"There is no such thing as tropical medicine." Often have we heard that there should be no such thing as "western medicine," "Russian medicine," or "Chinese medicine." Of course he is right: medicine is one, the whole is always greater than the part. Yet in practice we cannot manage without words that set limits to that part with which we happen to be concerned. Tropical medicine has long been a convenient if illogical term. But if, in accordance with the implications of the penultimate paragraph of Dr. Shattock's letter, it were to be replaced by terms suitable for the particular needs of every country we could finally have as many types of medicine as there are members of the United Nations, which is absurd. Tell me someone, assuming as I do that we need a geographical classification of medicine, what it should be. —I am, etc.,

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### Maintenance Therapy in Myeloma: Risk versus Benefit

SIR,—The letter by Drs. Susan M. Sieber and R. H. Adamson (7 June, p. 557) drawing attention to the risks of maintenance therapy in myeloma emphasizes the current dilemma attending the treatment of patients with this disease. We have also recognized this complication[1] and, on the basis of some 100 new patients with myeloma admitted to the clinic in the past two years, we have become concerned about the whole approach to therapy.[2] Undoubtedly current treatment schedules have prolonged median survival, but we question the continued use of alkylating agents in the maintenance period when the labelling index has risen in response to treatment.[3] We have suggested that alternative chemotherapeutic regimens be employed at this time in which cycle-specific drugs are administered in an attempt to capitalize on the altered cell kinetics.[4] Acknowledging that these proposed programmes will impose a heavy load on medical staff, require additional sophisticated haematological support, and have at the present time a largely theoretical basis, we have mounted a prospective study to test this hypothesis. We would be interested to hear how other investigators currently view this therapeutic dilemma.—We are, etc.,

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DANNY DUBOVSKY
HELEN S. KING

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### False Positive Pregnancy Test in Uraemia

SIR,—Following our report (16 November 1974, p. 410) of two patients suffering from uraemia who had false positive pregnancy tests, a study of the incidence of false positive pregnancy tests in 120 uraemic patients with the Gravindex method has been completed with the following results.

(1) False positive pregnancy tests occurred in three out of 60 patients (5%) suffering from chronic renal failure (two women and one man). On haemodialysis the false positive pregnancy test reverted to normal within a period of three weeks. The false positive pregnancy test was unrelated to the degree of albuminuria, since the three patients with a positive pregnancy test only had a trace of albuminuria. (2) In 60 patients suffering from acute renal failure a false positive pregnancy test was not observed.

I suggest that a false positive pregnancy test does not occur in acute renal failure because a disturbance in the immunological state may require a period of time to develop. If a false positive pregnancy test does occur in uraemia the diagnosis would be compatible with chronic renal failure rather than acute renal failure.—I am, etc.,

Y. K. SEEDAT

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### Cot Deaths in Sweden

SIR,—Several investigations have shown a rather high incidence of sudden unexpected deaths in infancy in Britain, Canada, the United States, and many other countries. Figures between 2 and 3 per 1000 live births are commonly given and for certain places and certain strata of population even higher rates have been mentioned. As a consequence, much research has been done, and is still going on, in pathology, physiology, immunology, virology, and other fields to try to reveal the cause or causes of these deaths but, as yet, with no conclusive results.

Recently, Emery and his co-workers[1-3] have brought some evidence for the belief that certain cases of sudden unexpected death in infants are due to factors which might be prevented by rather simple measures such as intensified health supervision of an empirically defined high-risk group of children and advice to their mothers on feeding and care of the babies. During the last two years, while these measures were taken, the incidence in Sheffield of sudden unexplained deaths in infants has dropped by about half.[4] In Sweden and in some other countries (Czechoslovakia, Israel, the Netherlands) a much lower incidence of sudden unexpected death has been found in infancy. For the period 1968-72 rates between 0·4 and 0·8 per 1000 live births are reported from different parts of Sweden.[5] During these years the total infant mortality after the first week of life was only between 3·7 and 2·9 per 1000 live born in Sweden. This fact supports the belief that the Swedish rate of sudden infant deaths must really be much lower than the British.

Two questions seem to arise from these facts. (1) Is it justified to think that the so much lower rate of cot deaths in Sweden may be due partly to a more intense child health service which has managed to reach also most babies in the high-risk group defined by Emery? In Sweden virtually all children are followed by the child health service at least during their first year of life. Out of 112 273 babies born in 1972, 110 467 were supervised and had an average of 11·7 contacts with the doctor or nurse of the service during the first year. The rate of babies being entirely breast-fed for at least two months was still 30·7% that year. (2) Is the group of babies who still die suddenly and unexpectedly in Sweden, or their families, in any respect different from the corresponding group in Britain? In other words, are there two (or more) types of sudden infant death syndrome, one preventable by better care and feeding (plus, probably, certain socioeconomic factors), the other not preventable by these means? In our opinion, answers to these questions would be of great value.—We are, etc.,

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2 Emery, J. L., and Carpenter, R. G., *Proceedings of the F.E. Camps International Symposium on the Sudden Infant Death Syndrome*, p. 97. Toronto, Canada, 1974.
3 McWeeny, P. M., and Emery, J. L., *Archives of Disease in Childhood*, 1975, **50**, 191.
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### Glibenclamide-induced Hypoglycaemia

SIR,—We would like to draw attention to the dangers of accidental ingestion of the hypoglycaemic agent glibenclamide. Cases of poisoning with glibenclamide have been reported but complete recovery seems to have occurred.[1] In the following case of a patient who was admitted to hospital after accidentally taking glibenclamide sequelae still persisted 12 months after ingestion.

