effective drug, and there is no evidence that patients will escape from its therapeutic effect, or that oedema will be perpetuated, during prolonged treatment.

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

SIR,—We agree entirely with Dr Ramsay's "axiom." However, it is obvious that Dr Ramsay has failed to grasp the points we wished to make in our short report (16 June, p 1604).

It was not our intention to detail the principles of diuretic therapy. We merely pointed out the peculiar behaviour of renal allograft recipients in respect of diuretics, a phenomenon which appears to be more complicated than Dr Ramsay has appreciated. We have shown not only that urinary sodium excretion did not exceed intake indefinitely but that it actually returned to about baseline levels in about two weeks. The dose of the diuretic had to be increased to achieve the same saluresis in the presence of unchanged sodium intake, suggesting "escape" from the therapeutic effect of the drug.

Oedema often develops acutely during rejection episodes in renal allograft recipients. Since causative factors are usually removed if the rejection responds to immunosuppressive treatment, it is imperative to try to wean the patient off the diuretic after the rejection crisis as the maximal therapeutic effect is achieved in a short time. Patients who are inappropriately left on the diuretic after the rejection crisis will become dependent on the drug, since homeostatic mechanisms of salt retention are stimulated by the inappropriate use of the diuretic. Sudden withdrawal of the diuretic even when all causative factors have resolved (as was the case in our report) frequently produces severe yet transient "rebound" oedema.

We therefore wish to emphasise that frequent reassessment of individual requirements for diuretics is needed, and that one should not be dissuaded from weaning patients off potent diuretics after treatment of the cause of the oedema, since the "rebound" fluid retention is transient.

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Prostaglandins and impotence

SIR,—The answer to the question about impotence as a recognised side effect of indomethacin suppositories (16 June, p 1608) needs further elaboration.

According to Karim and Hillier,¹ the spontaneous activity of strips of corpus cavernosum muscle from human penis in vitro is abolished by inhibitors of prostaglandin synthesis (aspirin and indomethacin); this implies a role of endogenous prostaglandins in the activity of this tissue. They also have pharmacological effects on the muscle of human penis in vitro, producing relaxation or stimulation depending on the compound used. It has been speculated that a com-

bination of smooth muscle stimulation and vasodilatation brought about by prostaglandins may be involved in the physiology of erection and ejaculation.

Prostaglandins, being among the most potent biologically active substances, play a major role in the reproductive process. Assessing the in-vivo effects of indomethacin and other inhibitors of prostaglandin synthesis on the basis of information obtainable from subfertility or rheumatology clinics will provide us with better answers.

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¹ Karim, S M M, and Hillier, K, in *Prostaglandins and Reproduction*, ed S M M Karim, p 23. Lancaster, MTP Press, 1975.

Mental handicap and the BBC

SIR,—I was most interested to read the correspondence between my colleague Dr Bernard Laurance and Mr Ian Trethowan (30 June, p 1785), since, unknown to Dr Laurance, I have had similar correspondence.

The things that disturb me most about the forthcoming play are the very rare cause of handicap in the child (anaesthetic negligence) being portrayed and that they were looking for a handicapped child to exhibit in the play.

Like Dr Laurance I received a very bland and quite unsatisfactory letter from Mr Trethowan and in it is the fact that the disquiet of paediatricians about this programme is not going to influence the BBC, who clearly intend that it should go on.

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Drugs for epilepsy

SIR,—We applaud the advice of Dr P S Mehta (9 June, p 1565) to follow the accurate diagnosis of epilepsy by the use of a suitable single anticonvulsant drug in therapeutic dosage. However, the young epileptic described in our article (14 April, p 1000) had been considered resistant to single-drug therapy several years before he presented to our community clinic in clinical pharmacology, by which time he was receiving three different anticonvulsant preparations.

There is scant evidence to suggest that anticonvulsants given in combination have effects which are additive. Our initial objective therefore was to adjust the dosage of one drug (phenytoin) to an optimal level and then, once seizures had been controlled, to reduce the complexity of the regimen. Regrettably, he died before this strategy could be followed through.

We accept the point made by both Dr Mehta and Dr D P Addy (5 May, p 1217) regarding the merits of carbamazepine. It was not our intention to advocate the wider use of phenytoin, but rather to demonstrate how the dosage of this drug may best be adjusted.

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Drug-induced oesophageal injury

SIR,—Mr F J Collins and others (23 June, p 1673) clearly demonstrate the ability of emepromium bromide to cause oesophageal ulceration, but do not remark on the long latent period before symptoms occur. I myself have seen three cases of dysphagia caused by this drug, which I would like to describe briefly.

Case 1—A 9-year-old girl was admitted to the Bristol Royal Hospital for Sick Children with a 48-hour history of painful dysphagia for both solids and liquids. She has been taking emepromium bromide for three months for enuresis. Barium swallow showed no abnormality and all symptoms disappeared over three days with conservative treatment with intravenous fluids and mucaine. Emepromium bromide was discontinued.

