postpone the emergence of drug resistance. The cosmetic unacceptability of B663 and the emergence of resistance to rifampicin complicate the matter.

A daily dosage of 100 mg of dapsone from the onset of treatment, combined with good health education and alternative methods of supervised administration, especially for lepromatous patients, as suggested by Allard,¹ Pearson *et al.*,² and Warren,³ may be our best defences against the emergence of dapsone resistance for some time to come.

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¹ Elland, G. A. *Leprosy Review*, 1975, **46**, 149.

² Pearson, J. M. H., *et al.*, *Leprosy Review*, 1977, **48**, 83.

³ Warren, G., *Leprosy Review*, 1977, **48**, 113.

Indomethacin, prostaglandins, and schizophrenia

SIR,—Dr M W P Carney (15 October, p 994) reported an apparently drug-induced paranoid psychosis with hallucinations in a woman receiving indomethacin. Turner¹ reported a similar episode, this time acute, in a normal volunteer receiving both indomethacin and aspirin in a drug metabolism study.

I have suggested that schizophrenia may be a prostaglandin (PG) deficiency disease.² Natural schizophrenia seems to be related to a specific deficiency in PGE₁ since prolactin, whose secretion is stimulated by antischizophrenic drugs, specifically stimulates PGE₁ synthesis,³ and since platelets from schizophrenics off drug treatment fail to increase their PGE₁ synthesis normally in response to adenosine diphosphate.⁴ Since indomethacin inhibits synthesis of all the prostaglandins and related substances it is not to be expected that it will be able to cause a syndrome which imitates exactly the natural disease. However, the schizophrenia-like features reported by Dr Carney and by Turner support the concept that a prostaglandin deficiency may be playing a causal role in the natural syndrome.

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¹ Turner, P., *Lancet*, 1977, **1**, 1058.

² Horrobin, D. F., *Lancet*, 1977, **1**, 936.

³ Horrobin, D. F., *et al.*, *Psychological Medicine*. In press.

⁴ Abdullah, Y. H., and Hamadah, K., *British Journal of Psychiatry*, 1975, **127**, 591.

Alpha-fetoprotein in antenatal diagnosis of neural tube defects

SIR,—It was with interest and awe that I read the case reports in the article by Drs D J H Brock and Christine Gosden on "Early antenatal diagnosis of small open spina bifida lesions" (8 October, p 934). The advent of α -fetoprotein as the diagnostic tool to detect spina bifida early in pregnancy has certainly raised a number of false hopes, especially with those who are directly concerned with the management of these babies. The decrease in the numbers of babies born with spina bifida is still not evident in those centres that have to manage these deformities. A number of open spina bifida lesions are missed because screening is not advised to the pregnant patient or because they fail to go to antenatal clinics. However, the majority of closed

myelomeningoceles go undetected and α -fetoprotein is of no practical help.

What should be questioned at this stage in view of the second case in this article is the real danger of the false-positive elevated α -fetoprotein concentration which was the reason for the abortion of a perfectly normal fetus. Can any of the centres in Britain provide the information that many would like to have: how many false-positive levels are recorded and has the reason for these false-positives been investigated? Clearly the whole value of the screening is at stake on this issue. This argument extends also to the elevated levels found in cases with exomphalos and gastroschisis, which are treatable conditions, and it would be disastrous if one had to practise eugenics on a raised α -fetoprotein level.

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Asymptomatic gonorrhoea in men

SIR,—In their interesting report (29 October, p 1155) on the detection of antibodies in gonorrhoea Professor A A Glynn and Miss Catherine Ison state that as many as 68% of infected men may be asymptomatic. They cite a point prevalence study¹ of urethral gonorrhoea in US Army enlisted men, many of whom could have been in the incubation and presymptomatic phase of the disease while others may have had ignored or suppressed symptoms. Most men with urethral gonorrhoea develop symptoms within two weeks of contracting infection, and a US cohort study² showed that only 3% of men who became newly infected in South-east Asia did not develop symptoms within two weeks. The combination of effective and rapid contact-tracing and accurate diagnostic techniques in the UK is resulting in more infected males being seen with no symptoms, particularly in genitourinary and venereology clinics. In view of this and to facilitate monitoring of the extent of asymptomatic gonorrhoea in infected males it might be wise to confine the term "asymptomatic urethral gonorrhoea" in men to those cases which are seen two weeks or more after first contact with infection. Confusion with presymptomatic cases still incubating disease would then be excluded.

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¹ Handsfield, H. H., *et al.*, *New England Journal of Medicine*, 1974, **290**, 117.

² Harrison, W. O., *et al.*, Paper presented at the 13th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, DC, 1974.

SI units

SIR,—I am glad Dr J S Law and Dr J M Stansfeld have raised this matter again (5 November, p 1224). We are fed up with SI units too.

