peral lactation.⁴ It is important, therefore, to establish or exclude any effect the drug might have on bleeding or clotting mechanisms in patients treated with bromocriptine.

Seventeen patients (five males and five females with acromegaly, six females with anorexia nervosa, and one female with refractory obesity) were investigated. None was taking any drug known to disturb blood coagulation mechanisms. Coagulation studies including bleeding time were carried out on each patient, after which they started treatment with bromocriptine in doses increasing to 10 mg/day. The coagulation study was repeated after the patients had been established on this dose for at least one week (range 1 week-2 months).

No significant alteration was detected in any of the following coagulation indices: bleeding time, platelet count, Quick's one-stage prothrombin time, partial thromboplastin time with kaolin, fibrinogen, euglobulin clot lysis time, fibrin degradation products, and prothrombin consumption index.

The dose of the drug in our patients on a weight-for-weight basis was approximately one-hundredth of that given to the mice used in the study by Karmali and Horrobin, but a total dose of 10 mg/day has been shown to be effective in suppressing galactorrhoea² and puerperal lactation.⁴ Although doses of as much as 60 mg/day have been used in acromegaly,³ there are probably few patients who require so much.

Our evidence indicates that patients can take a clinically effective dose of bromocriptine without showing any tendency to a "hypercoagulable" state as might be suggested by a shortened bleeding time or a change in any other of the coagulation variables listed.

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¹ Karmali, R A, and Horrobin, D F, *British Medical Journal*, 1975, **3**, 307.

² Thorner, M O, et al, *British Medical Journal*, 1974, **2**, 419.

³ Sachdev, Y, et al, *Lancet*, 1975, **2**, 1164.

⁴ Varga, L, et al, *British Medical Journal*, 1972, **2**, 743.

Cephalosporins in meningitis

SIR,—I read with interest the letter from Dr M Phillips and others entitled "Hazards of cephalosporins in penicillin-allergic patients with meningitis" (14 February, p 397). I would, however, like to draw your attention to some data which seem to have escaped the authors.

It is stated in the article that "none of the cephalosporins efficiently penetrate the blood-brain barrier." My experience,¹ as well as animal experimental^{2,3} and human^{4,5} pharmacokinetic data, clearly shows that cefacetrile (Celospor) penetrates into the cerebrospinal fluid in an amount sufficient to eradicate most of the commonly encountered pathogens causing bacterial meningitis. In controlled clinical evaluations on the efficacy of cefacetrile therapy in bacterial meningitis Correa Lima⁴ and Lomar et al⁶ have confirmed its clinical and bacteriological efficacy in more than 100 patients. In these patients the success rate was more than 90% and the tolerance of the drug was good. It is to be noted that in no case

was cefacetrile given intrathecally but always intravenously or intramuscularly.

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¹ Dettli, L, and Lomar, A V, in *International Symposium on Cephalosporins, Munich, 1976*, ed E Gladtko and W Marget, in press.

² Sherertz, R, Dacey, R, and Sande, M, in *Abstracts of the IXth International Congress of Chemotherapy, London, 1975*.

³ Zak, O, personal communication.

⁴ Lima, M B C, et al, To be published.

⁵ Meyer-Brunot, H G, Schenk, C, and Lomar, A V, in *Chemotherapy: Proceedings of the IXth International Congress of Chemotherapy, London, 1975*, ed J D Williams and A M Geddes, vol 5, p 299. New York and London, Plenum Press, 1976.

⁶ Lomar, A V, et al, *Folia Médica*, 1975, **71**, 269.

Effects of methyldopa on growth hormone

SIR,—Dr J Steiner and others (15 May, p 1186) report an increased response of serum growth hormone (GH) to insulin hypoglycaemia in hypertensive patients treated with methyldopa for two to three weeks when compared with seven untreated hypertensive control patients. In contrast, patients treated for prolonged periods had a GH response indistinguishable from normal. In our studies¹ the GH response to insulin hypoglycaemia was similar before and after methyldopa treatment (250 mg three times daily for two to three weeks) when the hypertensive patients acted as their own controls. Neither did an intravenous infusion of methyldopa (250 mg) have any significant effects on serum GH levels in the same study.

