recommend prophylactic treatment of the pituitary only where there is definite radiological evidence of a tumour. The early identification of those patients at risk of tumour expansion, and their treatment, clearly requires further study.

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¹ Child, D F, *et al*, *British Medical Journal*, 1975, **4**, 87.

² Kelly, W F, *et al*, *British Journal of Obstetrics and Gynaecology*, 1979, **86**, 698.

³ Doyle, F H, and McLachlin, M, *Clinics in Endocrinology and Metabolism*, 1977, **6**, 53.

⁴ Kelly, W F, *et al*, *Quarterly Journal of Medicine*, 1978, **47**, 473.

Preventing postoperative thromboembolism

SIR,—Before answering the specific questions directed to our report (2 June, p 1447) by Professor V V Kakkar and other correspondents (14 July, p 127), we wish to make it clear that the present study was mounted to fill what we considered to be a gap in currently available studies. To our knowledge, no previous low-dose heparin study of a comparable patient population has employed as comprehensive a surveillance protocol for either deep venous thrombosis (DVT) or pulmonary embolism (PE), and in particular most have relied almost entirely on ¹²⁵I-fibrinogen leg screening, the sensitivity of which has recently been called into question.¹ It is for these reasons that we believe a cautiously worded interim report justified.

It is misleading to suggest that sublethal thromboembolic events are unimportant and thus unworthy of study. A DVT involving the axial system with or without PE is certainly important if it leads to therapeutic anticoagulation, prolongation of hospital stay, and the long-term risk of post-phlebotic symptoms. End-points such as these occur with sufficient frequency to justify an objective single-centre study.

The question of beta-effect in relation to trial size has been raised by Dr C R M Prentice and others (p 128). A major part of our conclusions however is based on alpha, confirming a reduced incidence of DVT in heparin-treated patients and locating the source of this difference as a reduction in calf vein thrombosis. Apart from the relatively low observed frequency of proximal segment thrombosis a further point at which the comment regarding beta could be relevant would be if only patients scoring 6/6 for PE were to be considered in isolation ignoring all lesser scores. As scoring criteria were stringent we believe that scores of 4/6 or greater are highly likely to represent PE (6/68 control patients). If heparin were capable of reducing the PE rate by 50% the probability of encountering PE in 9/95 heparin patients would be low ($P=0.0052$). Even if heparin were capable of reducing PE by 25% the probability of the findings in the heparin patients would be 0.054. While nearly a quarter of patients in both groups developed new postoperative perfusion defects, the majority were allotted low scores because of the difficulty in assigning "without doubt" validity to perfusion defects in the presence

of obstructive airways disease. That it is likely that at least a proportion of these patients did indeed suffer a PE is attested to by the high degree of correlation between the presence of phlebographic DVT and postoperative perfusion defects. The absence of even a trend towards reduction at this event-rate frequency after the entry of 200 patients is of concern. We do, however, intend to continue this study until a sufficient number of patients has been entered to place the results beyond reasonable doubt.

In his letter Professor Kakkar points out that a number of patients in our study developed post-operative perfusion defects in the absence of phlebographically demonstrable DVT. This is in accordance with the findings of Knight and Metrewelli.² Emboli may originate from the pelvic veins or from discrete iliofemoral thrombi that have already embolised by the time the phlebogram is performed. This merely serves to highlight the importance of combining adequate PE and DVT surveillance in studies of prophylactic agents.

In the light of Professor Kakkar's criticism of our technique of diagnosing PE we find it surprising that he quotes the study of Buttermann *et al*³ as confirming that low-dose heparin reduces the incidence of non-fatal PE. We wish to correct his statement that this latter study utilised combined ventilation-perfusion scanning. Not only was perfusion lung scanning used alone, but this was only done postoperatively and was only performed in ¹²⁵I-fibrinogen-positive patients. In addition this study was not adequately randomised.

Few would deny that the major goal of prophylaxis lies in the prevention of fatal postoperative PE. The dilemma lies in the daunting logistics of proving this beyond doubt. Pulmonary embolus mortality probably varies worldwide and from centre to centre. Of the small proportion of patients who do succumb to this event, an appreciable number will be patients with a terminal illness. Thus fatal PE in patients who would otherwise recover is a rare event and it is precisely for this reason that many surgeons have questioned the benefit-to-risk ratio of applying a prophylactic regimen, with a small but unquestioned risk of bleeding complications to all their patients over the age of 40.

Like Dr Prentice and his colleagues we would welcome a definitive and independently confirmed multicentre study if this were possible. Until such time, we believe that objective studies of sublethal thromboembolic events have a part to play in furthering our understanding of the efficacy of prophylactic regimens.

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¹ Sautter, R D, *et al*, *Archives of Internal Medicine*, 1979, **139**, 148.

² Knight, M T N, and Metrewelli, C, *British Journal of Surgery*, 1977, **64**, 712.

³ Buttermann, G, *et al*, *Medizinische Klinik*, 1977, **72**, 1624.