Case 2—A 24-year-old woman presented at the accident and emergency department of Bristol Royal Infirmary complaining of retrosternal discomfort on swallowing. She had been taking emepromium bromide for 10 days for frequency following a urinary tract infection. It is of note that she was "of no fixed abode." The dysphagia had resolved completely two days after stopping emepromium bromide therapy.

Case 3—A 79-year-old man was given emepromium bromide for urgency following a prostatectomy. After two weeks he developed dysphagia. This resolved on stopping the treatment with no adverse effect on his frequency.

The common factor in these three cases was that they were no longer taking an adequate quantity of fluid with their tablet. In cases 1 and 3 this was because of a desire to avoid a fluid load last thing at night and in case 2 because of the patient's general life style.

Patients who take emepromium bromide should be warned to take a good volume of fluid when swallowing the tablets and a reminder is appropriate when represcribing the drug. Neglecting this precaution while continuing to take the drug is probably the explanation of the latent period that occurs between starting therapy and dysphagia occurring.

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SIR,—With reference to the paper on drug-induced oesophageal injury by Mr F J Collins and others (23 June, p 1673), we wish to bring to the attention of your readers two more cases of oesophageal ulceration due to emepromium bromide (Cetiprin).

Case 1—A 26-year-old dental nurse was prescribed emepromium bromide (200 mg three times daily) for urinary frequency. She had taken the drug uneventfully for five days when she developed severe midretrosteral pain shortly after swallowing two tablets with a little water. She took no more tablets but continued to have painful dysphagia. Seven days later she was referred to this hospital, where fibreoptic oesophagoscopy showed a large, superficial ulcer in the mid-oesophagus. With the help of symptomatic treatment she made a full recovery from the symptoms and repeat oesophagoscopy two months later confirmed complete healing without scarring.

Case 2—A 30-year-old housewife had been taking emepromium bromide for 10 days when she suddenly developed retrosternal pain and dysphagia a few minutes after swallowing two of the tablets with a little water. For the next eight days she continued to take the tablets in the prescribed dose of 200 mg three times daily but could swallow them with only small amounts of water because of painful dysphagia. Fibreoptic oesophagoscopy nine

days after the onset of symptoms showed a large, superficial ulcer in the mid-oesophagus. She responded well to withdrawal of emepronium bromide and to oral analgesics and nine days later repeat oesophagoscopy showed that the ulcer had healed.

There have been a number of reports of oesophageal ulceration with emepronium bromide,¹⁻⁴ as well as a report of mouth ulcers,⁵ thought to be caused by prolonged contact of the tablet with the mucosa. The data sheet on this drug now suggests that the tablets should be swallowed with a glass of water, but it is apparent that this instruction is not always stressed by the doctor or followed by the patient. The tablet is formulated to disintegrate rapidly on contact with water but its hygroscopic nature can cause it to stick to the oesophageal mucosa if it is swallowed with too little water. Perhaps the time has come for the manufacturers to redevelop the presentation of this drug. Surely it will not be long before oesophageal perforation due to emepronium bromide is recorded.

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¹ Habeshaw, T, and Bennett, J R, *Lancet*, 1972, 2, 1422.

² Hale, J E, and Barnardo, D E, *Lancet*, 1973, 1, 493.

³ Kavin, H, *Lancet*, 1977, 1, 425.

⁴ Kenwright, S, and Norris, A D C, *Lancet*, 1977, 1, 548.

⁵ Strouthidis, T M, Mankikar, G D, and Irvine, R E, *Lancet*, 1972, 1, 72.

Sulphinpyrazone and warfarin after myocardial infarction

SIR,—We decided that all patients discharged from Stracathro Hospital after a myocardial infarct should receive sulphinpyrazone (Anturan), 200 mg thrice daily, from 1 January 1979. Early that month one patient had a recurrence of infarction while in hospital, and then we agreed to start the sulphinpyrazone as soon as the patient was admitted to the coronary care unit and to use it concurrently with anticoagulants. Between 1 January and mid-June 47 patients received warfarin and 31 subcutaneous heparin. As was to be expected, the dose of warfarin required was approximately halved. The anticoagulants were discontinued on the patient's discharge, usually after two to three weeks, the warfarin dose being tailed off over a few days. All patients were then continued on the sulphinpyrazone in a dose of 200 mg thrice daily. One patient on warfarin and sulphinpyrazone had a recurrence of infarction while in hospital and six in whom warfarin was discontinued have been readmitted with a fresh ischaemic episode, usually within two to three weeks of discharge and at the most after two months. One patient who received subcutaneous heparin plus sulphinpyrazone died suddenly, 16 days after discharge.

