particularly encouraging.

Drs Tulloch and Marr have reported an interesting observation worthy of further investigation, but it would be unwise to draw conclusions from it regarding beneficial or adverse effects of sulphinpyrazone, alone or in combination.

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* * * We sent a copy of this letter to the authors, whose reply is printed below.—ED, *BMJ*.

SIR,—Dr Domenet's letter, while of interest, suggests that he has missed the reason for our letter. However, to answer the points he raises:

(1) It was and still is our intention to compare the progress over one year (initially) in patients admitted during the first half of 1979 who received sulphinpyrazone and in those admitted in the second half who will not receive it. (2) All patients admitted up to 30

June who had an acute infarct or acute ischaemic episode did receive sulphinpyrazone. (3) All of these patients were anticoagulated—those admitted under JAT receiving warfarin and those under TCKM subcutaneous heparin. No patient had an absolute contra-indication to anticoagulation. (4) We have no information on the "coagulation status" of the patients after warfarin was withdrawn. (5) No details of the clinical course of the patients were given as it did not seem relevant to the point we were raising. (6) The recurrent attacks were "ischaemic episodes" rather than major infarcts. In our experience six attacks among 41 patients in the course of a few months is unusually and alarmingly high.

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Sodium in peritoneal dialysis solutions

SIR,—We read with interest the paper by Dr P G Bisson and Mr K M Bailey on sodium in peritoneal dialysis solutions (19 May, p 1322). Dialysate sodium concentration is no doubt critical in the management of patients on regular dialysis treatment, whether they are on peritoneal dialysis or haemodialysis. Optimal dialysate sodium concentration in regular dialysis treatment remains a controversial subject. Whereas there are only two types of peritoneal dialysis solution available in the United Kingdom (Na 130 and 141 mmol(mEq)/l), we are alarmed by the fact that on our last count 21 haemodialysis solutions with varying sodium concentration (range 115–145 mmol/l) were commercially available in the United Kingdom.

The need for varying the type of dialysate for haemodialysis stems from the days when haemodialysis machines with fixed proportioning units were used. The modern generation of haemodialysis machines, and indeed the ones used during the past decade, have variable proportioning units, which deliver a desired dialysate sodium concentration, at site, and obviate the need for so many types of haemodialysis solutions.

In the light of these developments we suggest the reassessment of our requirements and standards of dialysis technology.¹

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¹ Ahmad, R, *Proceedings of European Dialysis and Transplantation Association*, 1979, 16 (in press).

Seizures after aminophylline by suppository

SIR,—A 19-year-old girl without a previous history of epilepsy presented in status asthmaticus. She had been ventilated on two previous occasions during the preceding nine years.

She weighed 36 kg and her arterial oxygen pressure (PaO₂) was 10.1 kPa and arterial carbon dioxide pressure (PaCO₂) 3.3 kPa. Within 12 hours of admission, following the failure of conventional treatment to prevent carbon dioxide retention, she was treated with positive-pressure ventilation for three days, intravenous salbutamol, hydrocortisone, and ampicillin. Off the ventilator on

28% oxygen, her PaO_2 was 20.22 kPa and PaCO_2 4.5 kPa. Prior to her return to the ward she was started on aminophylline suppositories 360 mg twice daily, prednisolone 20 mg twice daily, salbutamol, and becotide inhalers. Three days later she had three grand mal seizures within one hour, commencing on the right side of her body. Intravenous diazepam (10 mg) given after the first seizure did not prevent the two further attacks. Treatment with aminophylline suppositories was stopped and no further fits occurred. An electroencephalogram on the following day was normal.

In children, convulsions have followed the rectal administration of aminophylline,¹ but this effect has rarely been described in adults. Absorption from suppositories is unpredictable.² In adults convulsions have occurred following intravenous administration.³ The patient described above was given 720 mg/day = 0.8 mg aminophylline/kg/h for three days. It has been recommended that adults with severe asthma should be given no more than 1 g/day of aminophylline intravenously,⁴ or no more than 0.9 mg/kg/h.⁵ This case illustrates the danger of aminophylline suppositories and prolonged treatment at high doses. We suggest that this drug should be prescribed by weight at specified intervals rather than in terms of the number of tablets or suppositories, particularly in small adults.

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¹ Bacal, H L, *et al*, *Canadian Medical Association Journal*, 1959, **80**, 6.

² Martindale, *The Extra Pharmacopoeia*, 27th edn, ed A Wade, p 279. London, the Pharmaceutical Press, 1977.

³ Zwillich, C W, *et al*, *Annals of Internal Medicine*, 1975, **82**, 784.

⁴ *British Medical Journal*, 1975, **4**, 65.

⁵ Mitenko, P A, and Ogilvie, R I, *New England Journal of Medicine*, 1973, **289**, 600.

Management of maternal phenylketonuria

SIR,—In a recent article Dr G M Komrower and others (26 May, p 1383) report their experiences with phenylketonuria in pregnancy and quote a case of ours.¹ Unfortunately in his table III, owing possibly to a transcription error, the final IQ of our patient's child was given as 65. This child's latest IQ, at the age of 9 in 1976, was: WISC verbal 86; performance 90; full scale 87.

The IQ figure in the last column should therefore read 87. This is of some importance in supporting the conclusion of Dr Komrower's article that a low-phenylalanine diet provides some protection to the fetus in maternal phenylketonuria.

