danger of development of carcinoma of the breast. Clinical examination reveals merely the usual wide variations in consistency and nodularity of normal breasts, and the condition has no organic significance.

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Self-assessment tests

SIR,—Your leading article on "Antibiotics again" (8 May, p 1107) drew attention to the use in America of self assessment programmes in continuing education based on simulated patient problems. It concluded by commenting that "a British programme of this type might be difficult to finance." In the same issue another leading article, "Politics and pharmaceuticals" (p 1105) reported criticisms of expenditure in the pharmaceutical industry.

Over the past year a similar self-assessment exercise has been carried out in the United Kingdom¹ and this has been supported financially by a British drug company. A programme in six parts was mailed over a period of six months to 29 000 doctors. This presented the history of a patient with both physical and psychological disease. Readers were invited to make decisions about the management of the patient, including history-taking, examination, further investigations, treatment, and follow-up or referral for a specialist opinion.

The programme was so designed that the reader was able to compare his own decisions with those of his colleagues and of a panel which included general practitioners, general physicians, and specialists. It is estimated that 15 000 doctors took part in the programme, although some did not complete all stages of the series. As in the American study some surprising results emerged. For example, only half of the respondents wished to take a drug history in the patient with erythema nodosum and 20% did not arrange to see her for two weeks when she became depressed and potentially suicidal. A full report of the experience gained in the exercise will be published and a further programme is at present under way.

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¹ *Medical Education*, 1976, 10, 138.

Fitness to drive

SIR,—There is a disquieting example of double standards in the assessment of applications for disabled persons' car badges as opposed to the assessment of medical fitness to drive. For the former a person declares his disability, be it an amputated limb, defect of spine or central nervous system, motor defect, or permanent and substantial disability causing difficulty in walking, and the disability is certified by his or her general practitioner or an authorised member of the social services department, without any reference to the person's fitness to drive.

It is evident from those applications referred to me for a further medical opinion by the social services department that many "relevant" or "prospective" disabilities are unlikely to have been notified to the licensing centre by

the applicant as the law requires. Furthermore, with the possible exception of the Greater London Council, authorities which issue badges are not prepared to pass on any information to the licensing centre. Much of the detailed and valuable advice which has gone into the booklet *Medical Aspects of Fitness to Drive*,¹ and the legislation to which it refers, is therefore inapplicable.

Until the situation has been clarified between the DHSS and the Department of the Environment the least that local authorities could do would be to require applicants to state whether or not they have declared their disability to the licensing authority. GPs and local authorities could also inform applicants of their obligations by means of a suitable leaflet.²

M J BALL

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¹ Medical Commission on Accident Prevention, *Medical Aspects of Fitness to Drive*, ed P A B Raffle, 3rd edn. London, MCAP, 1976.

² Central Office of Information, *Driver Licensing System, Changes in Medical Assessment of Drivers*. London, HMSO, 1975.

Depot neuroleptics

SIR,—Dr J P R Young and his colleagues (8 May, p 1116) conclude that flupenthixol is a useful treatment for depressed outpatients and they raise the question of using depot flupenthixol in the management of depression.

Depot neuroleptics are marketed primarily for the management of chronic schizophrenia, but there have been reports on the use of these drugs for other conditions.^{1,2} Clinical experience at this hospital would indicate that depot neuroleptics can usefully be given to a variety of non-psychotic patients. By and large the patients so treated have been suffering from either severe behavioural disorders, aggressive psychopathy, or alcoholism.

A heterogeneous group of eight resistant neurotic patients have been given fluspirilene in a dose ranging from 2 to 4 mg each week. This type of intramuscular therapy has been successful in resolving symptoms where previous oral therapy with antidepressant drugs and benzodiazepines had not been successful. The responsive patients presented with paranoid, depressive, or phobic symptoms associated with behavioural irritability. Patients whose symptoms were entirely subjective did not respond to fluspirilene.

It does appear that the long-acting tranquillisers can be usefully prescribed in a variety of psychiatric conditions. We feel that this finding should be further explored because the intramuscular route of administration of tranquillisers has certain advantages over the oral route.

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¹ Bennie, E H, and Kinnell, H G, *Lancet*, 1975, 2, 1303.
² O'Flanagan, P M, *British Medical Journal*, 1974, 3, 258.

Daily antihypertensive therapy

SIR,—Drs A P Douglas-Jones and J M Cruickshank (24 April, p 990) suggest that mild hypertension could be adequately controlled by a single daily dose of the beta-adrenergic blocking drug atenolol.

