dose, adjuvant has been reintroduced, and the recommended schedule for the vaccination of children has been changed.

In Israel a similar improvement in the efficacy of pertussis vaccine has been noted,[7] but with fewer accompanying changes. In that country the improvement dates from 1968, when the inclusion of agglutinogen 3 in their vaccine was ensured. The earlier vaccine, which gave unsatisfactory protection, did, however, contain adjuvant and it also achieved a mouse-protective potency of four international units per human dose.[8] Moreover, the vaccination schedule in Israel has not been altered.

The one feature common to the improvements in British and Israeli vaccines is that their manufacturers now make deliberate attempts to ensure that their products contain enough agglutinogen 3. But ought our hopes for the wellbeing of vaccinated children to be based merely on the good-will of present well-informed staff, adequate though this proves to be at present? Or should we formulate requirements which would ensure that present knowledge is not forgotten?

To conclude: though there is evidence that for some years before 1967 the pertussis vaccine of Glaxo Laboratories was less effective than that of Wellcome Laboratories, there is ample reason to believe that this does not apply to vaccine made during the last six years. There is also further evidence that effective pertussis vaccines are those that contain sufficient agglutinogen 3.—I am, etc.,

NOEL W. PRESTON

Department of Bacteriology and Virology, University of Manchester

1 Preston, N. W., *British Medical Journal*, 1963, 2, 724.
2 Preston, N. W., *British Medical Journal*, 1965, 2, 11
3 Preston, N. W., *British Medical Journal*, 1965, 2, 1001.
4 Abbott, J. D., Preston, N. W., and Mackay, R. I., *British Medical Journal*, 1971, 1, 86.
5 Preston, N. W., and Stanbridge, T. N., *British Medical Journal*, 1972, 3, 448.
6 Perkins, F. T., *British Medical Journal*, 1969, 4, 429.
7 Shmilovitz, M., Preston, N. W., Zaltser, H., and Cahana, A., *Israel Journal of Medical Sciences*, 1972, 8 1936.
8 Singer, E. D., 1973. Personal communication.

Discrimination against Rhodesian Nurses

SIR,—In Personal View (28 April, p. 238) Professor Levy says that regulations governing the entry of Rhodesian students into the U.K. have recently come into effect and are manifestly discriminatory against the young Rhodesian girl who seeks to train as a nurse in the U.K. It would even appear that the discrimination is maximal against the less well-educated girl who wishes to train for the S.E.N. diploma rather than for the S.R.N. The raised educational standards demanded by the new regulations apply exclusively to applicants from Rhodesia.

Personally I have no sympathy with the present rebel Rhodesian regime and I would approve any whole-hearted action our Government might take against it. When, however, the action involves petty discrimination against trainee nurses, then surely it is time our nursing institutions and the B.M.A. united to protest that the professions of nursing and medicine have a long tradition of international co-operation and have in the past striven to rise above national disputes. Our British institutions should protest against the new discriminatory measures.

World opinion is hardly likely to view our new regulations as evidence of our Government's firm determination to deal with the Rhodesian problem, but our colleagues abroad will note the profession's silent acquiescence as evidence that we care less about our international obligations than we did.—I am, etc.,

PETER DIGGORY

London W.1.

Resources and Needs in Africa

SIR,—In your leading article (5 May. p. 255) you commented with editorial sympathy on the first International Congress on Basic Medical Sciences in Africa, held at Lusaka in March.

Will you allow me, in the name of the trustees of the Commonwealth Foundation, to mention that the presence of many of the distinguished Commonwealth African delegates at this meeting was made possible by a Foundation grant of £4,250? This does not in the slightest detract from the imaginative and far-sighted planning of Professor Ezeilo and his colleagues, with whom the writer had the privilege of discussing plans for the conference as far back as November 1971. The main point is that you have commended the value of this meeting—a judgement which will certainly not be lost on our trustees.—I am, etc.,

JOHN CHADWICK
Director,
The Commonwealth Foundation

London S.W.1

Prescribing Mandrax

SIR,—I was interested to read the letters of Drs. G. C. Mathers and R. W. Green (28 April, p. 243) and of Dr. H. J. S. Matthew (12 May, p. 367) commenting on my letter published earlier in the *B.M.J.*, (7 April, p. 54).

