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Multiplication of *Mycobacterium leprae* in the Mouse Footpad

To the Editor:

Little progress has been made in the field of leprosy compared with other bacterial infections because it has not been possible to cultivate the causative organism or transmit the infection to experimental animals. It is obvious that until these two basic requirements for studying an infectious disease are achieved, leprosy research will remain restricted and pitifully slow. Therefore, despite the innumerable unsubstantiated claims in the past of cultivation or transmission, every new claim must be thoroughly investigated. Since 1960 Shepard ([5, 6]) in a series of papers has set out very clearly and convincingly the methods by which he claims human leprosy can be transmitted to the footpads of mice. It is obvious that a claim of such importance must be confirmed by workers in other laboratories before it can be accepted and, if confirmed, the resulting experimental infection should be ruthlessly exploited to fill the vacuum in our knowledge of the pathogenesis of leprosy. Nevertheless, those undertaking the confirmatory experiments must approach them on a scientific basis and it is their duty to carry out their experiments repeating precisely every essential detail laid down by the originator. For these reasons we are compelled to criticize both the work of Dr. Kirchheimer in his paper entitled "Attempts at growth of *Mycobacterium leprae* in footpads of mice and guinea-pigs" (The Journal **32** (1964) 9-17) and The Journal for publishing the paper as presented. Dr. Kirchheimer makes it clear in his introduction that he set out to corroborate Shepard's findings. This he has inadequately undertaken for three important reasons: *a*. The footpads were not inoculated with *M. leprae* from man but with acid-fast bacilli recovered from mouse embryomata inoculated with *M. leprae* three months previously. *b*. The acid-fast bacilli obtained from the mouse embryomata for inoculation of the footpads contained a high proportion of granular bacteria; yet there is now overwhelming evidence that such organisms are dead ([3, 4, 8]), and *c*. 10^5 acid-fast bacilli were inoculated into the mouse footpads, an inoculum size that Shepard ([6]) has shown is not optimal for subsequent multiplication of *M. leprae* in the footpad. Moreover, the assessment of multiplication in the footpads at the time of death or sacrifice was determined only histologically and not quantitatively by counting the total number of bacilli harvested from the footpads, a prerequisite for any accurate assessment of limited multiplication.

It is true that Dr. Kirchheimer fully admits some of these deficiencies and it is also true that in a footnote he states that experiments in progress where he has inoculated mouse footpads with fresh suspensions of *M. leprae* obtained from nasal washings of untreated patients indicate multiplication. We submit that these admissions fully justify our criticism.

We consider it most unfortunate that THE JOURNAL of the International Leprosy Association should have accepted a paper that to the general reader would indicate that *M. leprae* cannot be transmitted to the mouse footpad when its own Association at the recent International Congress in Rio fully accepted Shepard's work (THE JOURNAL **31** (1963) 473). The Technical Committee on Pathology and Experimental Transmission were satisfied that the claims of Shepard had been fully substantiated and extended by one of us, Rees ([2, 3, 4]), by Janssens and Pattyn ([1]), and substantially similar results had been obtained in the hamster ear by Waters and Niven ([7]).

We therefore note with pleasure (THE JOURNAL **32** (1964) 87) that Dr. Shepard has been honored with the Gorgas Medal and the Timble Award for his success in producing multiplications of *M. leprae* in the footpads of mice, which undoubtedly represents the most significant experimental advance since Hansen first identified the organism in human lesions.

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November 1964

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