CORRESPONDENCE

This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters. The mandate of this JOURNAL is to disseminate information relating to leprosy in particular and also other mycobacterial diseases. Dissident comment or interpretation on published research is of course valid, but personality attacks on individuals would seem unnecessary. Political comments, valid or not, also are unwelcome. They might result in interference with the distribution of the JOURNAL and thus interfere with its prime purpose.

Survival of *Mycobacterium leprae* in Mice Administered Several Antibiotics *per Os*

TO THE EDITOR:

Treatment of mice by the oral administration of combinations of antibiotics, the majority of which are not absorbed from the gastrointestinal tract, has been proposed as a means of improving the survival of bacterially contaminated congenitally athymic (nude, *nu/nu*) mice ([1]). We wished to determine whether treatment of *Mycobacterium leprae*-infected mice with several of these antibiotics would be contraindicated. In the absence of previous reports in the literature, we measured the activity against *M. leprae* of six antibiotics and antibiotic combinations, employing conventionally reared, immunologically normal mice.

Ninety locally bred, male, weanling BALB/c mice, divided among nine groups, were inoculated in both hind foot pads with *M. leprae,* $10^{3.7}$ per foot pad, of a strain that has been intensively studied by the Leprosy Research Unit, Public Health Service Hospital, San Francisco, California, U.S.A. ([2, 5]). Mice of the experimental groups received bacitracin, neomycin, bacitracin plus neomycin, oxytetracycline, polymyxin or oxytetracycline plus polymyxin dissolved in the drinking water, as shown in The Table. Mice of the three control groups were administered tap water *ad libitum. M. leprae* were harvested from the pooled tissues of four foot pads and counted by established methods ([3, 4]).

During the first month of treatment (The Table), the mice administered bacitracin, neomycin or bacitracin plus neomycin had a smaller water intake, and those administered bacitracin, bacitracin plus neomycin,

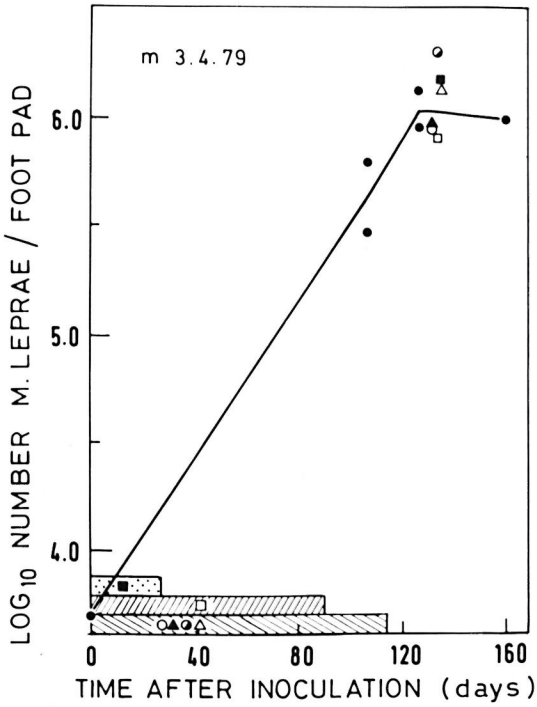
THE TABLE. *Antibiotic dosages.*

Antibiotic[a]	Mean water intake[b] (ml/kg/day)	Mean weight gain[b] (g/day)	Mean drug dosage[b] (mg/kg/day)
Control 1	230	0.13	—
2	230	0.13	—
3	220	0.17	—
Bacitracin	200[c]	0.05[c]	817
Neomycin	200[c]	0.13	805
Bacitracin plus Neomycin	160[c]	0.01[c]	632 632
Oxytetracycline	220	0.14	109
Polymyxin	240	0.12[c]	61
Oxytetracycline plus Polymyxin	230	0.08[c]	117 58

[a] Bacitracin was purchased from the Commercial Solvents Co., Terre Haute, Indiana, U.S.A.; neomycin was purchased from the Upjohn Co., Kalamazoo, Michigan, U.S.A.; oxytetracycline and polymyxin were purchased from Pfizer, Inc., New York, New York, U.S.A. The antibiotics were administered in the drinking water in the following concentrations: bacitracin and neomycin, 4 g per l; oxytetracycline, 0.5 g per l; polymyxin, 0.25 g per l. Bacitracin, neomycin, bacitracin plus neomycin and oxytetracycline were administered for 114 days, beginning on the day of inoculation; polymyxin alone was administered for 90 days, and the combination of oxytetracycline plus polymyxin for 27 days, beginning on the day of inoculation.

[b] Measured during the first month only.

[c] Different from control values ($p < 0.05$).



THE FIGURE. Multiplication of *M. leprae* in the mouse foot pad as a function of time after inoculation. Harvests of *M. leprae* from the various groups of mice are represented as follows: ●—control; ○—bacitracin-treated; ▲—neomycin-treated; ◑—bacitracin plus neomycin; △—oxytetracycline; □—polymyxin; ■—oxytetracycline plus polymyxin. The solid line represents the bacterial growth curve in untreated mice.

The shaded bars along the abscissa represent the periods of administration of the various antibiotics and antibiotic combinations.

or oxytetracycline plus polymyxin experienced a weight gain smaller than that of the untreated controls. The only deaths during the first month occurred among mice treated with bacitracin (1 of 10) and those treated with bacitracin plus neomycin (3 of 10).

M. leprae had multiplied to the level of $10^{5.63}$ per foot pad in control mice 106 days after inoculation, and to $10^{6.04}$ per foot pad 20 days later (The Figure). Harvests from treated mice, performed between 132 and 135 days after inoculation, yielded between $10^{5.89}$ and $10^{6.31}$ *M. leprae* per foot pad, indicating that treatment with none of the antibiotics or antibiotic combinations had inhibited multiplication of the organisms.

Aside from considerations of efficacy, the choice of antibiotic combinations may be influenced by considerations of toxicity and cost. Bacitracin plus neomycin was clearly the more toxic of the combinations; oxytetracycline plus polymyxin, the more expensive. Therefore, because neither combination showed activity against *M. leprae*, there appears no compelling reason to choose one over the other. It might be most efficient to employ both combinations in sequence, as recommended by Gullino, *et al.* [1].

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