I would like to stress that I did not write my letter to extol the virtues of Mandrax (methaqualone and diphenhydramine). My complaint was of a communication I had received from the senior medical officer. I can assure Dr. Mathers that I am aware of the addictive qualities of Mandrax, and if he will refer to my letter again he will note that only a little over 1% of my patients had been prescribed this drug, and all the recipients were of a mature age. I cannot ever remember prescribing the drug to a youngster —in fact I find it unusual for a teenager to come to me with a sleep problem, and when they do it is usually amitriptyline which they receive.

I completely reject the advice of Dr. Green that I should accept the S.M.O's communication "in the manner intended." I considered that the letter was unnecessary, and it is my interpretation, devoid of paranoia, that the "manner intended" could have had but one object, and that was to intimidate me, and I think that intimidation should be resisted. I should imagine that the S.M.O. has powers that he can exercise over erring doctors, and I am very pleased that he should have such power, but he should abandon his tactics of attempted intimidation.

I have before me the last published details of suicidal poisoning in England and Wales during the year 1971 which have been extracted by the General Register Office.[1] The list of drugs is a very formidable one and, as one would expect, deaths due to barbiturates outweigh those due to any other listed drug; contrary to Dr. Green's and Dr. Matthew's assertion there were six listed deaths attributable to Mogadon (nitrazepam).

Though as I stated earlier the intention of my letter was to draw attention to a letter I received from the S.M.O. and not to discuss the virtues or otherwise of drugs, I would like, if I may, to comment on Dr. Matthew's letter. Dr. Matthew suggests that a voluntary ban on Mandrax could help to prevent thefts from chemist's shops. Why did he not follow his suggestion to its logical conclusion and suggest a ban on barbiturates as well? It is not my experience to find that Mandrax is a drug that my patients become addicted to. There is not a demand for increasing dosage by those to whom the drug is prescribed. A half to one tablet at night are the requirements of my patients. and I could count on the fingers of one hand those who require two tablets at night. I am in no position to know the most popular drug of addiction apart from alcohol—and I'll wager that most of us have a tipple at this—but my guess would be that barbiturates would far outweigh all other prescribable drugs put together, and as to the cause of death by drug overdosage there were 286 deaths from Tuinal (quinalbarbitone and amylobarbitone) alone in 1971, and 43 from Mandrax.[1]

That the S.M.O. should "politely draw" my attention to those of my patients to whom I prescribe Mandrax is what irritates me, besides the implied threat already mentioned. I regard it as an impertinence that a remote Ministry official should write and tell me what I'm prescribing for my patients. I do not prescribe sleeping tablets willy-nilly; it often happens that patients with a sleeping problem do not require hypnotics at all. I wish to remain master of my own house, and be free to practise as I see fit. If I err, then let officialdom act.

The day has drawn to a close and bedtime has arrived. Rather than risk taking half a Mandrax to soothe me off to sleep I'm going to have a nice stiff whisky instead. Good health and good night.—I am, etc.,

C. G. BROWN

Slough, Bucks

1 General Register Office, *Pharmaceutical Journal*, 1973, **210**, 77.

Behçet's Syndrome and Oral Fibrinolytic Therapy

SIR,—We were interested to read the paper of Drs. T. Chajek and M. Fainaru (31 March, p. 782) and, by reference to a similar case, would like to support their observation that impaired fibrinolysis is an important factor in the pathogenesis of Behçet's syndrome.

We have under our care a male patient now aged 32. For eight years he has had recurrent attacks of deep venous thrombosis and one episode of pulmonary embolism. During this time he has also suffered from recurrent mouth ulcers, scrotal ulcers, erythema-nodosum-like lesions, and superficial phlebitis. When referred to us he had lower inferior vena caval obstruction but there was no proteinuria, suggesting that the renal veins were not affected. For a few years he had been treated with intravenous heparin and oral anticoagulants. Though this had

helped the immediate episodes of deep venous thrombosis, recurrences had not been prevented and his other symptoms also were not influenced by this treatment.

