of environmental medicine, the whole of public health as local authorities have administered it, the departments of social medicine and, indeed, much psychosomatic medicine contravene the medical ethic.

A century ago, when the world's human population was a quarter of what it is now, open sewers in English cities and contaminated water supplies stirred Chadwick and others to promote public health legislation. They were already dealing with the symptoms of local overpopulation. I intend no lack of respect for their great achievements when I point out that what the public health acts have treated have been the symptoms and not the cause. The cause is overpopulation.

Is it really against the medical ethic to treat the cause of much potential disease?—I am, etc.,

KENNETH BARLOW

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SIR,—I fear Lord Brock (12 February, p. 440) is too late to stop the rot. Doctors have long encouraged public health measures and immunization to prevent infectious disease for the general good, and not on medical grounds in the individual patient.

Overpopulation, partially the result of this successful prophylaxis, produces medical and psychiatric as well as social disease. Yet now we have the means of prevention by the control of conception. Let doctors encourage and practise the prophylaxis of this new disease with as clear a conscience as they did the old.—I am, etc.,

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SIR,—I was not a little surprised to read Lord Brock's comments (12 February, p. 440) on the "Doctors and Overpopulation" letter (8 January, p. 108). In particular, his statement "I find it difficult to see that *as doctors* we have a concern with the problem of overpopulation" (the italics are his) seem to ignore a number of cogent and highly relevant facts. For example, as already mentioned in the original letter, overpopulation is to a certain extent clearly iatrogenic. Again, would Lord Brock "write off" the efforts "*as doctors*" of the medical officers of health and their numerous medical assistants whose major efforts lie in the field of preventive and social medicine? We take their work as much for granted as we do the seasons of the year; until an emergency situation such as a potential smallpox or typhoid epidemic appears in our midst.

Is it not reasonable to suggest that the more civilized a community the greater the emphasis on and effectiveness of preventive medicine; that much of hospital doctoring as many of us know it boils down to a tentative situation of reparative medicine, where the fundamental goal of discharging home a patient with a totally integrated and wholly functioning mind and body is as yet more a concept of fantasy than fact.—I am, etc.,

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Status Epilepticus

SIR,—Your leading article on status epilepticus (19 February, p. 460) mentions the treatment regimen of intravenous diazepam as a slug dose followed by drip infusion. An intravenous dose of 10 mg repeated if necessary is a valuable and readily available emergency measure, and may be immediately effective; but if status or serial epilepsy recurs response to further diazepam is often poor. We therefore tend to use paraldehyde 10 ml intramuscularly followed by a drip (30 ml in 500). The method is safe and control once established is prolonged, thus allowing a more easy transfer from intravenous to oral therapy with standard anticonvulsants, and to normal levels of responsiveness. This second phase of treatment is often the more difficult.

In our experience status presents in two groups: one where response to initial treatment by any of a number of methods is rapid and lasting, the other in which seizures recur early and are very difficult to control. These two populations account for some seeming contradiction in therapeutic results. The latter group constitutes the problem of treatment and its early recognition is not easy. Since many cases of status will present initially to those unfamiliar with it, the establishment of simple and effective treatment regimens is the more important.—We are, etc.,

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Renal Function and Plasma Digoxin Levels

SIR,—We note with interest the work reported by Dr. E. Mary Baylis and others (5 February, p. 338) concerning renal function and plasma digoxin levels, which parallels a project proceeding in our own hospital.

From the results presented we would suggest that it is a little premature to state that creatinine clearance measurements are of no value as a guide to digoxin dosage. Our own results for creatinine determinations in plasma using the method indicated by the authors¹ show considerable variation and have proved unacceptable for a study of this type. We are currently evaluating a method outlined by Cook² which follows the rate of colour development at 510 nm after the addition of alkaline picrate to aqueous dilutions of plasma.

We have also found the Lanoxitest method for digoxin assay to be of insufficient sensitivity for research work of this nature. Results in our own laboratory suggest that considerable care is required when determining urinary digoxin by radioimmunoassay, particularly with regard to the medium chosen for dilution of the sample, and in the process of quench correction.

While not disputing the conclusions the authors have made we feel that the above points should be considered before the original work of Jelliffe and Blankenhorn³ and Jelliffe⁴ is dismissed.—We are, etc.,

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- ¹ Henry, R. J., *Clinical Chemistry: Principles and Technics*, p. 292, New York, Hoeber, 1964.
- ² Cook, J. G. H., *Clinical Chimica, Acta*, 1971, 32, 485.
- ³ Jelliffe, R. W., and Blankenhorn, D. H., *Circulation*, 1967, 35, 36, Suppl. II, p. 150.
- ⁴ Jelliffe, R. W., *Annals of Internal Medicine*, 1968, 69, 703.

