being reported. The physician should be aware that dystonic reactions can occur while swimming and could be potentially fatal.

MAURICE W DYSKEN
JOHN M DAVIS

Illinois State Psychiatric Institute,
Chicago, Illinois

Persistence of barbiturate prescribing

SIR,—Drs J B and Elspeth T Macdonald in their paper on barbiturates and fractures (20 August 1977, p 483) commented that although it had been reported that barbiturate prescribing was declining at 7.5% a year their results indicated that this might be a complacent view. My experience when taking over a practice in south-east London earlier this year seems to confirm this opinion.

It was found that 47 patients, the majority being in the 61-80-year age group, asked for repeat prescriptions for barbiturates and, having very strong views on the use of these drugs as hypnotics, I refused them as a matter of policy to everyone except epileptics and patients with terminal illnesses. Instead they were given either nitrazepam or flurazepam. Of the 47 patients, 28 readily accepted flurazepam, seven accepted it with difficulty, and four preferred nitrazepam, while two refused both drugs. Of the remaining six patients, four left the practice because they were refused a prescription for barbiturates and the other two left the district.

In view of the authors' findings that the incidence of mental status questionnaire scores of under 12 dropped from 39% to 1% on stopping barbiturates and that the clinically important degree of confusion found in the old people following the use of barbiturates is reversible when the drugs are withdrawn the substitution of barbiturates by non-barbiturate hypnotics is a worthwhile exercise.

I would also agree with these authors (1 October 1977, p 891) that the lives of a large number of elderly people throughout the country would be made less confused and miserable if their barbiturates were stopped.

J A SHEIKH

London SE6

Solving clinical questions by research

SIR,—Following the Horizon programme (BBC2, 8 September) your correspondent WFW (16 September, p 825) concludes that work on synthetic membranes is "just looking for the sake of looking with no practical benefit in sight." This conclusion undermines the fair-minded circumstances which stimulated it and is critical of teams tackling complex clinical questions, their funding, and the educational standards and pool of knowledge to which they contribute.

The programme appeared complicated but then so is the subject. How then are clinical questions solved in the supposedly utopian arena, outside the usual experience, but of which WFW writes, where funds seem plentiful and obsessions unrestrainedly pursued? A difficulty facing investigators and committees alike is to produce answers for man. Did WFW predict at the time of the solution of the molecular structure of DNA that it might be possible to produce a genetic

implant capable of producing insulin? It seemed clear from the programme that vision alone would not, for example, prove whether an artificial membrane approach could be used to render insulin injections unnecessary in diabetic patients, control coagulation defects, improve cancer chemotherapy, restore genetic mishaps, and so on. It is necessary to conceive and do the appropriate molecular experiments and clinical studies.

The critique appears also to be directed at the creation and funding of the right blend of clinical and biochemical talents to study such complex questions. Perhaps the programme did not emphasise enough this difficulty. An interdisciplinary team is probably the best instrument by which to hold a principal clinical question in constant perspective so that the eventual solution is clinically justified, ethically acceptable, and scientifically valid. By even appearing to argue against use of funds in this way WFW does a grave disservice to investigators and to the Medical Research Council, Department of Health, independent grant-awarding bodies, and pharmaceutical companies who supported studies mentioned in the programme. Further consequences of the implementation of such an uninformed constraint would be the strangulation of some of the best sources of future clinical, teaching, and research staff and the lowering of morale of present workers.

N G L HARDING

University Department of Pathological
Biochemistry,
Royal Infirmary,
Glasgow

Hypertension and oral contraceptives

SIR,—We have some comments about the letter from Dr F B Pipkin and others (22 July, p 278) on this subject. On the basis of their results with the infusion of the angiotensin II antagonist Saralasin they reach the conclusion that "the renin-angiotensin system is not immediately involved in the pathogenesis of this form [contraceptive] of hypertension." Their preliminary results add interesting information in connection with the pathophysiology of hypertension from oral contraceptives. However, we feel that there is an alternative explanation for their results.

A review of the literature and studies in our own laboratory lead us to conclude that there is more than one mechanism simultaneously at play in the production of contraceptive hypertension. Oestrogens increase the renin substrate and this in turn results in an associated increase in renin activity, angiotensin II, and aldosterone.¹ In addition, oestrogens have a mineralocorticoid effect directly on the renal tubules.² The direct mineralocorticoid action causes a decreased renal renin secretion. The net effect of these two countering actions is a normal or only slightly elevated plasma level of renin activity, angiotensin II, and aldosterone. In some patients the direct mineralocorticoid effect appears to be relatively greater than the effect of the oestrogens on the renin substrate and the renin activity levels tend to be in the low range.

In addition to those two effects of the oestrogens the synthetic progestational agents with an alpha side radical on carbon 17 of the steroid molecule have a direct mineralocorticoid effect.³ This action is in contrast to natural progesterone, which has an anti-mineralocorticoid effect.³ Synthetic gestogens

would thus tend to lower the actual values of renin activity and aldosterone even further.

A patient, then, who is taking an oral contraceptive agent would have a two-pronged attack on the renin-angiotensin-aldosterone system. One mechanism (oestrogen) increases the circulating angiotensin II and aldosterone; the other mechanism (oestrogen-synthetic gestogen) acts as a mineralocorticoid to suppress angiotensin and aldosterone. Which of these mechanisms is the cause of the hypertension? The answer is probably one or the other or both. It would depend on whether the patients were responding more to the stimulatory effect on the renin-angiotensin system with a high plasma renin activity or whether they were responding more to the mineralocorticoid activity of the contraceptives.

One would expect those who are hypertensive solely from the mineralocorticoid action of the oral contraceptive to respond to Saralasin with no change or a slight increase in blood pressure. On the other hand those who were hypertensive solely as a result of an inappropriately high level of angiotensin II would respond to Saralasin by a decrease in blood pressure. The patients who had hypertension from a combination of both mechanisms should not exhibit a drop in blood pressure from Saralasin.

MILTON G CRANE
JOHN J HARRIS
WILLIAM WINSOR III

Department of Medicine,
Loma Linda University,
Loma Linda, California

- ¹ Crane, M G, Harris, J J, and Winsor, W, *Annals of Internal Medicine*, 1971, **74**, 13.
- ² Thorn, G W, and Harrop, G A, *Science*, 1937, **86**, 40.
- ³ Crane, M G, and Harris, J J, in *Oral Contraceptives and High Blood Pressure*, ed M J Fregley and M S Fregley, p 100. Gainesville, Florida, Dolphin Press, 1974.

Patient package inserts

SIR,—Dr J Deane Collinge's comments on patient package inserts (30 September, p 958) prompt me as a pharmacist to put forward my own comments as follows:

With an increasing trend towards "original pack" dispensing of medicines, whether from hospital, general practice, health centre pharmacies, or dispensing practices, many medicinal products now reach the patient as supplied by the manufacturer. Often included in the pack, whether it be a dermatological preparation, inhaler, suppositories, course of tablets, etc, is literature, some of which is intended solely for the patient's benefit in addition to the labelling added by the pharmacist, so enabling optimum results to be obtained from the medication and which should therefore be left in the pack when issued to the patient at the time of dispensing. Many manufacturers, however, still include in their products literature intended only for the use of the medical and allied professions regarding indications, contraindications, dosage, etc, of the product. This literature should not, of course, reach the patient for various reasons, one example being quoted by Dr Collinge.

I feel that it is one of the duties of the pharmacist to ensure that the patient receives only that information which is necessary for the correct use of the medication prescribed together with any relevant precautions—for example, antihistamines and driving—and