The sulphinpyrazone is given in the expectation that it will lessen recurrence of myocardial infarction. Six recurrences of infarction within a short period among 41 patients is remarkably high. We therefore wonder if the combined use of warfarin and sulphinpyrazone for two to three weeks, followed by the withdrawal of the warfarin, results in an unstable state—making the patients more vulnerable to reinfarction rather

than, as hoped, partially protected. The fact that only one of 31 patients treated with subcutaneous heparin plus sulphinpyrazone has had a recurrence supports this possibility.

We have discontinued the warfarin-sulphinpyrazone combination from 1 July. Comments on this finding would be helpful.

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Oral choline in cerebellar ataxia

SIR,—I reported last year¹ the case of a patient whose cerebellar ataxia responded to oral treatment with choline chloride. Since then I have given the same treatment to a further 13 patients with cerebellar ataxia, in doses of up to 20 g a day. The causes of the ataxia included hereditary familial cerebellar ataxia, with or without upper motor neurone signs; sporadic cerebellar degenerations; multiple sclerosis; ischaemia; and trauma. No patient has shown any significant improvement.

Because of the known role of γ -aminobutyric acid (GABA) as a synaptic transmitter within the cerebellum I have tried in these patients the effects of drugs calculated to enhance gabanergic activity. They have received baclofen, a GABA analogue; or sodium valproate, which at least in large doses is thought to increase brain GABA levels; or the two drugs in combination. Not only has there not been any improvement, but most patients have reported a significant deterioration, and in several this was confirmed objectively. Deterioration has not been apparent in patients with accompanying upper motor neurone signs, presumably because the associated spasticity has been benefited whether or not the ataxia has been made worse; and the overall functional state has thus remained static.

This observation is interesting, as it suggests the possibility that lowering gabanergic activity might benefit cerebellar ataxia. Unfortunately, the drugs which are known to have such an effect experimentally tend to be convulsants; so it may not prove possible to obtain the desired effect on the ataxia without provoking fits. These results will be reported in more detail shortly.

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¹ Legg, N J, *British Medical Journal*, 1978, 2, 1403.

Prurigo and pets

SIR,—As someone who has suffered for some two years from the unwelcome attentions of the canine mite *Cheyletiella yasguri* may I, from personal experience, comment on this interesting report?

Firstly, although Dr Marianne Kieffer and others (9 June, p 1539) state that all the animals with mite infestation had symptoms, my dog, a whippet, appeared clinically normal, was not scratching, and had no skin lesions. Secondly, they mention that the mites were identified in skin scrapings. I took skin scrapings on two occasions and saw precisely nothing; only when Mr L R Thomsett of the Royal Veterinary College vigorously combed

the animal for several minutes was the mite demonstrated in the material obtained. Without this technique it is not easily found. Lastly, although Kieffer *et al* mention that the mites were removed by washing the animals three to six times in the appropriate solution, the need for repeated bathing is not appreciated by vets, including the one I originally consulted. One or two baths are no good at all, and now, thanks to the correct advice at last (Mr Thomsett again) I am no longer under attack from *Cheyletiella*.

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Withdrawal of alclofenac (Prinalgin)

SIR,—Studies in recent years in the UK have shown a 20–30% incidence of rash with alclofenac. The high incidence of rash with this drug has received previous comment.^{1,2}

We have undertaken a series of studies designed to explore the mechanisms of this rash. These studies have failed to show any likely way of preventing the problem and indicate the advisability of adding to the available animal safety evaluation data. These additional studies would still not be expected to solve the presenting problem of the skin eruption and we have therefore decided to withdraw the drug.

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¹ Mansel-Jones, D, *Lancet*, 1974, 1, 97.

² Mansel-Jones, D, *British Medical Journal*, 1974, 1, 160.

Bedside library for medical students

SIR,—I wish to defend staunchly Sir William Osler from the incorrect claims made by Dr Peter Beattie (9 June, p 1551) in Reading for Pleasure.

Osler did indeed recommend a "Bedside Library for Medical Students" and this comprised 10 titles, not 30 as suggested. The list can be found on the last page of *Aequanimitas*, published by Blakiston's in 1904. For those who have not seen the book, the list reads as follows: (1) Old and New Testaments; (2) Shakespeare; (3) Montaigne; (4) Plutarch's *Lives*; (5) Marcus Aurelius; (6) Epictetus; (7) *Religio Medici*; (8) *Don Quixote*; (9) Emerson; (10) Oliver Wendell Holmes—*Breakfast Table Series*.

The list is not so very different, in profundity from Dr Beattie's after all—especially No 8.

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Coronary care

SIR,—Dr Clifford Lutton (23 June, p 1709) may be interested to hear that my general practitioner agreed that I took the correct decision in seeking direct admission to a coronary care unit, and having read my article in the Personal View series (14 April, p 1012), thoroughly approved of it, as did a large number of colleagues who wrote to me about it. Some of them, indeed, thanked me for giving publicity to an experience which they had suffered themselves.