Clotting Factor Concentrates

SIR,—Mr. T. W. Barrowcliffe and others (29 January, p. 309) raise several interesting points, some of which are worthy of emphasis and others of guarded caution. To the best of our knowledge this must be the first time that a group has got down to the problem of making a serious attempt to estimate the requirements of this clotting factor concentrate in their own area. On this item alone the authors deserve congratulations, for it is this type of regional market research that is lacking in the field of blood transfusion practice, and may be partially responsible for the slow development of adequate plasma fractionation capacity in the United Kingdom. Whether their predictions are accurate or not can be debated, but in the interests of such a dialogue it might be helpful to record the actual use of these type of concentrates for 1971 in the south-east of Scotland, which has a population of 1.25 million.

There are two preparations made available by the Scottish Plasma Fractionation Centre. The first is a product containing coagulation factors II, VII, IX, and X and the other contains factors II, IX, and X. This latter concentrate is reserved for the management of haemophilia B patients. The release of these products is strictly controlled from the regional blood transfusion centre, and is undertaken only after full discussions by a member of our medical staff with the clinician responsible for the patient's care. It is a pleasure to record the excellent co-operation we have received from our clinical colleagues. The use of these products in 1971 can be summarized as follows:

	Reason for Infusion	No. of Patients	No. of 10 ml vials
II VII IX and X Concentrate	Oral Anticoagulants (reversal)	20	45
	Acute Liver Failure	12	33
	Cardiopulmonary Bypass		
	Surgery	3	9
	Premature Infants	3	3
	Bleeding Varices	1	4
	Liver Biopsy	5	10
	Vitamin K Deficiency	1	1
		45	105
II IX and X Concentrate	Haemophilia B	3	135

We would seriously doubt the wisdom of the implied suggestion that regional blood transfusion centres should embark upon plasma fractionation programmes. In the interests of economy, high standards of quality and safety, and the satisfactory future general development of the national plasma fractionation units, this type of work should be centralized into perhaps no more than three centres in the United Kingdom. The regional blood transfusion centres should concentrate their efforts on the clinical supervision of the products made available, and provide the fractionation units with *in vivo* recovery data on different batches if required. In collaboration with their clinical

colleagues they should estimate the requirements for the next 12 months, and based on this assessment and the anticipated fractionation yields collect the necessary raw material within their region for the patients for whom they are directly responsible. This done, the ball is firmly in the court of the central fractionation units to make the necessary capacity available to prepare and deliver high quality products to the regional transfusion centres in the quantity requested. This principle should hold for all plasma fractionation products and would thus throw the burden of responsibility for patient care where it belongs—to the regional transfusion centres.—We are, etc.,

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The Red Cell

SIR,—Dr. G. W. G. Bird's article on "The Red Cell" (29 January, p. 293) prompts me to record some of my own observations. I have found¹ that the geometry of the avian egg is that of conic sections. This discovery was made possible by the assumption that the contents of the egg are paracrystalline and that the shape is derived from the figures related to liquid crystals.²

The following shapes are found in connexion with red blood corpuscles: biconcave discs, signet rings, crescents, cups, flattened elliptical discs in the camel family, and spheres when the cells are placed in hypotonic solution and pointed spines in the so-called "thorn apples" found when they are placed in hypertonic saline. Furthermore, the cells may range from 6-9 microns in any one individual.

These shapes are readily derived from conic sections. The biconcave disc is a cyclide figure, derived from confocal conic structure, that comprises a family of curves, so covering variation in size of the red cell. The signet ring is a cyclide with the hole or dimple off-centred and the crescent is a broken anchor ring; the cup a distorted anchor ring where the dimple in one side is exaggerated and in the other is everted. The red cell of the camel is a distorted ellipsoid figure, also found in the red cells of ovipara.

When placed in hypotonic saline, the red cell absorbs water and swells up into the form of a sphere that can be regarded as a limiting figure of the cyclide or ellipsoid. Placed in hypertonic saline, however, it loses water, ceases to be in the mesophase, assumes crystalline structure, and displays prismatic radiation. These findings will be of interest to haematologists, as red cells of signet ring shape are found in disease, notably malaria. Crescents are found in sickle-cell anaemia and spherocytosis is found in the disease of that name.

These observations provide strong evidence for the paracrystalline nature of haemoglobin in the red blood corpuscle. The outer "membrane," which might be described better as the sheet of the figure, is an interface between the mesophase in the cell and that of the plasma. The importance of the discovery, however, is in application to genetics. Sickle-cell anaemia, for example, is of genetic origin, likewise spherocytosis. The cyclides are derived from the ellipse and the

hyperbola and these have parametric descriptions, which, in turn, suggests a mathematical approach to the subject of genetics. It may well be found to apply to the theory of blood grouping.—I am, etc.,

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¹ Malcolm, J. E., Arris and Gale Lecture, Royal College of Surgeons of England, 20 January 1972, to be published.

² Hartshorne, N. H., and Stuart, A., *Crystals and the Polarising Microscope*, 4th edn. London, Edward Arnold, 1970.

