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 fiberoptic 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. Fiberoptic oesophagoscopy nine