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.

A D B HARROWER
P L YAP
N C ALLAN

Departments of Medicine and
Haematology,
Western General Hospital,
Edinburgh

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.

L DETTLI

Department of Internal Medicine,
University of Basle,
Kantonsspital,
Basle, Switzerland

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.

E K G SYVÄLAHTI

Department of Pharmacology,
University of Turku
Turku, Finland

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.

COLIN BREWER

University Department of Psychiatry,
Queen Elizabeth Hospital,
Birmingham

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

proportion have no pattern in time and are associated with stigmata of duct ectasia/periductal mastitis. The other patterns we recognise are Tietze¹ syndrome, trauma, sclerosing adenosis, and cancer (pain was the first symptom in 12 of 140 cancers, sometimes preceding other symptoms by many months). We shall shortly be reporting the diagnostic features of these various syndromes. Our clinical observations have been carried out in parallel with a questionnaire assessment of psychoneurotic traits² which shows overall that 80% of these patients have no gross psychological abnormalities.

We conclude that the presenting symptom of mastalgia is not purely functional and deserves the usual investigation and attempt at diagnosis that are appropriate to other breast complaints.

P E PREECE
R E MANSEL
L E HUGHES
I H GRAVELLE

Welsh National School of Medicine,
Cardiff

¹ Tietze, A, *Berliner klinische Wochenschrift*, 1921, **58**, 829.

² Crown, S, and Crisp, A H, *British Journal of Psychiatry*, 1966, **112**, 917.

Pseudomonas aeruginosa in hospital pharmacies

SIR,—The letter from Dr D C Shanson (17 April, p 958) reminded me of a similar incident in another London hospital that came to my notice some two years before the one which he describes.

It had been noticed over a period of some weeks that the tracheostomies of patients in the intensive care unit almost inevitably became colonised by *Pseudomonas aeruginosa* followed in some instances by an overt respiratory tract infection with this organism. A search of the unit resulted in the isolation of *Ps aeruginosa* from an unopened bottle of mouthwash and, following this lead, a large stock bottle of the mouthwash (closed by a bare cord) was discovered in the hospital pharmacy. *Ps aeruginosa* was also isolated from the contents of this stock bottle and from the cork. All of the environmental isolates and most of those from the patients were indistinguishable by phage or serological typing. The elimination of this source of infection was followed by a marked fall in the number of pseudomonas infections in the intensive care unit.

It is interesting to note that the warning given by Hughes¹ against the possible use of contaminated mouthwash had already been justified by this event.

J V DADSWELL

Public Health Laboratory,
Royal Berkshire Hospital,
Reading

¹ Hughes, M H, *Lancet*, 1972, **1**, 210.

Warning of severe asthma attacks

SIR,—I should like to comment on the paper on asthma deaths in Cardiff by Dr J B MacDonald and others (19 June, p 1493).

I am myself an asthmatic who has had to be admitted to hospital twice this year with severe attacks. As the authors indicate, the onset of bad attacks is often rapid and it is

difficult to predict when an attack will become severe on subjective symptoms alone. I have found from personal experience that the use of a peak flow meter is the best predictive instrument. A notable reduction in peak flow rate seems to occur before the symptoms become very severe and may give notice of an attack which is going to require medical help. I am now inclined to alert my doctor if my peak flow drops below 140 l/min. I would suggest that severe asthmatics be issued with peak flow meters and encouraged to keep a graphic record of their peak flow morning and evening and to inform their doctors immediately this drops below whatever their accustomed level is.

The use of a peak flow meter might also obviate calling the doctor when it is unnecessary. One can have quite severe asthmatic symptoms which prove to be transient, but on subjective evidence alone it is very difficult to tell which attacks are going to pass off and which are going to require medical help. Those who are reluctant to summon medical help in time, as obviously happened in some of the Cardiff cases, would find it useful to have an objective measurement which would indicate that they were not bothering the doctor unnecessarily.