Hyperprolactinaemia and cardiac disorders

SIR,—We were interested in the paper by Dr J Cohen and others (29 September, p 678) reporting two cases of life-threatening arrhythmias occurring during treatment with intravenous cimetidine. The authors have also seen two patients with prolactinomas and unexplained arrhythmia, and speculate on the possibility that hyperprolactinaemia might be involved in the pathogenesis of cimetidine-associated arrhythmias.

We have recently described a woman with long-standing prolactinoma who presented with unexplained cardiomegaly and heart failure, and eventually died suddenly.¹ A preliminary survey of 35 prolactinoma patients showed five with raised blood pressure and four (two of whom were normotensive) with cardiomegaly. We also speculated on the possible pathogenetic role of prolactin hypersecretion in cardiac disorders associated with pituitary tumours, but our data suggest that long-standing hyperprolactinaemia is required for any possible effect of the hormone on the heart to be manifested.¹

Sudden death has been reported in some patients chronically treated with phenothiazines,² drugs known to stimulate prolactin secretion. Several actions of prolactin on the heart have been described in animals. The hormone induces changes in rhythm and amplitude of cardiac contraction, and it has been suggested that stress-induced hyperprolactinaemia might contribute to cardiac arrhythmias during myocardial infarction³ or, alternatively, dampen the tachycardia-inducing effect of isoprenaline in experimentally-induced myocardial infarction in the rat.⁴ Although the possibility that drug-related hyperprolactinaemia of short duration may precipitate cardiac arrhythmias is far from established, further study is obviously needed on the cardiovascular effects of prolactin overproduction.

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² Leestma, J E, and Koenig, K L, *Archives of General Psychiatry*, 1968, **18**, 137.

³ Horrobin, D F, *et al*, in *Progress in Prolactin Physiology and Pathology*, ed C Robyn and M Harter, p 189. Amsterdam, Elsevier, 1978.

⁴ Lewis, B K, and Wexler, B C, *Proceedings of the Society for Experimental Biology and Medicine*, 1975, **150**, 712.

Vasodilators in senile dementia

SIR,—I would like to comment on your leading article (1 September, p 511) and certain letters in response to the editorial (6 October, p 866), in which a literature review of mine was quoted.¹

I am in complete agreement with your basic stance that "cerebral activators" are backed by more positive clinical studies than are "vasodilators." I would disagree, however, with your strong contrast between dihydroergotoxine mesylate (Hydergine) and naftidrofuryl (Praxilene, Nafronyl). The use of both of these compounds is supported by large numbers of positive double-blind clinical studies and neither seems to have serious side effects at recommended doses. It seems as though the side effects of ergotamine have been confused with those of dihydroergotoxine.

I do also share your concern for the "practical" impact of such compounds. Certainly they do not work miracles; nevertheless, they do seem to have some effect. In the attempt to increase the practical effects of such medications we have been concerned with finding the proper dosage for the individual, selecting drug-responsive patients, and combining these medications with psychotherapies aimed at improving cognitive function.² It is hoped that the application of some of the standard techniques of general

pharmacology and psychiatry to such relatively neglected geriatric compounds may yield better practical results.

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¹ Yesavage, J A, *et al*, *Archives of General Psychiatry*, 1979, **36**, 220.

² Yesavage, J A, *et al*, *Journal of the American Geriatric Society*, 1979, **27**, 80.

What are accident and emergency departments for?

SIR,—The accident departments that claim to have become an alternative to the surgery deserve our sympathy (6 October, p 837). I have worked for 20 years as a clinical assistant in a casualty department where the relationship between consultants and general practitioners is excellent and few patients abuse the system.

One problem is that in hospital technical expertise is not always combined with an awareness of social problems. How many accident consultants have visited their patients' homes or factories, know when the weekly bus from outlying villages runs, or know the facilities of the local surgeries?

I believe that such knowledge is essential for effective as well as humane care. Satisfactory home conditions as well as strict medical criteria are necessary before a child, for instance, is discharged home after a minor head injury. The intelligence of the mother, the proximity of a telephone, and the willingness of the general practitioner are just three factors to be considered.

Patients are sometimes brought back to the hospital when they might easily have been referred to their own doctor. A few years ago a mother and son died in a car crash near here when the latter was asked to return to a hospital 10 miles away to have sutures removed. His doctor, I know, would willingly have done this simple task for him.

General practitioners working in casualty departments can see that these social factors are not forgotten and help to narrow the gap between hospital and home care.

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Disasters, flying squads, and immediate care

SIR,—The Inter-service Co-operation and Disaster Planning Subcommittee of the British Association of Immediate Care Schemes (BASICS) is currently engaged in a study of major accident plans and is reassessing the planned disaster intervention.