It would seem to me that there are three problems. Firstly, it is difficult to acclimatise to the *significance* of these new units. This is true in general but is particularly a problem with measurements that one only uses

occasionally. Secondly, certain of the changes have resulted in contraction of the range: calcium and blood gas measurements are a good example. As a result, changes which were only small in the old units, but which were clinically significant, are now almost imperceptible and, particularly in the case of blood gases, the management of patients is much more complicated. Thirdly, we have the additional problem that the Americans are apparently not changing to SI units and therefore in reading the literature one is going to require double knowledge for a long time to come. This will be relatively easy for some of us who have grown up with the old units, but for the new generation it will be very hard indeed.

I am glad to say that we have persuaded our own biochemistry department to give way on their principles of purity and present us with figures which are clinically meaningful, which is after all their prime function. We are now receiving our blood gases both in SI units and in mm Hg.

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Cancer of the lung and bladder

SIR,—Dr S Dische and others (13 November 1976, p 1174) and Dr T A W Edwards (5 March, p 637) have reported cases of the development of primary carcinoma of the bladder subsequent to carcinoma of the lung and vice versa in patients with a long history of cigarette smoking.

To assess whether routine urological follow-up is indicated in patients treated for squamous-cell carcinoma of the lung, we studied a series of 99 consecutive patients treated over the two-year period 1960-1 for squamous-cell carcinoma of the lung. Information was obtained about necropsy findings in 92 out of 94 patients. None of these had bladder cancer. The remaining five patients, who were alive, had no symptoms of bladder tumour according to their family doctor. The interval from the detection of the squamous-cell carcinoma of the lung to death or follow-up was less than two years in 78 cases, 2-5 years in six, 6-10 years in seven, and more than 11 years in eight.

Hence in this 2-year series of consecutive patients with squamous-cell carcinoma of the lung an incidence of bladder malignancy of zero was found (95% confidence limits, 0-4). In our opinion, this does not justify routine urological follow-up of patients treated for squamous-cell carcinoma of the lung.

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Long-term Althesin infusion and hyperlipidaemia

SIR,—The intravenous anaesthetic Althesin may be used for the long-term sedation of patients in intensive care units.¹ Its active components, alphaxalone and alphadolone, are presented for injection as an aqueous solution containing 20% of the surface-active agent Cremophor EL (polyethoxylated castor

oil). This agent has been implicated in the production of an unusual hyperlipidaemia in patients receiving an intravenous preparation of the antifungal drug miconazole which also contains Cremophor EL.²

We have observed a similar pattern on lipoprotein electrophoresis of the plasma of a 33-year-old man with post-traumatic pulmonary insufficiency who had been sedated for seven days with a continuous infusion of Althesin at the rate of 72 ml/day. The pattern is that of disappearance of the α -lipoprotein band and the appearance of a densely staining abnormal band running in the β -lipoprotein region. The total plasma cholesterol concentration was 4.3 mmol/l (166 mg/100 ml) (normal range 3.6-6.2 mmol/l (140-240 mg/100 ml)) and the triglyceride concentration was 2.6 mmol/l (230 mg/100 ml) (normal range 0.6-1.7 mmol/l (53-150 mg/100 ml)). Bagnarello *et al*² pointed out that this unusual lipoprotein pattern is similar to that seen in dogs during continuous infusion of the surface-active agent Triton, which, over a period of a few months, produces severe arteriosclerosis.

We suggest that patients receiving long-term infusions of Althesin or other preparations containing Cremophor EL should have their plasma lipids monitored and that development of the electrophoretic pattern described could be a justification for discontinuing such infusions unless the benefit of the therapy is thought to outweigh the potential risk. We would also suggest that the transitory rise in plasma free fatty acids associated with the induction of anaesthesia with Althesin³ may be due to its Cremophor EL component.

We thank Mr P M Scott, FRCS, for permission to report this case.

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¹ Ramsay, M A E, *et al*, *British Medical Journal*, 1974, **2**, 656.

² Bagnarello, A D, *et al*, *New England Journal of Medicine*, 1977, **296**, 497.

³ Mehta, S, and Burton, P, *British Journal of Anaesthesia*, 1975, **47**, 863.

Management of children with nephrotic syndrome

SIR,—Your leading article (29 October, p 1103) concerning the treatment of nephrotic syndrome in children requires comment.

A low-sodium diet is traditional and easily prescribed but is unpalatable, tedious for the mother to cook, and unnecessary. A high-protein diet is expensive and illogical: the stimulus to albumin synthesis is hypoalbuminaemia itself and not ingestion of excess protein.

Setting aside these points, the precise indications for steroid therapy are not discussed. The natural history of minimal-change glomerulonephritis is one of relapse and remission. Why should not loop diuretics be used to control oedema until remission occurs? Frusemide and bumetanide are very well tolerated and much less toxic than steroids. Because a condition responds to steroids this does not necessarily imply that steroids are indicated. Is proteinuria per se injurious, provided that oedema is controlled by diuretics? Only a very few nephrotic patients

develop hypoalbuminaemic hypovolaemia of clinical importance.