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¹ Arthur, L J H, and Hulme, J D, *Pediatrics*, 1970, **46**, 235.

Pressure in cuffed tubes

SIR,—Dr T H S Burns (21 July, p 212) is quite correct in drawing attention to the rise in pressure if the cuff is inflated with air when nitrous oxide is the anaesthetic used. This is due to permeation of the cuff membrane by the nitrous oxide. The rate of permeation depends on a variety of factors—for example, the nature of the respective gases, their partial

pressure, the thickness of the membrane, and the nature of the membrane. The last factor is by far the most important, and it has been found that plasticised polyvinyl chloride (the material used in Portex tubes) has a very much lower permeability coefficient than either natural rubber or silicone rubber, the other materials commonly used.

For maximum safety, however, it is nevertheless advisable to inflate the cuffs with the anaesthetic mixture and not air, to inflate only to the minimum pressure needed, to use release valves, and to release at least every hour any excess build-up of pressure that may have occurred.

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Management of self-poisoned patients

SIR,—Drs D R Blake and M G Bramble (30 June, p 1763) raise the question of whether self-poisoning patients need to be admitted to hospital to await psychiatric assessment. Dr E J Salter (21 July, p 205) is right in assuming that in some parts of the country the number of patients being discharged either from casualty or before psychiatric assessment takes place is larger than in the Newcastle survey (13.5%).

I recently surveyed patients falling into this category at a local general hospital over a six-month period. One-hundred and eighty-one patients were involved in 193 self-poisoning episodes, of which 71 (39%) patients were not seen by a psychiatrist, 55 (30%) of these not being admitted from the casualty department. A search of hospital records in psychiatric hospitals serving the general hospital plus continual recording of self-poisoning episodes revealed that, of those patients not seen by a psychiatrist, 14 were already known to the psychiatric services, though half of these had come into contact only because of previous overdoses. In a four-month period following self-poisoning, two patients were seen following subsequent overdoses—a 15-year-old girl, who was referred to child guidance, and a 61-year-old woman with depression secondary to hypocalcaemia. There was also one patient who was referred following a medical admission for psychogenic vomiting with hypokalaemia. Three patients were admitted as psychiatric inpatients within one month of their overdose, two being diagnosed as having personality disorders and one as a depressed alcoholic. Two further patients were referred by their general practitioners for psychiatric assessment because of worries about further overdosing. In all, 11% of the patients discharged home were seen by a psychiatrist subsequently, with continuing psychiatric contact in the majority of cases.

Although no patients appeared to have committed suicide (from a search of coroners' records) as a result of discharge before psychiatric assessment, this superficial survey of records suggests a high rate of psychiatric morbidity in these patients. I would seriously question the ability of overworked casualty officers or medical staff to make adequate assessments of these patients in a busy casualty department, where the patients may still be under the influence of the drugs that they have taken. There are obviously many hospitals like the one described above where shortage of

acute beds and lack of immediate psychiatric assessment mean many patients are sent home without adequate assessment. Written guidelines and discussion of self-poisoning assessments with psychiatric staff would help those staff who have to make the decision about whether a patient should be sent home. Provision of personnel with expertise in assessing these patients might be one way of reducing medical admission without unnecessary risk to the patients concerned.

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Diverticular disease in Kenyan Africans

SIR,—I am interested in the comments by the Reverend H C Trowell and Mr D P Burkitt (30 June, p 1795) on my article on diverticular disease in Kenyan Africans (2 June, p 1465). The heading of their letter is, I feel, misleading as diverticular disease occurs not only in urban but also in rural Kenyan Africans. The Kenyatta National Hospital is the major referral hospital for the whole country and the fact that the patients were examined there does not mean that they lived in Nairobi. As the series was a retrospective radiological one and much of the clinical information was not available, I was unable to differentiate the patients according to their place of residence or social class. In Nairobi, however, most Africans in the upper social classes attend one of the private hospitals and the Kenyatta National Hospital deals largely with the lower income groups. It should also be noted that in the article by Archampong *et al*¹ that Dr Trowell and Mr Burkitt mention in their letter the patients with diverticular disease, though mainly upper class, had all lived on traditional African high-residue food. The authors concluded that other factors may contribute to the pathogenesis of the disorder.

I agree that quantitative data and dietary surveys are needed. I have just completed such a survey and hope to publish the results in the near future.

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¹ Archampong, F Q, Christian, F, and Badoe, E A, *Annals of the Royal College of Surgeons of England*, 1979, **60**, 464.

SIR,—Dr John F Calder has reported an unusually high incidence of diverticular disease of the colon for Africans (2 June, p 1465). If others have not found this, it is not necessarily from lack of looking. During a 17-month period (1972-3) at Mulago Hospital, Kampala, I found only one patient with diverticular disease, and he had only one diverticulum.

A 40-year-old Ugandan official was referred for barium enema. He gave a six-month history of left iliac fossa pain and intermittent blood in his stools. Stool examination was negative. A single sigmoid diverticulum was seen, associated with localised narrowing and a "saw-tooth" mucosal pattern. A noteworthy feature of barium enema examination in Ugandan patients was the very large capacity of the colon. Two litres of contrast could be introduced without filling of the caecum. Over-