Eighteen months ago investigations showed a persistently impaired plasma fibrinolytic activity (euglobulin lysis time[1] 320 min; normal range 80-220 min). All other investigations were within normal limits. He was treated with slow-release phenformin (50 mg twice daily) and either ethyloestrenol (2 mg twice daily) or stanozolol (2 mg four times daily). These drugs are known to enhance plasma fibrinolytic activity.[2] Since then he has remained well; he has had no episodes of deep venous thrombosis but has had one episode of superficial phlebitis. He has had no scrotal or mouth ulcers or erythema-nodosum-like lesions. Fifteen months ago he returned to full-time work for the first time for several years and is now working seven days a week. The details of the patient's fibrinolytic activity before and during treatment are shown in the table, the fibrinolytic activity becoming normal with treatment. Fibrin degradation products were estimated but were always normal.

Effect of Treatment with Phenformin and an Anabolic Steroid

	Euglobulin Lysis Time (min)
Before treatment (*a*)	320
" (*b*)	289
At " 1 month "	136
At 3 months	122
At 6 months	190
At 9 months	192
At 12 months	83
At 18 months	98

To prove conclusively the value of this patient's treatment we ought to stop the treatment, but we do not consider this procedure to be ethical.

We consider that this report supports the observations of Drs. Chajek and Fainaru and our own observations[3] that fibrinolytic mechanisms should be investigated in patients with Behçet's syndrome and that it emphasizes the value of oral fibrinolytic therapy. —We are, etc.,

W. J. CUNLIFFE
B. E. ROBERTS
B. DODMAN

General Infirmary, Leeds

1 Menon, I. S., *Lancet*, 1967, **1**, 116.
2 Fearnley, G. R., and Chakrabarti, R., *Journal of Clinical Pathology*, 1964, **17**, 328.
3 Cunliffe, W. J., and Menon, I. S., *Lancet*, 1969, **1**, 1239.

Toxicity of Benorylate

SIR,—Dr. M. Aylward's letter regarding the incidence of salicylism in patients taking benorylate and aspirin (14 April, p. 118) poses some interesting questions regarding the numerous factors in patients which may render them more liable to develop these symptoms. His clinical experience is, however, in complete contrast to our own. We have recently reported[1] a double-blind, double-dummy, crossover trial in 26 patients admitted to hospital for the treatment of active rheumatoid arthritis. A dosage of 10 ml (4·0 g) of benorylate twice daily was compared with 1·2 g soluble aspirin four times daily. The clinical measurement of efficacy showed no difference between the two treatment regimens, but the incidence of salicylism was significantly different, 10 of the patients developing this symptom while taking aspirin and only two while taking benorylate. Other side effects were uncommon in either group. This difference was explicable when the plasma salicylate concentrations were considered, the mean values being 203 μg/ml at 6 a.m. and 217 μg/ml at 6 p.m. while taking aspirin, and 114 μg/ml at 6 a.m. and 123 μg/ml at 6 p.m. when taking benorylate. These plasma levels are similar to those achieved by Robertson *et al.* when giving benorylate to normal volunteers.[2]

The high incidence of salicylism in the patients taking aspirin in the study is probably due to the fact that they took their medication under careful supervision by the nursing staff. The lower incidence of tinnitus in outpatient studies probably reflects the inability of most patients to take 16 aspirin tablets daily with regularity. Some increase in the overall incidence of tinnitus might be expected in patients taking benorylate, as many of them, despite having been treated with apparently effective doses of aspirin previously, are in fact achieving therapeutic salicylate levels for the first time. It has been shown that aspirin must be given in high doses (up to 5 g daily)[3] in order to achieve measurable anti-inflammatory effect.[4] Doses of this size will produce symptoms of salicylism in some patients. Because of its simplicity of dosage and considerable patient acceptability, benorylate will produce plasma salicylate levels in the therapeutic/toxic range more frequently than conventional salicylate therapy as it is generally taken, but this should be taken as an indication for tailoring the dose to effective levels which do not induce these mild toxic symptoms rather than substituting a therapeutic regimen that is non-toxic but may be ineffective.—We are, etc.,

