cephradine (given as 11 μg/ml after a 500-mg oral dose) readily exceeds the M.I.C. in all cases and exceeds the M.B.C. for all except the methicillin-resistant strains. These results are far more persuasive than those quoted in the promotional literature.—I am, etc.,

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SIR,—While accepting that it is the duty of experts like Drs. J. D. Williams and A. M. Geddes to keep a watchful eye on the advertising of antibiotics, I would like to refute the implications of that part of their letter (14 April, p. 116) dealing with the advertising of amoxycillin. It is my opinion that this letter may itself mislead doctors into believing that amoxycillin and ampicillin are the same compound, which is completely untrue.

Amoxycillin is absorbed, distributed in the body, and eventually excreted from the body as amoxycillin and at no time is it converted to ampicillin. As is correctly stated, the two antibiotics differ in structure only by an OH group but, as any pharmacologist can confirm, this can make a radical change in the properties of a drug. One only has to consider L-dopa, which differs from L-tyrosine merely by the possession of an OH group, and the remarkable difference in properties between benzylpenicillin and ampicillin resulting from the substitution of an NH_2 group.

Certainly amoxycillin and ampicillin have a similar (but not identical) antibacterial activity. Amoxycillin, however, has been shown to be more effective in experiments in vivo and this has recently been shown to be associated with higher bactericidal activity against many Gram-negative organisms (G. N. Robinson, to be published). The absorption of the two antibiotics is quite different. May[1] has shown that some patients with infections that have failed to respond to ampicillin have, indeed, been improved by amoxycillin with conversion of purulent sputum to mucoid.

Finally, the two antibiotics differ in the frequency with which they induce rashes in patients with infectious mononucleosis. Whereas ampicillin causes rash in about 90% of patients suffering from this disease, a search of our records of over 5,000 patients treated with amoxycillin reveals seven patients with an eventual diagnosis of infectious mononucleosis, only two of whom developed a rash. Although it is too early to draw any definite conclusions, our present information suggests that the incidence of rash is less than that of ampicillin and more in line with that of other oral antibiotics.

Of course amoxycillin is closely related to ampicillin, but therapeutic progress frequently results from a close study of the differences between two related drugs rather than from overstating their similarities. This is one of the directions, therefore, that we shall continue to explore for new and more effective antibiotics.—I am, etc.,

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1 May, J. R., and Ingold, A., *British Journal of Diseases of the Chest*, 1972, **66**, 185.

Serum Lithium Estimations

SIR,—Dr. J. G. Weir (10 February, p. 356) must have been unfortunate with his serum lithium determinations. The disparity which he quotes between simultaneous determinations in different laboratories (0·6 and 1·0 mEq/l., 0·2 and 0·46 mEq/l.) is considerably larger than that found in parallel determinations in most laboratories. With a reasonably sensitive flame photometer it is not difficult to achieve relative standard deviations of 2% or less. (For those who use Eppendorf flame photometers it may be worth knowing that photomultiplier RCA 931 A is more sensitive at 671 nm than the previously recommended photomultiplier RCA IP 22).

Dr. Weir also reports that the serum lithium concentration might vary considerably from time to time even in patients who meticulously maintained constant lithium intakes. In one of his patients the serum lithium level was usually around 0·4—0·6 mEq/l., it then suddenly rose to 2·0 mEq/l., and a fortnight later it was 0·2—0·5 mEq/l., all with a constant lithium intake. This variation may of course have been due to analytical error, but it seems unlikely. If the blood samples were drawn at different time intervals after the intake of lithium—and nothing to the contrary appears from Dr. Weir's letter—variation was in fact to be expected.

The variation has two main causes, one during the first 10 to 12 hours after the intake of lithium and another thereafter. During the hours following the intake of lithium, when the lithium ion is being absorbed from the gastrointestinal tract, the serum lithium concentrations shows marked variations (fig. 1), and since the rate of absorption differs from one person to another (fig. 2) as well as in the same person from day to day serum lithium concentrations during the period of absorption are ill-suited as guides for treatment. With ordinary lithium tablets complete gastrointestinal absorption may last 6 to 8 hours and with retard preparations 8 to 10 hours. Blood samples drawn for monitoring purposes should accordingly not be drawn earlier than at least 10 hours after the last intake of lithium—perhaps, to be on the safe side, 12 hours would be better.