We have recently completed a study of the pharmacokinetics of another beta-blocker, metoprolol, in a small group of young healthy volunteers. The beta-blocking effect of the drug was assessed by measuring the reduction in tachycardia induced by standardised exercise on a bicycle ergometer. After a single 200-mg dose of metoprolol there was a significant effect in 30 min ($P < 0.05$) which persisted throughout the day and was still significant at 12 hours ($P < 0.01$). Furthermore, the pre- and post-exercise pulse rates had not returned to those obtained 24 hours after placebo administration. These results suggest that when 200 mg or more of metoprolol is prescribed a single daily dose, particularly if taken first thing in the morning, would be rapidly effective and would maintain significant beta-blockade while the patient is awake and active and should provide adequate control of milk to moderate hypertension.

This suggestion will have to be evaluated by further clinical trials when the control of blood pressure over 24 hours and the incidence of adverse effects on once-and twice-daily regimens can be compared. Once-daily treatment with metoprolol and perhaps other beta-blockers is likely to improve patient compliance and make long-term therapy for hypertension and angina more acceptable.

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Multiple sclerosis and poliomyelitis

SIR,—Your leading article (1 May, p 1030) does not mention the name of the person who first drew attention to the analogy between the epidemiology of acute anterior poliomyelitis and multiple sclerosis. This was Dr David Poskanzer,¹ who, with his colleagues Drs Schapira and Miller, published his ingenious hypothesis in 1963. It is important that this point should be made, as confirmatory evidence of an epidemiological pattern along the lines they suggested is now beginning to appear.

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¹ Poskanzer, D C, Schapira, K, and Miller, H, *Lancet*, 1963, 2, 917.

Unexplained bitemporal swelling

SIR,—A minor but puzzling syndrome was recently encountered on our teaching medical service and we wonder if your readers have previously observed it or can give us any suggestions.

The patient was a 27-year-old white woman who presented with bilateral temporal swelling accompanied by blurred vision, sweats, nasal congestion, and an oral temperature of 38.6°C. There was no history of trauma, diplopia, tenderness, rashes, or joint complaints. She had a long medical and psychiatric history, including a seizure disorder for which she was maintained on diphenylhydantoin. The other medications included desipramine, chlorpromazine, loxapine succinate, and benzhexol hydrochloride.

She was a healthy, alert young woman, somewhat apprehensive but in no distress. Symmetrical areas of soft-tissue swelling about 4 cm in diameter were noted in the temporal regions protruding

about 1 cm without discoloration or tenderness. The remainder of the physical examination, including visual field and ophthalmoscopic examination, was normal.

Laboratory investigations, including complete blood count, differential white cell count, serum electrolytes, chest x-ray, urine analysis, blood urea nitrogen, creatinine, and glucose, examination for antinuclear antibody and rheumatoid factor, and serum protein electrophoresis, were normal and serological test for syphilis was negative. The erythrocyte sedimentation rate (Westergren) was 4 mm in 1 h on three determinations.

After the third day in hospital the swelling decreased by about half and, since the patient remained free from other symptoms, she was discharged home. Diagnoses entertained included cranial arteritis, trauma, autoerythrocyte sensitivity, and allergic reaction, but none was established.

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International units and standards for proteins

SIR,—Those working in clinical immunology and protein immunochemistry will welcome the letter from Drs J H Humphrey and I Batty (10 April, p 898), of the International Union of Immunological Societies, listing some of the existing standards in this field and indicating others to be developed.

While agreeing with the need for sound, common standard preparations, we feel that the assigning of international units to such preparations is another matter. Total proteins and a number of individual serum proteins have been measured in weight per volume units for decades, and we would urge that for such measurements international units have little place in routine clinical practice, where clinicians have come to learn and accept results expressed in more conventional terms. Also, the International Federation of Clinical Chemistry Standards Committee has an expert panel on proteins which is aiming to have standards calibrated where possible in g/l by the best criteria currently available. The profession has already experienced an upheaval with the introduction of SI units, and there seems little practical advantage in causing another tremor by changing the mode of reporting of many human serum proteins.

We agree that when a pure preparation of a substance is not available and it is not possible to assign a weight value to a standard, there is obviously a good case for reporting in international units. We hope, however, that editors of journals will not adopt the suggestion in the last sentence of the letter from Drs Humphrey and Batty; in our opinion that would be a retrograde step and would discourage the search for a more rational mode of reporting based on weight or (when appropriate) molar equivalents.