ANTHONY STORR

Warneford Hospital,
Headington, Oxford

Pathological parasites in food handlers

SIR,—The otherwise valuable report by Dr A P Hall and others on intestinal parasites (19 June, p 1542) is marred by the incorrect conclusion that screening is desirable. The Public Health Laboratory Service, the majority of delegates to a WHO seminar on food hygiene, and most doctors working in the food industry in the UK all condemn such screening as being ineffective.

The widespread prevalence of parasites so ably demonstrated by the authors should be seen as justifying appropriate expenditure on adequate toilet facilities and confirms the importance of sound hygiene training and disciplines among food handlers. Such measures are effective and do not waste money which comes ultimately from the consumer.

JOSEPH L KEARNS
Head of Health and Safety,
J Lyons Group of Companies

London W14

Unexplained hepatitis following halothane

SIR,—Dr W K Slack (19 June, p 1532) raises an interesting point in the story of unexplained hepatitis following halothane. He suggests that it might be rewarding to consider whether hypoxia may have occurred during the course of the anaesthetic. The same idea has occurred to me and no doubt to many others. Some years ago I began to wonder whether the techniques of administration were receiving a fair share of attention.

The liver may be particularly vulnerable to hypoxia because of its dual blood supply from the hepatic artery and portal vein; the mixing of these two sources results in the liver being normally exposed to a lowered oxygen environment. In certain pathological conditions—for example, in congestive cardiac failure—an increased systemic venous pressure subjects

the liver to a state of stagnant hypoxia and a centrilobular pattern of hepatic pathology is set in train. An anoxaemic anoxic state will be expected to produce a similar pattern.

Halothane is a powerful cardiorespiratory depressant. With spontaneous ventilation a patient can all too easily reach a state of hypoxia and profound hypotension which can be accentuated by positioning on the table. Is it not reasonable to suggest that the combination of a lowered alveolar oxygen tension and reduced tissue oxygen availability could provide the appropriate conditions for liver failure according to the degree and duration of exposure?

Although I am no longer directly employed in anaesthetic practice, I am interested in following the search for a solution to this mysterious ailment. Whenever I gave a halothane anaesthetic I was always impressed with its ease of administration and often I wondered whether this was its gravest danger.

F C SHELLEY

Bovingdon, Herts

Diamorphine for postoperative pain

SIR,—When someone as eminent as Professor Ian Donald draws our attention to the inadequacy of post-operative analgesia (leading article, 19 June, p 1491) then those responsible for the welfare of patients should pull their fingers out smartly, and we should be grateful to him for trying to ease us out of our habitual attitudes and take stock.

After the 1945 war there were many thousands of patients with tuberculosis, many of whom came to surgery for the then fashionable three-stage thoracoplasty, performed under local analgesia, a formidable prospect for the most courageous. Choice of drugs was limited in those days, but it soon became apparent that diamorphine was the drug of choice, both before and after operation. It provided not only excellent analgesia but also that mental tranquillity which was such an essential feature for patients who knew they must endure three such episodes at short intervals. I always believed that much of their calm courage was due in no little measure to the use of this drug, and so satisfactory was it that it passed into use for all forms of thoracic surgery for the next quarter of a century, proving overall a better drug than some of the newer analgesics, which were neither as efficacious, nor as free of side effects.

I well remember many years ago Ronald Jarman proclaiming to a meeting of anaesthetists in Dublin that diamorphine was the "only analgesic" for him after his major operation. I never saw a case of addiction, as patients were kept unaware of the drug used, and I would end by making a plea that more, responsible, use be made of this excellent calming analgesic.

LAURENCE O MOUNTFORD

Emsworth, Hants

Hepatitis in patients with chronic renal failure

SIR,—With reference to the article by Dr R M Galbraith and others (19 June, p 1495) it is worth placing on record that there have been three patients in Newcastle who, although negative for hepatitis-B surface antigen, have