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Beige Mice Infected with *Mycobacterium leprae*

TO THE EDITOR:

Infection of the beige (c57/6/BG^1/BG^1) mouse with *Mycobacterium avium* complex (MAC) by different routes (e.g., oral, rectal, subcutaneous, intraperitoneal, and intravenous), unlike that in BALB/c mice, results in widely disseminated disease and early mortality ([6, 7]). Disseminated MAC infections in AIDS patients are often encountered near terminally where they commonly cause bacteremia and may contribute to the patient's demise ([13]). The beige mouse model of MAC infections has been used extensively by several investigators to monitor the effectiveness of antimicrobial and cytotoxic therapy whereby the level of bacilli in the liver, spleen, lungs and the blood stream, as well as survival have proved useful parameters of efficacy ([2–4, 9]).

Recently, Gangadharam and Dhople ([5]) reported the utility of the beige mouse model to leprosy research. Specifically, they infected beige mice and BALB/c mice in parallel both intravenously (i.v.) and intraperitoneally (i.p.) with 1×10^7 *M. leprae* and in the foot pad with 6×10^3 *M. leprae*. They noted that while BALB/c mice infected i.v. or i.p. did not develop liver or spleen infections, beige mice infected by both routes developed infection at both sites, peaking at 4 months with *M. leprae* levels of 3.3–6.2×10^5 bacilli/g of tissue which fell somewhat but was maintained at 1.3–2.1×10^5 bacilli/g at 12 months. In these studies beige mice infected in the foot pad attained levels of *M. leprae* peaking at 3.42×10^6 from 4 to 9 months postinfection, a level 30%–50% higher than that found in BALB/c mice in-

THE TABLE. M. leprae *in tissues of* M. leprae-*infected mice.*[a]

Group	Tissue	Months after infection		
		8	13	22
		(*M. leprae*/foot pad)		
Right hind foot pad-infected beige mice	Right hind foot pad	1.6×10^5	1.6×10^5	1.6×10^5 3.2×10^4 3.8×10^5
	Left hind foot pad	$< 8.2 \times 10^4$	$< 8.3 \times 10^4$	
	Spleen	$< 3.0 \times 10^4$	$< 3.7 \times 10^4$	
	Liver	$< 3.0 \times 10^4$		
i.v.-infected beige mice	Right hind foot pad	$< 8.0 \times 10^4$	$< 8.2 \times 10^4$	$< 1.0 \times 10^4$ $< 1.0 \times 10^4$ $< 1.0 \times 10^4$
	Left hind foot pad	$< 8.5 \times 10^4$	$< 8.2 \times 10^4$	
	Spleen	1.25×10^5	$< 3.2 \times 10^4$	
	Liver	$< 3.7 \times 10^4$		
BALB/c mice infected in hind foot pads	Hind foot pads	2.21×10^5		

[a] Numbers represent amounts of AFB in single foot pads or tissues, except foot pads from BALB/c mice which represent numbers of bacilli in four hind foot pad pools.

fected in parallel but not at the level found in nude mice, averaging 10^9/foot pad ([10, 11]). Because of the more luxuriant growth and dissemination found in those studies, we also infected beige and BALB/c mice in parallel utilizing both the foot pad and i.v. routes.

We infected two groups of beige mice with 5×10^3 mouse-derived and logarithmically multiplying *M. leprae* in either the right hind foot pad or intravenously. In parallel, a group of BALB/c mice was infected in both hind foot pads with the same *M. leprae* inoculum. At 8, 13, and 22 months subsequently, the number of bacilli in the right hind foot pads of one or more beige mice infected by each route was evaluated, as well as the number of *M. leprae* in spleens (8 and 13 months after infection), livers (8 months after infection), and the contralateral left hind foot pad (8 and 13 months after infection). Also, from three beige mice infected by the foot pad route (8 and 13 months after infection) and the intravenous route (8 months after infection) various tissues were examined microscopically following both hematoxylin-and-eosin (H&E) as well as Fite-Faracco staining. These generally included the nose, tail, liver, ears, thymus, spleen, sciatic nerve, kidney, and skeletal muscle. Finally, the number of acid-fast bacilli (AFB) in four hind foot pools of BALB/c mice were enumerated microscopically 8 months after foot pad infection.

The number of *M. leprae* obtained by foot pad and i.v. inoculation in these studies at 8, 13, and 22 months later is presented in The Table. It is noteworthy that while *M. leprae* grew in BALB/c mouse foot pads to 2.21×10^5 by 5 months, the level obtained in individual right foot pads of beige mice at several time intervals was only minimally higher in one mouse and at one time interval. Furthermore, AFB from right hind foot pad-infected beige mice never disseminated to the left hind foot pad or to other organs (no granulomas or AFB seen). Of the i.v.-infected beige mice there was only one instance, a spleen obtained 8 months after inoculation, wherein the presence of *M. leprae* was detected (2×10^5 *M. leprae*/foot pad or 2×10^6 *M. leprae*/g of tissue). In no other organ system or in the spleen at other time intervals were either granulomas or AFB found.

In these studies in beige mice following foot pad inoculation we found no evidence of superior growth to that of BALB/c mice and no evidence for systemic dissemination. Gangadharam, *et al.* ([5]) found essentially the same results in their foot pad-infected mice. However, the numbers of *M. leprae* found in beige mice in their study were slightly greater than in BALB/c mice, but not to levels obtained in nude mice ([10, 11]). Gangadharam, *et al.* ([5]) found that using much larger (10^7) i.v. and i.p. inocula than we used (5×10^3) consistent infection

in the liver and spleen resulted, the intensity of which decreased with time after 5 months. In our study we found early infection in the spleen only, which resolved entirely, and no evidence of infection to the liver or elsewhere. The differences between the study done by Gangadharam, *et al.* ([5]) and our own in the level of visceral involvement following i.p. infection may well be a function of the different inoculum sizes utilized. In any event, in neither Gangadharam's nor our own study did visceral involvement of the liver and spleen approximate that found in nude mice (2×10^8/g of tissue) ([12]) or that in beige mice infected with MAC (10^8–10^9 bacilli/g of tissue) ([1]).

In beige mouse-infected foot pads local growth was not found in both studies to be substantially higher than in BALB/c mice, and not to levels in nude mice (10^8–10^{10}) or neonatally thymectomized Lewis rats (10^8) ([8]), and even i.p. or i.v. inoculation did not result in a profound, progressive, systemic infection comparable to that obtained in *M. leprae*-infected nude mice or MAC-infected beige mice. We, therefore, see no reason to utilize the beige mouse model in future studies of leprosy chemotherapy.

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