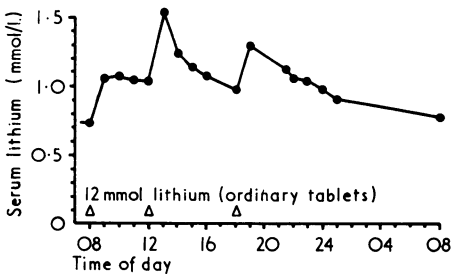

FIG. 1—Serum lithium concentrations throughout 24 hours in a patient on lithium maintenance treatment with drug administrations at 8 a.m., 12 noon, and 6 p.m.

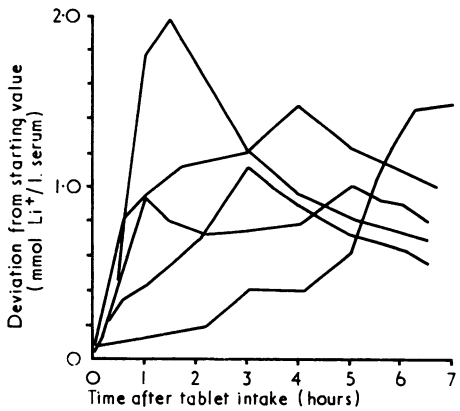

FIG. 2—Changes in the serum lithium concentration of five patients given a single dose of lithium carbonate, 0·7 mmol lithium per kg body weight, at time zero.

When gastrointestinal absorption of lithium is finished the serum lithium concentration falls evenly and the fall follows an exponential course. Blood samples drawn, for example, 18 or 24 hours after the last intake will therefore show lower lithium values than blood samples drawn at 12 hours. So far as Dr. Weir's patient is concerned it seems possible that the serum lithium values of 0·2—0·5 mEq/l., and 0·4—0·6 mEq/l., were found in blood samples drawn, for example, 18 hours after the last intake of lithium and that the value of 2·0 mEq/l., was found in a sample drawn before the gastrointestinal absorption had been finished.

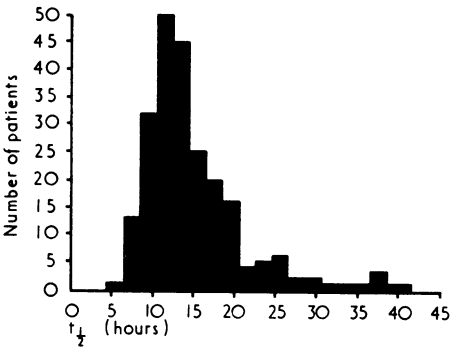

FIG. 3—Distribution of 226 patients according to their serum lithium half-time, $t_{\frac{1}{2}}$, during the interval between 12 and 20 hours after the last intake of lithium.

The rate at which the serum lithium concentration falls after absorption is finished is determined primarily by the renal lithium clearance. Since this varies considerably from one person to another the rate at which serum lithium falls also shows great variation (fig. 3), and consequently one cannot employ a common factor for converting 18-hour or 24-hour values to 12-hour values. This means that standardization of the time interval between the last intake of lithium and the drawing of blood is essential when using serum lithium concentrations as a reliable guide for treatment and adjustment of dosages. A time interval of 12 hours seems recommendable for both theoretical and practical reasons. Employment of the term "12-hr standard serum lithium" might serve to emphasize the importance of having the time interval standardized.—I am, etc.,

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Acute Pancreatitis in Mycoplasma pneumoniae Infections

SIR,—Several complications of respiratory tract infections with *Mycoplasma pneumoniae* have been described, including meningoencephalitis, pericarditis, and various skin manifestations.[1 2] We have recently seen four patients (aged from 15 to 69 years) with acute pancreatitis after pneumonia caused by *M. pneumoniae*. In three of the patients the pancreatitis developed in the third week after the onset of cough, by which time the respiratory tract symptoms had almost disappeared.

The diagnosis of *M. pneumoniae* infection