The article by your special correspondent (20 October, p 973) mentions the need for standardisation. We plan to standardise and clarify the expected response to a disaster situation from the medical and paramedical (ambulance) services. For example, a recent edition of the journal *BASICS* carried a summary of the role of the site medical officer. Clear guidance is urgently needed now to clarify terminology and the designation of doctors to certain duties. Another urgent requirement is for standardisation of triage and casualty labelling. Every hospital and ambulance service seem to have their own ideas.

I should like to ask if readers responsible for area health authority and hospital major accident plans would be prepared to send me copies of their plans for the BASICS library, and also to enable us to extract the many good ideas and systems which have been developed locally and which deserve much better publicity. Any other comments pertaining to the medical response to a major accident would similarly be much appreciated.

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Appendicectomy during caesarean section in a developing community

SIR,—I cannot agree with the opinion of Mr W O Chukudebelu and Dr W B Onuigbo (18 August, p 423) that appendicectomy during caesarean section in a developing community is worthwhile, nor do I believe that they have shown it to be safe.

Appendicitis is known to be extremely uncommon in the rural African woman taking a traditional diet, which has a high fibre content. My own experience in Malawi confirms this in that I saw only one case of appendicitis in pregnancy from approximately 200 000 pregnancies from which such cases would have been referred over a period of years. To see an appendicectomy scar was also a rarity.

As regards the safety of appendicectomy, the series reported included no cases of paralytic ileus and apparently none of severe puerperal sepsis. But such cases are bound to happen from time to time, especially in developing communities, and if appendicectomy has been carried out it will be a source of danger when ileus does occur, and a source of diagnostic difficulty where there is sepsis and abscess formation. Mr Chukudebelu and Dr Onuigbo have shown the supposed safety of the procedure under teaching hospital conditions with the operation performed by a consultant obstetrician and gynaecologist. It has to be remembered that the great majority of caesarean sections in developing communities are carried out by district medical officers or mission doctors who are non-specialists and only part-time surgeons. Appendicectomy in these conditions must be less safe, and in any case such doctors have many more valuable things to be doing with their time.

To show convincingly that appendicectomy at caesarean section is worthwhile and safe it would be necessary to measure the morbidity and mortality from appendicitis in a population of adult women, and show to what extent that could be diminished by appendicectomy at caesarean section, account being taken of the morbidity and mortality associated with the procedure. This would need a series of many more than 100 cases.

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Appendicectomy and family history

SIR,—In their letter (20 October, p 1003), Mr Lionel Gracey and Dr Stuart Sanders relate their unusual experience of operating on a pair of twins for acute purulent appendicitis on the same day, and they draw attention to the interesting fact that whereas in one of the twins a

faecolith was present (acute obstructive appendicitis) this was not so in the other (acute non-obstructive appendicitis.)

I would like to suggest the strong possibility that the only reason why no faecolith was found in the one case was that it had slipped back into the caecum before the operation; a faecolith fugax. Many years ago I had the rare experience of feeling such a faecolith slip back into the caecum at operation, without any encouragement on my part, and before I had made any attempt to mobilise the caecum and appendix. But for this observation the appendix would have been regarded as another example of acute non-obstructive appendicitis, a pathological concept which I have since come to regard with suspicion.

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Fulminating meningococcal septicaemia

SIR,—This clinical condition described in your leading article (20 October, p 953), known as the Waterhouse-Friderichsen syndrome, has salient features of sudden onset, fever, collapse, haemorrhages in the skin, and bilateral adrenal haemorrhage. This last grave feature was overlooked in your article, and there was no mention also of any post-mortem findings in another contribution dealing with 10 deaths from this condition in young children (25 August, p 468) or of corticosteroids being used in their treatment, but the authors quite rightly emphasise the urgency of treatment and suggest that the medical attendant should bring the victim to hospital in his car without delay. The presence of petechiae and large ecchymoses in the skin is diagnostic in a very ill patient and the practitioner should not be misled by the absence of meningismus. The other condition that might simulate this is typhus fever.

When serving as a resident medical officer at a large infectious diseases hospital during the cerebrospinal epidemic in 1940, I saw nearly 300 cases, among them six of the fulminating variety. Although treated immediately on admission with sulphathiazole and deoxycortone acetate, they all died within a few hours of admission.

Even after nearly 40 years my clearest recollection is of the post-mortem findings—massive haemorrhages into the suprarenals, liver, and other organs being the most striking features. We undertook our own laboratory work and I succeeded in demonstrating diplococci, two or three pairs in every high-power field in a blood film from one of these fatal cases; the memory of the technique of this escapes me, but as evidence of the overwhelming septicaemia it would appear to be unique.

The only hope of a recovery lies in early diagnosis and immediate treatment with suitable antibiotics together with steroids and treatment of shock; one should not delay by undertaking a lumbar puncture or waiting an hour for the result of a limulus endotoxin assay mentioned in a letter from America (7 April, p 953). In the unlikely recurrence of a countrywide epidemic of cerebrospinal meningitis, one would expect to have an incidence of 1-2% of the fulminating variety and not many medical practitioners would come across one.