A 30-month-old, previously normal child was admitted 48 hours after ingesting an unknown but small number of 5-mg tablets. Since taking them he had been drowsy and delirious and had had screaming attacks and difficulty in feeding. On admission he was pale, limp, perspiring freely, and had a generalized convulsion with right focal features. The Dextrostix test was non-reactive for blood glucose. He was promptly given a bolus of 50% dextrose solution intravenously and a slow intravenous infusion of 10% dextrose solution. He did not recover consciousness after the convulsion and two hours after starting therapy his blood glucose was 0·38 mmol/l (7 mg/100 ml) and cerebrospinal fluid glucose 1·38-2·77 mmol/l (25-50 mg/100 ml). Further 50% dextrose was given statim. Ten hours later he was more deeply unconscious. His pupils were dilated and fixed and the plantar responses extensor, though he responded to painful stimuli. There was continual multifocal twitching. Though the fundi appeared within normal limits his deterioration was believed to be due to cerebral oedema, and intravenous dexamethasone, mannitol, and glycerol were given sequentially. His conscious state improved but fluctuated over the next 48 hours. After 72 hours he was conscious but very irritable. Plasma insulin was estimated daily for several days from the third day after admission. The values were not raised and were appropriate for the simultaneously measured plasma glucose levels. Blood samples were not available for plasma insulin before the third day.

When discharged 12 days after admission the patient had a persisting left third nerve palsy but he was alert and happy. There had been no attacks of drowsiness or twitching for seven days. He was maintained on anticonvulsant therapy. When last seen 12 months later the left third nerve palsy was still present, there seemed to be a diminution of visual acuity in the left eye, and the left optic disc appeared paler than the right. He was dyslalic and his vocabulary was limited for his age, but his parents thought his comprehension was normal. He had had a number of epileptic seizures, a few grand mal but mainly minor motor seizures, including akinetic seizures. Plasma glucose estimations performed at these times had been within normal limits.

The hypoglycaemic reaction to glibenclamide in adults has been reported as not

protracted and symptoms are relieved within half an hour of receiving glucose.[2] On the other hand, in a study of normal children (5 to 15 years of age) as little as 2·5 mg of glibenclamide produced a marked decrease in blood sugar with lower than normal blood sugar values persisting for more than six hours (six hours being the total investigation time).[3] In our patient there appeared to be a prolonged hypoglycaemic effect lasting 48-72 hours. Moreover, we can only conclude that the hypoglycaemia has caused permanent cerebral damage with epilepsy. Mental retardation cannot be excluded.—We are, etc.,

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2 Davidson, M., *et al.*, *Lancet*, 1970, **1**, 57.
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## Potentiation of Warfarin by Co-trimoxazole

SIR,—I was interested to note the observations of Dr. J. M. Hansen and others (21 June, p. 684) on their finding of co-trimoxazole "as an inhibitor of drug metabolism in man." Their remarks were prompted by previous correspondence discussing potentiation of the action of warfarin by co-trimoxazole and consequent increased hypoprothrombinaemia.

In several years' experience in supervising a long-term anticoagulant clinic now comprising about 1000 patients, about 95% of whom are treated with phenindione, I cannot recollect a case of potentiation of hypoprothrombinaemia to untoward levels (less than 5% thrombotest control) whenever co-trimoxazole was added for intercurrent infection. I would, therefore, recommend the use of this drug whenever an oral broad spectrum antibiotic is needed in patients with phenindione—especially since the latter group of anti-infective agents usually does cause troublesome hypoprothrombinaemia with warfarin or phenindione. This clinical advantage in using phenindione rather than warfarin is, in my experience, one reason for preferring the former anticoagulant for routine use.—I am, etc.,

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## Clomiphene in Investigation of Ovulatory Failure

SIR,—I cannot accept as reasonable the conclusion of Dr. Jean Ginsburg and others (19 July, p. 130) that "clomiphene's failure to evoke a response when there was a positive response to LH/FSH-RH suggests a functional defect at hypothalamic level or above." They state correctly that "clomiphene is thought to act essentially through competition with oestrogen at hypothalamic receptor sites," but are incorrect in adding: "stimulating release of LH/FSH-RH and gonadotrophins by negative feedback."

