diabetic acidosis, primary aldosteronism, and sometimes after the removal of a parathyroid adenoma. Hypomagnesaemia is often associated with postdiuretic electrolyte imbalance; furthermore, hypomagnesaemia of more than a slight degree is usually due to diuretic therapy in general, and thus is not specific to metolazone.

In the first case reported the female patient had received 2·5 mg daily for three days before the onset of symptoms. An EEG was reported as being possibly indicative of epilepsy. There was no laboratory report of serum magnesium. The information on this case does not support an adverse reaction to metolazone, especially with such a small dosage over a short period of time.

In the second case a 70-year-old male was receiving diuretic therapy consisting of daily theophylline, salbutamol, frusemide 160 mg, and spironolactone 150 mg; later frusemide was increased to 200 mg. This treatment was continued for 14 days. Five days later one dose of 5 mg metolazone was given, following which the described epileptiform seizures occurred. The EEG, blood urea, serum sodium, potassium, and calcium were described as normal. Serum magnesium was given as 0·32 mmol/l. All drugs with the exception of metolazone were continued with no recurrence of symptoms. A past history recalls an episode of syncope two years previously, when the patient was not receiving any medication; this episode was preceded by a leg cramp.

In the second case, it would seem more reasonable to assume the low serum magnesium was due to the previous 14 days' diuretic therapy rather than a single 5 mg dose of metolazone.

A leading article in the *British Medical Journal* (25 January 1975, p 170) draws attention to the fact that most established diuretics such as thiazides and frusemide will increase magnesium clearance in the long term. The article also mentions that certain patients with heart failure are already magnesium-depleted before the beginning of drug therapy.

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Abortion and maternal deaths

SIR,—It is surprising that Dr Ann Cartwright (24 July, p 232) should now describe as a "random sample of women having an abortion" the 272 patients used for the study by her "Institute for Social Studies in Medical Care," commissioned by the Lane Committee and published as vol III of their report. Actually there is no reason at all to suppose that the sample will have been a random one, being seriously biased by the fact that 7 of the 30 NHS hospitals approached and over half (6 out of 11) of the private abortion clinics (only 25 of the private patients were from clinics *not* associated with the Pregnancy Advisory Service) refused requests to participate in the inquiry. This was correctly pointed out on p 3 of the introduction to the report as follows: "Our sample has an unduly high proportion of women having abortions in NHS hospitals, an appropriate proportion having them in clinics associated with the PAS, but women having them in other private clinics are greatly under-represented."

Extrapolating conclusions from a small sample can be justified only if the original sample really was a random one and representative of the whole population. This particular study seems to have been done under great pressure, and its results may well have been the best that could have been achieved in the time available. But it certainly was not (and wasn't even claimed to have been) truly representative. It should surely therefore not be used as an argument against your proposal (10 July, p 70) for "well-planned prospective studies in large, representative communities" as a basis for future policy decisions.

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Febrile fits

SIR,—Recent correspondence (19 June, p 1530 and 10 July, p 112) on this subject may have led people to ignore the potential seriousness of this condition. To divide the fits into "simple febrile convulsions" and "epileptic seizures precipitated by fever" certainly separates the mild from the severe, and obviously the former are not likely to result in brain damage. However, this reasoning seems to exclude the facts that all these seizures are epileptic and that epilepsy in any form is a symptom. All of us are liable to certain symptoms under particular conditions, and this seems to be especially so in the case of epilepsy.

It is not known why fever is a precipitating factor for epileptic seizures any more than why certain people are photosensitive. It is no doubt a complex matter, and in the case of febrile convulsions pyrexia is unlikely to be the only cause. Therefore if any child appears to be liable to the onset of fits when the temperature rises, he is at considerable risk of a complication which may lead to death or lifelong handicap, and the matter must be considered as an emergency. Any argument over terminology in the absence of knowledge about causation is likely to distract from the most important issue. If such seizures are not prevented or treated urgently, a number of children will suffer.

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BCG in cancer

SIR,—The writer of your leading article under this title (19 June, p 1487) recommends that more clinical trials are needed "if the potential benefits of BCG used in malignant disease are to be fully realised." Leaving aside this optimistic anticipation of the results of trials not yet done, we should point out that over 150 registered clinical trials of BCG in the treatment of cancer are currently in progress or projected.[1] It can be surmised that many unregistered trials also are in progress.

The question arises whether any limit is envisaged for the number of trials required to determine whether BCG does or does not make a realistic contribution to therapy. Many examples could be given from other branches of medicine in which a single fair clinical trial of a mooted form of therapy has been found sufficient to decide the issue. Immunotherapy of cancer is peculiar in that various techniques have been subject to clinical trial for over 80 years.

Your leader writer refers to preferential modification of cancer cells by BCG-induced macrophages independently of the exertion of any tumour-specific antigenicity. However, the reference[2] is exclusively to studies in vitro. The fact is that the principal instigation of clinical immunotherapy has been the favourable results of in-vivo studies using rodent tumours induced by powerful chemical carcinogens or oncogenic viruses. A recent communication[3] seriously questions the validity of these experimental systems as models of clinical cancer and reports a total failure to demonstrate immunogenicity in a wide variety of rodent tumours of *spontaneous* origin.

Projection to clinical trial of the results of immunotherapy experiments using animal tumours requires fastidious attention to the validity of the animal systems employed as models of the human disease. We believe that, very largely, this requirement has not been met. Until it has, the recommendation of yet further clinical trials of BCG in cancer signifies more domination by an idée fixe than a logical progression from laboratory experiments to clinical measures.

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[1] *Compendium of Tumor Immunotherapy Protocols*, No 3, October, 1975, Bethesda, National Cancer Institute.
[2] Hibbs, J B, *Science*, 1973, **180**, 868.
[3] Hewitt, H B, *et al*, *British Journal of Cancer*, 1976, **33**, 241.

Raynaud's disease and the oral contraceptive pill

SIR,—Your reply to this question (17 July, p 156) is an oversimplification, which though it may be true in primary Raynaud's disease takes no account of the problem that may be arising in patients who are developing the secondary condition. My own experience has shown that apparently typical primary cases in young women coincided in their onset with the taking of ovarian steroids. Two girls proved to be diabetic, and one has since shown unmistakeable evidence of scleroderma. In all cases there was an improvement when the pill was stopped.

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Economy in prescribing

SIR,—I must take issue in part at least on this matter with Dr P M Morris (31 July, p 304), in particular with his implication that cheaper drugs are inferior. I would suggest that very often the converse is true and that well-established *National Formulary* preparations are equally effective with fewer side effects. Three examples which come readily to mind are phenoxymethyl penicillin instead of ampicillin and tetracyclines for upper respiratory infections, thiazide diuretics in place of combined or loop diuretics in maintenance treatment of congestive failure, and aspirin or paracetamol rather than expensive and often highly dangerous proprietary analgesic/steroid mixtures in chronic rheumatic conditions.

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