The great individual differences in GH response to insulin hypoglycaemia are well known. Therefore the findings of Dr Steiner and his colleagues may also be partly due to the small number of patients and control subjects studied. In any case, when discussing the possible effects of methyldopa on GH secretion the role of central alpha-adrenergic receptors is worth considering. Methyldopa, like clonidine, probably stimulates these receptors,² and clonidine is known also to augment GH secretion,³ apparently through stimulation of central alpha-adrenoreceptors.¹ Thus the central stimulative effects of methyldopa may be relatively weak or perhaps the peripheral effects of the drug could inhibit the stimulative effects of the drug on GH secretion.

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¹ Syvälahti, E, Seppälä, P O, and Ilisalo, E, *Acta Pharmacologica et Toxicologica*, 1975, **37**, 257.

² Zwieten, P A van, *Journal of Pharmacy and Pharmacology*, 1973, **25**, 89.

³ Lal, S, et al, *Journal of Clinical Endocrinology*, 1975, **41**, 827.

⁴ Ganong, W F, et al, *Abstracts of the Sixth International Congress of Pharmacology, Helsinki, 1975*, p 93.

Suicide with tricyclic antidepressants

SIR,—Last year¹ I tried to draw attention to the increasing and disproportionate share of deaths from suicidal poisoning attributable to tricyclic antidepressants. The latest figures—for 1974—have just become available² and they make depressing reading.

Calculating on a rather conservative basis (details of which have been published elsewhere³) the number of tricyclic suicides has increased from 127 in 1973 to 167 in 1974.

Although the total of suicidal poisonings has also increased from 1737 to 1875, the proportion due to tricyclics has risen from 7.3% to 9.0%.

Tricyclic antidepressants are of undoubted benefit in some cases of depressive illness, but I find it difficult to believe that this is what the majority of those who receive these drugs are suffering from. Furthermore, in the past few years many journals—including the *BMJ*—have carried advertisements urging doctors to prescribe tricyclics to induce sleep. After all the campaigning to reduce the prescribing of barbiturate hypnotics it is disturbing to see a contrary campaign to replace them with drugs which seem to be just as dangerous—indeed, perhaps more dangerous, for, while not every consumer of barbiturate is unhappy, almost everyone who receives tricyclics is by definition unhappy and therefore a suicide risk. To judge by the latest suicide figures this new campaign is proving rather successful.

You already carry an advertisement for a non-barbiturate hypnotic which points out that many people commit suicide with barbiturates. If no antidepressant competitor will do the same for tricyclics, will you consider asking tricyclic advertisers themselves to point out that they are marketing a product which is much more lethal than most doctors seem to realise? An annual total of 167 deaths seems a rather high price to pay for a drug which has had remarkably little effect on the prevalence of the condition which it is alleged to cure.

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¹ Brewer, C, *British Medical Journal*, 1975, **4**, 409.

² Office of Population Censuses and Surveys Monitor, DH4 76 5.

³ Brewer, C, *World Medicine*, 1976, **11**, No. 12, p 37.

Benign proliferative lesions of the breast

SIR,—Mr D H Patey (5 June, p 1403), with his characteristic ability to reduce a problem to basic principles, helps clarify the perhaps confusing account of benign proliferative lesions of the breast in your leading article (8 May, p 1106).

While agreeing with his first two groups, we would dissent from the opinion that the symptom of pain in the breasts is a distinct "functional" entity which merits the term "the pain syndrome." Because we were impressed by the apparently stable temperament of many of the women complaining of breast pain and the degree of disability this caused we have studied over 200 consecutive women in whom this was the presenting symptom. Full clinical evaluation has been usefully complemented by the detail provided from xeromammography and by correlation with histological findings from biopsy in appropriate cases. We have come to recognise that six patterns account for over 90% of our 200 patients. Those with cancerphobia and those with simple premenstrual discomfort which could be regarded as "normal" were first eliminated; such patients would form a much larger group than the 200 patients we have investigated in detail.

Cyclical mastalgia, pronounced either in duration or intensity to a degree that separates it from "normal" premenstrual discomfort, is the commonest of these. As your article states, lumpiness, particularly premenstrually, commonly accompanies this. Almost as large a