A negative feedback is, by definition, inhibitory, and clomiphene exhibits a positive feedback by blocking without stimulating the hypothalamic receptors that would otherwise transmit to the anterior pituitary the negative feedback effect of oestrogens. When the ovaries are producing no oestrogens the negative feedback is already virtually nil, and clomiphene cannot be expected to have an effect. Hence a failure of gonadotrophins to rise in response to clomiphene can reasonably be ascribed to a hypothalamic defect only if levels of oestrogen sufficient to produce a negative feedback have been demonstrated before the administration of clomiphene (given also, of course, that a functional anterior pituitary has been demonstrated by a response to LHRH).

No data about oestrogens are given in the paper, but support for my argument is provided by the finding that among the abnormal women all the five who were menstruating, and who must therefore have been producing substantial amounts of ovarian oestrogens, responded to clomiphene with a rise in LH.—I am, etc.,

P. BYE

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## Serum α-Fetoprotein in Cystic Fibrosis

SIR,—Paediatricians and geneticists have been looking forward to a reliable method of diagnosing cystic fibrosis in children and also in identifying clinically unaffected heterozygote carriers. Professor R. K. Chandra and others (29 March, p. 714) suggest that estimation of serum α-fetoprotein (AFP) might help in detecting carriers in families at risk. Their patients with cystic fibrosis had significantly raised levels of serum AFP, and the patients' parents and some siblings, presumed to be heterozygotes, also had moderately but significantly raised levels. Observers in the U.K. (17 May, p. 392) have been unable to confirm these findings, whereas Dr. J. A. Smith of New York (17 May, p. 392) supports them. More reports may be on the way. Perhaps the crux of the matter lies in the technique of estimating serum AFP.

Professor Chandra and others state that "In autosomal recessive traits the proportion of carriers to normal subjects in a sibship should theoretically be 2:1, whereas this ratio was 1:1 in our study." Their patients numbered 18, parents 16, and siblings 14, with seven presumed heterozygotes and seven presumed normal. Presuming that all the parents and all the siblings were studied, there were a total of eight families and 32 children, with an average of four children per family. Theoretically, an average of about eight affected children, eight normal children, and 16 heterozygote carriers could have been expected, but this was not so. Theoretically, 1 in 4 of the siblings is affected if a large number of families are analysed.[1]

If a small number of families is analysed the proportion of affected individuals may differ from the expected. By chance some families may have all normal children whereas some may have all affected children. For example, nowadays, since families tend to be small, the appearance of an autosomal recessive condition is often sporadic with only one affected person in the family.[2] This could well apply to cystic fibrosis.

There are about 1 in 25 heterozygote carriers of cystic fibrosis among Europeans and North American Whites.[3] Perhaps the time will come when these heterozygotes will be identified as part of their routine medical care. When two heterozygotes married each other the risk would be known in advance.—I am, etc.,

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Ministry of Health,
Al-Ain, Abu Dhabi, U.A.E.

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2 Emery, A. E. H., in *Textbook of Paediatrics*, ed. J. O. Forfar and G. C. Arneil, p. 66. Edinburgh and London, Churchill Livingstone, 1973.
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## Junior Hospital Staff Contract

SIR,—We, the undersigned junior hospital staff at the Aberdeen teaching hospitals, agree with the views expressed by the junior staff at the National Hospitals for Nervous Diseases, Queen Square and Maida Vale (5 July, p. 43).

We are opposed in principle to the proposed junior contract and support the call for a halt to the present negotiations; it is our opinion that the views of all the junior staff in the country should be sought by a national postal ballot before such ill-advised arrangements are finalized.—We are, etc.,

C. J. ALLISON

Aberdeen Royal Infirmary,
Aberdeen

*** This letter had 62 signatures appended to it in addition to that of Dr. Allison.—ED., *B.M.J.*

SIR,—As a "flying doctor" from the outback of Western Australia, I am appalled at the conditions of service that the junior hospital doctors have obtained in Britain. The rate of emigration of junior doctors from this country speaks for itself—there is only one way to reverse this trend and that is to obtain better working conditions for junior doctors. Fortunately there is one way of obtaining this and that is by pressing for a 40-hour contract.

Mrs. Barbara Castle promised us the 40-hour contract in January of this year. Even the Review Body in its Fifth Report pointed out (para. 15) that the work load on junior staff will continue to increase. Since the G.M.C. has at last tightened up the regulations there will be fewer overseas doctors available to staff the hospitals in Britain. The crunch of the matter is that the peripheral hospitals will be the first affected and hence they will need to lead the rest of the junior hospital doctors in their fight to secure better working conditions.

As I said at the Annual Representative Meeting you obtain from the Government what you think that you are worth—and I sincerely believe that a houseman who works well in excess of 80 hours (many of these being unsocial hours) is worth £6000 per year. However, you can only achieve this figure if you can obtain a solid basic 40-hour contract. For comparison, just look at