V. WRIGHT
IAN HASLOCK

Rheumatism Research Unit,
School of Medicine,
Leeds

1 Sasisekhar, P. R., Penn, R. G., Haslock, I., and Wright, V., *Rheumatology and Rehabilitation*, in press.
2 Robertson, A., Glynn, J. P., and Watson, A. K., *Xenobiotica*, 1972, **2**, 339.
3 Fremont-Smith, K., and Bayles, T. B., *Journal of the American Medical Association*, 1965, **192**, 1133.
4 Boardman, P. L., and Hart, F. D., *British Medical Journal*, 1967, **4**, 264.

Eclampsia and Social Change in the Tropics

SIR,—The epidemiology of eclampsia in tropical Africa has been poorly studied, but the incidence is thought to be much lower than in Europe. Precise data are lacking and the explanation is speculative, but social, climatic, and dietary factors may be contributory.[1] I believe that the general educational level is related to the incidence of eclampsia, which can be expected to rise considerably over the next decade or so in those countries where the western way of life is replacing the traditional pattern.

The evidence for this has been apparent to me working in a hospital in an urban community in a developing tropical African country which is socially transitional. Over 3,000 pregnancies are supervised by trained staff each year. Medical services are easily and quickly available to all, and we believe that for practical purposes no serious illness associated with pregnancy, such as eclampsia, in this area escapes our knowledge. The majority of patients, including the youngest, have received only an incomplete primary education and English is infrequently understood or spoken. Having noticed that all the eclamptic patients I could remember spoke English, I conducted a prospective study of all subsequent eclamptic patients over a period of 12 months. Five cases were seen. All these patients spoke English sufficiently well to conduct a satisfactory doctor/patient conversation and were educated to at least first-year secondary school level. They were matched for age and parity with 45 normal controls, only eight of whom had reached the same educational level. This difference is highly significant ($P < 0.01$ by Fisher's test).

Awareness of the effect of the western way of life on disease patterns is increasing. Which aspect affects the incidence of eclampsia is unknown, but the frequency can be expected to increase very considerably in line with the rapid social change. Doctors working in similar situations can expect an increase in eclampsia and it may be useful to be aware of the growing at-risk group.—I am, etc.,

DOUGLAS JENKINSON

Nchanga North Hospital,
Chingola, Zambia

1 Lawson, J. B., and Stewart, D. B., *Obstetrics and Gynaecology in the Tropics*. London, Arnold, 1967.

Diagnosis of Multiple Pregnancy

SIR,—We write to suggest a simple and reliable method for the early diagnosis of multiple pregnancy.

When, because the uterus is larger than would be expected, the possibility of multiple pregnancy arises, the patient herself may have this in mind and is naturally anxious for a prompt and reliable ruling, and in any case the sooner the diagnosis is made the better from the obstetrician's point of view. An *x*-ray may leave little doubt, but one prefers to avoid this if possible, and as yet few maternity hospitals have the highly sophisticated equipment which enables a confident diagnosis of multiple pregnancy to be made at eight weeks. However, a Doptone ultrasonic device should generally be available.

The traditional method of attempting to establish the presence of two fetal hearts by timing them and finding a difference in rate is notoriously unreliable, and though the Doptone makes this easier, and possible at a much earlier stage in the pregnancy, the method is still very liable to observer error. We have employed two Doptones, attempting to find two separate sites at which a fetal heart is clearly audible, and then switched both machines on at once. If there is more than one fetal heart the sounds on the two machines are not synchronous, and this is very quickly apparent, the slightest difference in rate soon showing that two separate hearts can be heard.

We suggest that, at the point at which the possibility of a twin pregnancy should be faced—say, at 24 weeks—and the patient given a confident answer instead of being told that she must rest content to await developments, our use of two Doptones to confirm asynchrony of fetal hearts can establish safely an accurate diagnosis of multiple pregnancy.

We should like to thank Mr. A. P. B. Mitchell for permission to report this technique. —We are, etc.,

PETER BARKER
DENIS CASHMAN

North Shields