Bacteriological Aspects of Mycobacterial Infections

SIR,—Professor D. A. Mitchison (12 February, p. 424) lists mycobacteria and, although writing in a section under the general heading of tuberculosis, includes *M. marinum* (*M. balnei*) and *M. ulcerans*, which cause ulceration of skin. *M. leprae* is not mentioned, perhaps because it cannot be cultured on artificial media. It may, however, be found in sputum of patients with advanced lepromatous leprosy involving the larynx and trachea. Although the diagnosis of leprosy will not be in doubt, as pulmonary tuberculosis not infrequently complicates neglected lepromatous leprosy, confusion between the mycobacteria may arise.—I am, etc.,

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Tropical Splenomegaly, Sickle-cell Trait, and P. falciparum Infection

SIR,—The letter of Dr. D. I. K. Evans and others (22 January, p. 250) entitled "Tropical Splenomegaly, Sickle-cell Trait, and P. falciparum Infection" needs to be commented upon from this part of the world, where enlarged spleens, sickle-cell traits, and *P. falciparum* infections are an everyday occurrence. In spite of the fact that the authors stated "This case has all the features of tropical splenomegaly syndrome" the evidence they presented could easily be interpreted to mean that the little Nigerian boy was not suffering from the tropical splenomegaly syndrome (T.S.S.), which, surely, has well known and accepted clinical and diagnostic features. Some of these features are:

A large spleen, which various investigators quoted in the authors' own letter specified to be at least 10 cm below the costal margin.^{1,2} The boy described had a spleen of 7.5 cm, a size which literally hundreds of West African boys would have without being considered here to be in the T.S.S. range.

Abdominal discomfort as a result of the size of spleen, with dragging pain, debility, and sometimes fever and anaemia.^{3,4} There were no febrile episodes in the case reported, and the abdominal pain could as well be explained by ascariasis, which the patient had.

There is a tendency to an increase in IgM, with IgG levels not significantly different from normal.² The authors found the very opposite, stating "Hyperglobulinaemia is present, but IgM is not so often raised as IgG", and in support of this statement they cited three authors,^{1,2,5} none of whom,

in fact, support their statement. It was surprising that Dr. Evans and colleagues omitted to refer to the work of Loewenthal *et al.*,⁶ who measured IgM values in 17 of 19 cases of suspected T.S.S. and found all greatly increased.

It usually takes at least 3-6 months' continuous drug therapy before shrinkage of the spleen occurs.^{5,6} The Nigerian boy's spleen shrank to one-third its original size after six weeks of antimalarial therapy.

In view of the above (and there was no liver biopsy, which, I agree, would not have been justified merely to prove T.S.S. in this boy), may I suggest, Sir, that there was no evidence whatsoever that this boy had the tropical splenomegaly syndrome. I submit that the cause of the splenomegaly which responded so well and fast to antimalarial therapy was chronic falciparum malaria infection. The child came from an endemic area and had by then developed a considerable amount of immunity. As immunity develops, parasitaemia decreases, but malaria parasites can still be found in small numbers. He also had multiple helminthic infestation, a likely cause for abdominal pain and even splenomegaly in children. Chronic malarial infection and helminthic infestation would account for the high IgG.

Finally, as tropical splenomegaly is not proved, the problem of sickle-cell trait in this case is irrelevant, and so are the authors' recommendations. Indeed, workers here have long ceased to call every AS pattern sickle-cell trait. The authors do not tell how they excluded sickle-cell β -thalassaemia, in which 8-year-olds often have a large spleen, an AS pattern, and *P. falciparum* infection.—I am, etc.,

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¹ Watson-Williams, E. J., and Allan, N. C., *British Medical Journal*, 1968, 4, 793.

² Saooe, A. S., *British Medical Journal*, 1970, 3, 378.

³ *British Medical Journal*, 1970, 3, 360.

⁴ Marsden, P. D., and Hamilton, P. J. S., *British Medical Journal*, 1969, 1, 99.

⁵ Stuijver, P. C., Ziegler, J. L., Wood, J. B., Morrow, R. H., and Hutt, M. S. R., *British Medical Journal*, 1971, 1, 426.

⁶ Loewenthal, M. N., O'Riordan, E. C., and Hutt, M. S. R., *British Medical Journal*, 1971, 1, 429.

Prevention of Deep Vein Thrombosis

SIR,—We are delighted that Mr. N. H. Hills and others (15 January, p. 131) have confirmed our finding (13 November, p. 394) that intermittent calf compression is an effective prophylactic against deep vein thrombosis and would congratulate them on presenting such a thorough analysis of their trial.

Our own trial of the efficacy of intermittent calf compression was preceded by a rigorous haemodynamic study, which was conducted both in greyhounds¹ and in patients² in order to find the most effective method of applying the compression. This investigation, as well as our previous one into the effects of passive flexion (10 July 1971, p. 78), revealed, despite Mr. Hills's reservations to the contrary, that when changing the flow in one leg the flow in the other remains largely unchanged. The techniques of statistical analysis used by ourselves and by Mr. Hills and his colleagues are, therefore, equally acceptable.

It is, however, surprising to find that our