The place of diet, of diuretics, and of corticosteroid therapy in the minimal-change glomerulonephritic nephrotic syndrome are yet to be evaluated by adequate clinical trials.

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Obstetric audit in general practice

SIR,—I was interested to read Dr G N Marsh's audit of a general practitioner maternity unit (15 October, p 1004). The previously unpublished retrospective figures for our GP maternity unit from 1965 to 1976 cover 3410 births, of which 96.2% were normal deliveries, 2.8% deliveries with forceps, 0.6% breech, and 0.1% twins. Post-partum haemorrhage occurred in a further 2.4% and the flying squad was called out for 1.7% of deliveries. The perinatal mortality was 3.8 per 1000 births, although this is falsely low owing to patient selection, etc, and the maternal mortality was nil. These figures merely show that a GP maternity unit is a safe place to have an anticipated normal delivery.

Between 1965 and 1973 54% of patients were breast-feeding on discharge. It was then decided to improve the combined approach of the primary care team and this involved a setting up of a GP unit booking clinic at which patients were separately interviewed by a midwife and a health visitor, and a clerk and practice nurse were involved in routine blood tests, etc. Also the previously separated hospital and district midwives joined together to become truly community midwives. Our patients are therefore cared for in hospital by their midwife who will follow them up at home, they are informally visited by their health visitors who will follow up later, and supervision is by their GP.

Coincident with this change in approach, the incidence of breast-feeding on discharge has risen to 63%. As the advantages of breast-feeding are now so well documented I wonder how many specialist units can claim such a degree of preventive health care for their normally delivered babies on discharge.

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Advisory Committee on Borderline Substances

SIR,—It is now several years since the Advisory Committee on Borderline Substances (ACBS) in their wisdom classified the powder formulation (but not the tablets) of Optimax (L-tryptophan compound), a drug used currently in the treatment of depression, as a food, creating a situation on which bureaucracy thrives, confusion abounds, and common sense goes by the board.

To the manufacturer who has the same product classified as a drug and as a food it is, to say the least, irritating. One attracts VAT and the other does not. Both are prescribable in hospitals; only the tablet is prescribable outside in family practice. To the committee it must sometimes seem to be a most regrettable classification, involving them in numerous tribunals and a great deal of paper work, not to

mention abuse from general practitioners up and down the country surcharged for prescribing "non-prescribable" medicines. In the case of Optimax powder, after three tribunals and one high court action that involved a great deal of expense and much wasted time, the situation remains unresolved.

Professor Barbara E Clayton in her lucid, informative letter (24 September, p 834) indicates that "the committee is always ready to reconsider any of its decisions in the light of new evidence." What is not spelt out, however, is what constitutes "new evidence." In the early days the clinical efficacy of Optimax was questioned by the committee; accordingly new evidence was generated attesting to the amino-acid's role as a safe, effective antidepressant,¹ etc. Regrettably the ACBS would neither change their mind nor advise on the sort of data they were seeking in respect of our petition to change the status of Optimax powder from food to drug—a classic "Catch 22" situation.

Although the ACBS's recommendations are "never... more than advisory," the implementation of their simple "guidelines" leaves a trail of confusion and frustration for administrators, clinicians, pharmacists, and, not least of all, the patient. However the ACBS sees itself, it is certainly not fulfilling the role of guide and mentor either to the clinician or to the pharmaceutical industry.

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¹ Jensen, K, *et al*, *Lancet*, 1975, **2**, 920.

² Rao, B, and Broadhurst, A D, *Lancet*, 1977, **1**, 460.

³ Herrington, R N, *et al*, *Psychological Medicine*, 1976, **6**, 673.

Matching resources to needs

SIR,—Our resources are finite and our desires to improve health care are not. After an evening spent considering the RAWP Report¹ and "The Way Forward"² I was irresistibly reminded of Macaulay's dictum that nothing is so useless as a general maxim. I must applaud the initiative of the Department of Health and Social Security in attempting to rationalise the planning of the Health Service for the future, but the more I read those documents the more uneasy I became. I appreciate the difficulties of equating the health needs of, say, Yorkshire with those of East Anglia, though it is much easier to contrast Trent with the North-west Thames Region. However, the more closely I study the RAWP formula the more I am impressed by how much we are to depend in the underprivileged areas upon a formula of pseudo-science for our future financial allocations.

"The Way Forward" encourages us to spend more upon community services, and they may be right, though we have no evidence that community health care is either better for the patient or cheaper. It may be both, but we just do not know. I suspect that the DHSS are recommending it because they think it is cheaper. Very large assumptions are being made by such a policy, and to attempt it in the absence of firm information as to its efficacy seems very unwise. Could we not have a trial of it in one region first and see if it is right before plunging the whole Health Service into a course of action which is based upon scant knowledge? We already have the uncomfortable consequences of Sir Keith Joseph's reorganisation to live with—a good