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.,

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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.,

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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.,

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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.,

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