sodium as well as ultrafiltration-induced movements of sodium and of water across the dialyser. Conventional hyponatric dialysis is thus inherently more difficult to control clinically, and would seem even more so when combined with individualized oral doses of Slow Sodium as advocated by Dr. Catto and his colleagues.—We are, etc.,

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1 Stewart, W. K., Fleming, L. W., and Manuel, M. A., *Proceedings of the European Dialysis and Transplant Association*, 1972, **9**, 111.
2 Stewart, W. K., Fleming, L. W., and Manuel, M. A., *Lancet*, 1972, **1**, 1049.
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The Magic Diploma

SIR,—Professor James H. Hutchison, in his Personal View (4 August, p. 288), expressed a view that is of great concern and interest to doctors from the developing countries.

While the problem is particularly related to the M.R.C.P., the F.R.C.S., and M.R.C.O.G., diplomas are desired by the majority of doctors from developing countries, because of possible new techniques and knowledge. On the other hand, if teaching centres were to be established in the developing countries, there would be more opportunities for many tropical doctors to acquire the basic skills in more fields than they would do in Britain. Britain is a small country expected to cater for a large number of postgraduates in surgery, obstetrics, gynaecology, and medicine, while the vast materials and opportunities available in the developing countries are left untapped. Clearly, only a very small minority of doctors from developing countries who acquire their postgraduate diplomas from Britain can claim to have had good clinical experience and opportunities of the type they had hoped for. Furthermore, most of them, "while they may become more aware of the importance of good history taking and clinical examinations, the right kind of doctor/patient relationship, the mutual respect which should exist between nurses and doctors, and the value of the health visitor and the social worker . . . concentrate more on the advances of 'Modern Medicine'." The former, which is of great importance and the one that becomes most useful on their return home, should be given as much attention as the latter.

Finally, I must add that postgraduate doctors from developing countries in search of diplomas do not enjoy the disruption of their families as a result of leaving their homes. It will be well for developing countries who are interested in the medical progress of their countries to carry out a true survey into the suffering and frustration of their "silent" doctors in Britain and elsewhere and this may, among other factors discussed by Professor Hutchison, help to increase the need for the development of postgraduate centres in these countries.—I am, etc.,

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SIR,—I read with interest Professor James H. Hutchison's "Personal View" (4 August, p. 288). It really was thought-provoking, and lucidly states the conditions of foreign doctors in Britain.

Being an Indian myself, I endorse some of the points raised by Professor Hutchison. However, I disagree with one statement most strongly, that being: "The Indian graduates who come unsponsored to the United Kingdom today tend to be those who have not made the grade in their own centres." I am sure there are many other reasons which have escaped the attention of the professor.

Firstly, the glamour of British qualifications still carries much weight in Indian society. This is a sad relic of our colonial past. Even a layman in Indian society seems to think that an F.R.C.S. is much superior to an Indian M.S. or M.D. This surely is a wrong conception, which fortunately is being rectified in most states of India by giving preference to local M.D. or M.S. postgraduates to foreign qualified doctors.

Secondly, the postgraduate educational system in India is very different from here, there being no free access to examinations as is the case in this country. Every Indian university has a very limited number of seats for M.D. or M.S. in all branches of medicine, so, naturally they cannot cater to the needs of so many young aspiring doctors who would like to take these examinations. Moreover, though in many cases the doctors are given seats for these examinations, they are not given any financial help—in other words, they are treated as supernumerary candidates. For these reasons so many young doctors, unsuspecting and unaware of the conditions, flock to Britain, which they find is no longer a promised land. Since a majority of doctors come over here within a year or two of graduation, they have certainly had no time to make the grade in their own centre, let alone fail.

What I would like to see is better organization of medical education in India so that there will be no need for young doctors to leave their own country and waste valuable years in pursuit of elusive British degrees, which are of secondary value when they return to India.—I am, etc.,

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SIR,—I wish to comment on Professor James H. Hutchison's Personal View (4 August, p. 288), and on Dr. M. D. Miller's letter (1 September, p. 503), on the above.

The M.R.C.P. so far as I know, is a test of the principles of fundamental medicine, and knowledge of the complexities quoted—for example, radionuclides, gamma cameras, chromosome abnormalities, radioimmunoassay, etc.—is not essential to pass the exam. As one with the M.R.C.P. who comes from, and has worked continuously for many years (including in what some people call "bush stations") in a developing country, I found the possession of this diploma most useful. I do not agree with Professor Hutchison that it is "designed to meet the needs of British medicine" only, since with increasing knowledge of the natural history of disease and diagnosis there are no frontiers political or national in medicine. Further, I wish to point out that doctors from developing countries with the M.R.C.P. are appointed specialists on return to their homeland only after prescribed years of local experience and apprenticeships and the M.R.C.P. is not worshipped as possessing magic powers.

