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	16
12	F	5	2	
		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
		6	5	
40	F	4	1	7
		6	6	
10	M	4	5	6
13	M	4	7	7
6	F	4	8	8
57	M	4	1	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 Domm¹ 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.

Gsell² 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 test² and by the rank sum method³ 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