

Minimal Bactericidal Dietary Concentration of Minocycline for *Mycobacterium leprae*-infected Mice is Very Low and Similar to its Minimal Inhibitory Dietary Concentration

TO THE EDITOR:

Previously it was found, by both the kinetic and proportional bactericidal method, that minocycline was consistently bactericidal for *Mycobacterium leprae* in infected mice (^{2, 4}). This activity was obtained at levels which were exceeded several fold by standard doses in man (²). Furthermore, we found that for seven different *M. leprae* isolates continuous administration of 0.01% and 0.04% w/w minocycline in the mouse diet consistently inhibited the growth of *M. leprae* (serum levels 0.11 µg/ml and 0.31 µg/ml, respectively), while 0.004% inhibited 5 of 7 strains and 0.001% was consistently inactive (serum levels ≤ 0.08 µm/ml) (³). These present studies were initiated to determine by the proportional bactericidal method (¹) minocycline's minimal bactericidal dietary concentration for a single strain of *M. leprae*.

In this study, groups of BALB/c female mice (Jackson Laboratories, Bar Harbor, Maine, U.S.A.) were infected in both hind foot pads with 10¹, 10², or 10³ *M. leprae* and fed diets for 60 days thereafter containing various concentrations of minocycline (0.004%, 0.01%, 0.04%, 0.06%, 0.1%); controls = 0%. One year after the discontinuation of therapy, foot pads of 8 or more mice (generally 10) from each group of mice were harvested, and the number of *M. leprae* counted microscopically (⁶). If ≥ 10⁵ *M. leprae* were found, multiplication was considered to have occurred (⁶). From these results the percentage of bacteria killed was quantitated by the method of Spearman and Kärber (⁵).

The results of these studies are summarized in The Table. Minocycline 0.004% was found to have had no significant bactericidal activity for *M. leprae* (p = 0.14). On the

THE TABLE. Killing of *M. leprae* by various dietary concentrations of minocycline.

Minocycline dietary concentration	No. <i>M. leprae</i> inoculated			% Killed ± S.E.	Probability that killing occurred
	10 ¹	10 ²	10 ³		
	No. foot pads in which <i>M. leprae</i> grew/No. foot pads inoculated				
0.0% (Control)	3/10	3/10	8/10		
0.004%	2/10	6/14	5/18	68 ± 25	0.14
0.01%	0/14	4/14	3/10	85 ± 11	0.01
0.04%	0/10	0/10	12/18	82 ± 12	0.01
0.06%	1/10	1/10	3/8	85 ± 12	0.02
0.1%	0/10	1/10	3/10	90 ± 7	0.001

other hand, all other dietary levels of minocycline tested (0.01%, 0.04%, 0.06%, and 0.1%) were bactericidal for *M. leprae* ($p \leq 0.02$).

Unfortunately, in this study the control inoculum itself had low viability. This may account for why the percentage of *M. leprae* killed was less than had been found in previous studies (^{2, 4}). Nonetheless, it would appear that concentrations of minocycline required to inhibit and kill *M. leprae* are similar (^{2, 3}) and easily attainable in man.

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