bral lactation. 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; 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 mean weight of 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 galactorrhoea and puerperal lactation. Although doses of as much as 60 mg/day have been used in acromegaly, 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 "hyper-coagulable" 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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2 Thorner, M. O., et al., British Medical Journal, 1974, 2, 419.

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, as well as animal experimental1 and human2 pharmacokinetic data, clearly shows that cefaz cetil (Celospor) penetrates into the cerebrospinal fluid in an amount sufficient to eradicate most of the drug in our patients causing bacterial meningitis. In controlled clinical evaluations on the efficacy of cefazetil therapy in bacterial meningitis Correa Lima1 and Lomar and al 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 cefazetil given intrathecally but always intravenously or intramuscularly.

L Dettili

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3 Zuck, O., personal communication.
4 Lima, M. B. C., et al., To be published.

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 stimulation in acromegaly patients treated with metyldopa 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 metyldopa (range 0.7 to 8.6 mg/kg) and in doses ranging from 10 mg to 60 mg/day. Neither an intravenous infusion of metyldopa (250 mg three times daily for two to three weeks) nor the hypertensive patients acted as their own controls. Neither did an intravenous infusion of metyldopa (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 metyldopa on GH secretion the role of central alpha-adrenergic receptors is worth considering. Metyldopa, like clonidine,2 probably stimulates these receptors, and clonidine is known to augment GH secretion,3 apparently through stimulation of central alpha-adrenoceptors.4 Thus the central stimulative effects of metyldopa 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., Seppäla, P. O., and Ililau, E., Acta Pharmacologica et Toxicologica, 1979, 47, 257.

Benign proliferative lesions of the breast

Sir,—Dr M D Patey (5 June, p 1403), with his characteristic ability to reduce a principle to basic principles, helps clarify the perhaps confusing account of benign proliferative lesions of the breast in your leading article (8 May, p 1108).

As we agreed 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 complaint. 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 carcinoma and those with simple premastitic discomfort which could be regarded as “normal” were first excluded. We have now also defined such a large group that separates it from “normal” premastitic discomfort, in the commonest of these. As your article states, lumpiness, particularly premenstrually, commonly accompanies this. Almost as large as...
Pseudomonas aeruginosa in hospital pharmacies

Sir,—The letter from Dr D C Shannon (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 *P. 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. *P. 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.

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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 training and disciplines among food handlers. Such measures are effective and do not waste money which comes ultimately from the consumer.

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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 halothane 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 centriflobular pattern of hepatic pathology is set in train. An anaoxamic anoxic state will be expected to produce a similar pattern.

Halothane is a powerful cardiosuppressant. 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. It is 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 wondered whether this was its gravest danger.

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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 anaesthesia, 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 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 20 years, and I would end by making a plea that more, responsible, use be made of this excellent calming analgesic.

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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...