I am sure that Professor Hutchison wrote in the interest of these countries, but surely the medical authorities and schools there, with their considerable local experience and knowledge, are capable of deciding what is good for them? It is only a question of time for these newly independent countries to solve their medical problems, but in the meantime they need all the friendliness and help from the developed countries. In the report[1] of the Director General of W.H.O. for 1972, the Minister of Health of Sri Lanka (Ceylon) is quoted as saying: "It is indeed a matter for regret that though amazing advances in medical research have been made in many fields, elementary sanitary conditions conducive to healthy living, appreciated nearly a century ago, are still denied to vast populations in many developing countries, including my own."—I am, etc.,

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1 Ariyadasa, W. P. G., *World Health*, September 1973, p. 30.

Co-trimoxazole in Bubonic Plague

SIR,—In the course of experimental studies conducted in 1971 with 50 strains of *Pasteurella pestis*, it was found that all these strains were highly sensitive to the combination of trimethoprim and sulphamethoxazole (co-trimoxazole). Trials in vivo in the mouse with this combination also gave positive results. Four clinical strains of *P. pestis* were inoculated into groups of 10 mice each. Solutions of $\frac{1}{2}$, 1, $1\frac{1}{2}$, and 2 tablets of co-trimoxazole (each tablet containing 80 mg of trimethoprim and 400 mg of sulphamethoxazole) in 100 ml of water were prepared and compared in the experiment with plain water. These solutions were given in place of drinking water to the mice, grouped in pairs for each drug concentration, two days before inoculation and during the whole trial. All the untreated control mice died 4-7 days after inoculation. All those which received co-trimoxazole survived the follow-up period of two weeks.

These experimental results led us to conduct a therapeutic trial of co-trimoxazole in cases of plague in man. Twelve patients suffering from bubonic plague (three with demonstrated septicaemia) were included in this study. The patients were admitted to hospital on day 1 (four cases), day 2 (four cases), day 3 (one case), day 4 (two cases), and one week after onset of the disease (one case). The diagnosis was based on clinical and epidemiological evidence and in six cases it was confirmed bacteriologically. Blood culture was positive in three cases.

The specific treatment lasted for 5-11 days in cases of uncomplicated bubonic plague and for 15-17 days for those with septicaemia. Co-trimoxazole was administered to these patients as the only antibacterial agent; the standard dose was two tablets twice daily, but some patients received somewhat higher doses (see table).

Apyrexia was obtained after two days (in six cases), three days in two, four days in

Treatment with Co-trimoxazole of twelve patients with Bubonic Plague.

Age of patient (years)	Sex	Daily Dose (tablets)	Duration of Treatment (days)	Duration of Hospital Stay (days)
*63	F	8	2	21
12	F	5	2 } 16	
		4	12	
12	F	4	7	7
47	F	4	10	11
15	M	4	10	12
*62	F	4	17	25
37	F	4	10	13
*61	F	4	10 } 15	16
		6	5	
40	F	4	1 } 7	7
		6	6	
10	M	4	5	6
13	M	4	7	7
6	F	4	8	8
57	M	4	1 } 11	11
		6	10	

*Septicaemia

one and five days in two; in only a single patient did the fever persist for more than one week. All patients were cured. This response must be regarded as highly satisfactory if compared with results obtained with other treatments. In our experience the mortality rate varies between 60 and 70% for untreated cases. With sulphonamides alone the mortality rate fell to between 5 and 10%. Our results with antibiotics (streptomycin, chloramphenicol, or tetracyclines) indicate a mortality rate in bubonic plague ranging from 0·5 to 5%.

Co-trimoxazole appears to be a promising chemotherapeutic agent for the treatment of plague; further clinical trials should be carried out for a conclusive evaluation.

We express our thanks to Dr. Nguyen-Dinh-Tiep, Director of the Cho-Quan Hospital, Dr. Nguyen-Nahn-Thuat, and the whole medical staff and paramedical service of this Hospital who have helped in performance of this study and also to Hoffmann-La Roche & Co. Ltd. for having supplied us with co-trimoxazole (Bactrim).

—We are, etc.,

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Penicillin in Leptospirosis

SIR,—Perusal of the literature does not suggest that antibiotics have any value in the treatment of leptospirosis. Failure of therapy is ascribed to delay in reaching a correct diagnosis and a missed opportunity to initiate early treatment. Edwards and Domm[1] state that the use of antibiotic agents in the treatment of patients seen in the first two days of treatment is permissible, though not to be recommended. My own experience has led me to conclude that antibiotics do not influence the clinical or serological picture whether they are given early or late in the disease. However, in my patients the predominant serogroup was canicola which causes a relatively benign infection of short duration. I would agree with Dr. L. J. Clein (11 August p. 354) that patients suffering from an icterohaemorrhagic infection should be given the benefit of penicillin.

