Comparison of B1912 and Clofazimine (B663) in *Mycobacterium leprae* Infections (35654)

CHARLES C. SHEPARD, LAURA L. WALKER, ROSALIND M. VAN LANDINGHAM, AND MARTHA A. REDUS

Center for Disease Control, Health Services and Mental Health Administration, Public Health Service, United States Department of Health, Education, and Welfare, Atlanta, Georgia 30333

B1912 is a newly synthesized type of rimino compound; it has about the same activity against tubercle bacilli in mice as clofazimine (B663) (1). Clofazimine is now generally accepted as the drug of choice in treating infections of man with sulfone-resistant *M. leprae*. Like clofazimine, B1912 deposits in the tissues of mice and other experimental animals, but it gives higher serum levels and lower tissue levels (except in fat) than clofazimine under similar conditions. We have compared B1912 and clofazimine in *M. leprae* infections in mice.

Materials and Methods. The methods were the same as those described in the accompanying paper (2).

Results. The activity of clofazimine and B1912 was compared (Fig. 1, Table I). The two drugs were administered from Day 70 to Day 140 after infection. Dosages of 0.00001% and 0.0001% of either drug in the diet were ineffective; 0.001% delayed the growth 233 and 209 days, respectively, and 0.01% delayed it 356 and 309 days. Thus, the results with the two compounds were very similar.

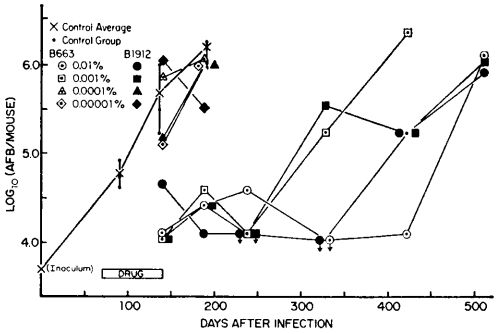

FIG. 1. Comparison of the effect on *M. leprae* of B1912 and clofazimine (B663). The drugs were administered in the diet in the concentrations shown. The values marked by arrows indicate maximal estimates in cases where no bacilli were found during the counting procedure.

TABLE I. Effects of Clofazimine (B663) and B1912 on the Multiplication of *M. leprae*.

Drug	Dosage[a]	Growth delay[b]
B663	0.01%	356
	0.001%	233
	0.0001%	0
	0.00001%	36
B1912	0.01%	309
	0.001%	209
	0.0001%	35
	0.00001%	0

[a] The drug was administered from Day 70 to Day 140 after infection.

[b] Days of delay relative to control curve.

In the case of rapidly eliminated drugs, growth delay that lasts distinctly longer than the period of drug administration can be interpreted as damage to the bacteria, resulting either in bactericide or in bacteriostasis that persists in the absence of drug. Clofazimine and B1912, however, are eliminated only very slowly, so the growth delay could have been bacteriostasis in the presence of drug.

Discussion. In spite of the difference in the pattern of tissue deposition of clofazimine and B1912, the two drugs had very similar activities against *M. leprae* growing in the mouse foot pad. In this experiment model most of the bacterial multiplication occurs in the fibroblasts (3) normally present in the tissues. Macrophages, cells in which clofazimine has been observed to accumulate, appear later in the growth curve at the end of the

logarithmic phase of bacterial growth. At the low levels characteristic of the minimal effective dosage for *M. leprae*, deposition of drug might not occur; the observations of deposition have been made at high dosages. Nevertheless, in this experiment the growth delay after the highest dosage, 0.01%, was very similar with the two drugs, and at this dosage tissue deposition of both of these highly pigmented compounds was clearly apparent.

The minimal effective dosage found in this experiment was higher than that found in the previous experiment (4). The difference is presumably caused by bacterial strain differences. In another experiment in progress, the lower dosage, 0.0001% has again been found active.

Summary. The effect of clofazimine was compared with another, more newly developed rimino-compound, B1912, in *M. leprae* infections in mice. The two drugs were found to have very similar activity.

This work was supported in part by an interagency agreement with the National Institute of Allergy and Infectious Diseases, National Institutes of Health, under the U.S.–Japan Cooperative Medical Science Program, Clofazimine (B663) was obtained through the courtesy of Dr. W. A. Vischer, J. R. Geigy S.A. Basel, Switzerland and B1912 through the courtesy of Dr. J. A. McFadzean, May and Baker Ltd., Dagenham, Essex, England.

1. Barry, V. C., Sci. Proc. Roy. Dublin Soc. Ser. A. **3**, 153 (1969).

2. Shepard, C. C., Walker, L. L., Van Landingham, R. M., and Redus, M. A., Proc. Soc. Exp. Biol. Med. **137**, 725 (1971).

3. Shepard, C. C., and McRae, D. H., J. Bacteriol. **89**, 365 (1965).

4. Shepard, C. C., Proc. Soc. Exp. Biol. Med. **122**, 893 (1966).

Received Jan. 8, 1971. P.S.E.B.M., 1971, Vol. 137