The practical value of assigning immunoglobulin weight equivalents to international units has already been recognised, as indicated by Drs Humphrey and Batty, and we hope that their committee is gathering the necessary information from reputable international centres to enable it to issue weight equivalents for other serum proteins in its standard preparations. In the meantime the supra-

regional protein centres will continue to express results in terms of weight per unit volume for the convenience of their users.

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A MILFORD WARD
Directors of Supraregional Specific
Protein Reference Units

Flupenthixol for depression

SIR,—Dr J P R Young and his colleagues (8 May, p 1116) are to be congratulated on their study showing the equivalence of flupenthixol and amitriptyline in the treatment of depressed outpatients. As they admit, however, "the improvement . . . may have been due partly to anxiolytic drug effects," and here lies the crunch. The scales used are designed to measure the severity of dissatisfaction with life rather than to separate those with specifically biological symptoms of depressive illness. Furthermore, the marked response of their patients within the first week, before the antidepressive effects of amitriptylene take effect, also supports the conclusion that their sample contained many patients with mixed neurotic illness, who are not only prone to respond to placebo but also to any drug with sedative properties.

To help the practising doctor choose the most effective drug for the individual patient could the authors tell us the degree to which their patients had biological symptoms (such as loss of appetite and libido, retardation, etc) and the relationship of these to drug response?

It would indeed be convenient if we could find a drug that worked in all psychiatric conditions, the only decision being that of choosing the dose, a development that would quickly lead to unemployment among psychiatrists. Unfortunately for the public, I doubt whether the evidence supports this conclusion.

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** We sent a copy of this letter to Dr Young, whose reply is printed below—ED, *BMJ*

SIR,—In reply to Dr Kellett's letter on the recent trial of flupenthixol and amitriptyline, all the subjects included in the trial were referred to hospital with predominant symptoms of depression; all were felt to be clinically depressed on initial psychiatric assessment. For each patient four standardised questionnaires¹⁻⁴ were completed serially to quantify the severity of depressive symptoms. Each questionnaire was designed to measure depression. In addition, with each patient a formal assessment of the common biological accompaniments of depression was made at each visit using a standardised inventory.⁵ Each patient included in the trial was rated for alteration in sleep pattern, appetite and

weight change, libido, and diurnal variation in mood and energy. Every patient in the series was recorded as showing some "biological symptoms" of depression. Variation in these several functions was found, as expected, to follow closely changes in rating scale scores for depression during the course of treatment. Raw data for all the above "biological symptoms" are available on request. The alteration in sleep pattern for the series as a whole was represented in the paper in graph form. Changes in appetite and weight recorded in the trial are to be published later with other data relating to carbohydrate craving previously reported with amitriptyline.

It is to misread the paper, therefore, to suggest that the trial subjects were simply "dissatisfied with life" or that the sample contained "many patients with mixed neurotic illness." How many depressed patients are not dissatisfied with life, anxious, or otherwise neurotic? As stated in the paper, "though not severely depressed, the patients studied seemed typical of those referred to hospital for antidepressant outpatient treatment, their mean Hamilton depression score being 24."

The apparent antidepressant properties of flupenthixol, of course, require further confirmation. A longer follow-up assessment is required and, as suggested in the paper, it would probably be worth while to evaluate the drug against more severe forms of depression. It would also be interesting to attempt to differentiate more clearly between the anxiolytic and antidepressant effects of the drug.

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Danger of instant adhesives

SIR,—Instant adhesives containing alpha-cyanocrylate and similar substances are both extremely rapid and efficient in action. Efficiency and rapidity combine to present dangers to patients and never more so than now and in the future owing to widespread television presentation and national sales.

The public should be warned of the dangers and the medical profession should learn of the difficulties ahead. The adhesives are quite capable of bonding surfaces, and these include human body surfaces, together in a matter of seconds, and once the surfaces are bonded the inanimate can be separated only by considerable force and the human by surgical intervention.

The containers of such adhesives that I have purchased have had explanatory leaflets enclosed with them in their cartons, but unfortunately sometimes the printing on these leaflets is so small that I am quite sure the public would not read it. On one leaflet there were five lines of print to the centimetre. I felt that the warnings were not written in strong enough terms, and, though the danger to eyes was mentioned, the fact that eyelids could be bonded together in seconds was missing. Furthermore, it was stated that immediate bathing of human surfaces with warm water or acetone would remove the