Gsell[2] claimed that early treatment might modify or prevent leptospiral meningitis. The opportunity was taken to study the cellular reaction of the cerebrospinal fluid in patients treated with penicillin in the early stage of the disease and in late untreated cases.[3] In the early group, eight patients were selected who were seen within five days of the onset of the illness and who had received penicillin for the first time on the day of admission to hospital. Lumbar puncture was performed on admission and seven to ten days later in the meningeal phase of the illness. The cell counts are as shown in the table at the foot of the page.

As anticipated, the cell count in the C.S.F. in the early cases was normal. The second lumbar puncture, with two exceptions, showed only a mild cellular reaction. In 18 cases admitted to hospital in the second week of illness the cell count at first lumbar puncture with one exception ranged from 120 to 1700/mm.[3] The difference between the two groups is statistically significant. It is therefore probable that penicillin given early enough in the disease modifies the pathological changes taking place in the cerebrospinal fluid.

In suspicious cases, penicillin should be administered in the leptospiraemic stage of the disease at least until the serogroup has been identified.—I am, etc.,

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1 Edwards, G. A., and Domm, B. M., *Medicine (Baltimore)*, 1960, **39**, 117.
2 Gsell, O., *Medical Science Publication*, no. 1, p. 34, Washington, U.S. Government Printing Office 1953 (quoted by Edwards and Domm, 1960.
3 Lawson, J. H., *British Journal of Hospital Medicine*, 1971, **5**, 357.

Epidemiology of Hypospadias

SIR,—We read with great interest the article by Dr. C. J. Roberts and Mr. S. Lloyd (31 March, p. 768) reporting their observations on the epidemiology of simple hypospadias. We were particularly interested in the remarkable cyclic pattern of the temporal frequency of hypospadias and in the proposed explanation that the pattern derives from the effect of daylight on maternal (and hence fetal) pituitary function (high frequency peak for winter conceptions). However, our own observations based on 145 consecutive cases of hypospadias do not appear to support this hypothesis.

During an 11-year-period (1955-65) 74,390 infants (live and stillborn) were born to women attending the Alexandra University Maternity Hospital of Athens. Of these infants 38,623 were males and among them There were 145 cases of hypospadias; only 10 of these cases had one or more malformations outside the genital system.[1] Temporal analysis of the dates of birth by Edwards's test[2] and by the rank sum method[3] showed no significant cyclic pattern. Nevertheless, Edwards's criterion did indicate a high frequency peak of hypospadias among mid-October births. This peak, though not significant, would be compatible with the observations and the hypothesis of Dr. Roberts and Mr. Lloyd, since the last menstrual period of a woman delivering in mid-October is usually in early January. Indeed, it would not be unreasonable to attribute the non-significance of our results to either of the following two reasons: the temporal analysis was done on dates of birth and not dates of conception; or the hours of daylight and the hours of darkness have a different distribution in South Wales and in Athens because of the difference in geographical latitude.

A more serious objection against the hypothesis that daylight is strongly negatively related to the frequency of hypospadias derives from the fact that in Athens the prevalence of this defect at birth is apparently more than 50% higher than in South Wales. It would appear therefore that either the effect of daylight variation is of relatively minor (if any) importance in the causation of hypospadias or that the causal factors of this defect are strikingly different in South Wales and in Athens.—We are etc.,

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1 Cadas, C., Observations on the epidemiology of congenital malformations in Greece, 1973, Thesis, Athens. In press.
2 Edwards, J. H., *Annals of Human Genetics*, 1961, **25**, 83.
3 Hewitt, D., Milner, J., Csima, A., and Pakula, A., *British Journal of Preventive and Social Medicine*, 1971, **25**, 174.

Returning Doctors

SIR,—The Department of Health and Social Security has recently sent a letter to secretaries of regional hospital boards and secretaries of Boards of Governors concerning payment of expenses for "British-trained doctors returning to the United Kingdom to take up hospital posts."

According to paragraph 3 of the letter, the term "British-trained doctors" is in fact confined to those receiving their undergraduate medical training in the United Kingdom.

This is certainly a step in the right direction, if our health service is to be manned

Case No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Early cases																		
1st week	4	1	9	6	1	4	1	4										
2nd week	25	36	16	118	2	25	440	25										
Late cases																		
2nd week	220	840	165	443	790	860	820	1700	390	739	369	105	128	412	1100	13	120	230