to other drugs, the knowledge of which would help to eventually identify groups at risk. This could be achieved by the undertaking of a case-control study in a population of individuals with leprosy in which the cases would be those who had ARF, and the controls a sample of those who did not. It is important to use incident cases and appropriate controls in such studies, but even cases which already occurred, such as those detected by the São Paulo state surveillance system, could be used insofar as the selection of controls is adequate ([6]). The identification of risk groups could be extremely helpful for health professionals, who could use this information to identify individuals who should either be monitored as to their renal function during WHO/MDT or should receive an alternative drug schedule to treat their leprosy with a lower risk of developing ARF as a drug reaction.

—Sergio de A. Nishioka, M.D., M.Sc.

Centro de Ciencias Biomedicas
Universidade Federal de Uberlandia
Av. Para 1720
38400-902 Uberlandia, MG, Brazil

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Bacillary and Histopathological Findings in the Peripheral Nerves of Armadillos Experimentally Infected with *M. leprae*

To the Editor:

The article by Scollard, *et al.* in the June 1996 edition of the Journal ([2]) raises a number of interesting points concerning the presence or absence of *Mycobacterium leprae* in the peripheral nerves of armadillos found to have disseminated infection at the time of sacrifice. The Table (page 147) indicates that of the three animals with disseminated infection at sacrifice, number 632 had bacilli in all 4 nerves, but number X5 had bacilli in only 3 out of 6 and number X6 in only 1 out of 7 nerves examined. Thus, out of a total of 17 nerves examined, no fewer than 9 (i.e., over 50%) were negative for *M. leprae,* despite disseminated infection at sacrifice.

These findings are strikingly reminiscent of those in a series of armadillos experimentally infected in the 1970s and 1980s by Dr. R. J. W. Rees, Laboratory for Mycobacterial Research, National Institute for Medical Research, London, U.K., as part of the Immunology of Leprosy (IMMLEP) arm of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), with the main objective of establishing a bank of *M. leprae* sufficient for leprosy projects worldwide, including efforts to develop a specific vaccine for human trials ([3]). The protocol included the submission to Oxford of a wide range of tissues for histopathological examination from all animals sacrificed ([1]). This invariably included right and left main

peripheral nerve trunks from the upper and lower armadillo limbs, from which we cut a minimum of 30 sections for examination with hematoxylin and eosin (H&E) and the Fite-Faraco stain for acid-fast bacilli (AFB). In all of the animals with disseminated infection, the commonest finding in nerve was of AFB in large numbers in all four nerves submitted, usually affecting the epineurial, perineurial, and endoneurial areas. However, this was not invariably the case, particularly in view of the heavy, often massive bacillary multiplication seen in other tissues where it was remarkable that AFB were absent in some of the nerve specimens examined. In several instances, this produced obvious asymmetry, i.e., positive findings on one side but negative on the other, in either the upper or lower limbs. The cellular responses in these animals were typically lepromatous (LL); borderline (dimorphous) changes were not seen in tissues submitted to Oxford.

In view of the main priority of the TDR project briefly described above, it was not possible to consider allocating time or money to the further investigation of a histopathological and essentially incidental finding, unlikely to be of relevance to the development of a bank of *M. leprae* for research purposes. No obvious correlation was seen between the presence or absence of bacilli in nerves and 1) the origin (source) of the inoculum (animal or human), 2) the route of inoculation, or 3) the time between inoculation and sacrifice. It was difficult then, and remains difficult now, to see what further line of investigation could reasonably be pursued by way of explanation. Clearly, it has to be recognized that there is a considerable difference between the time interval from inoculation to sacrifice in the armadillo (12–24 months) compared with the interval between infection and the development of lepromatous leprosy in the human being. However, while this might explain the differences in the extent or intensity of involvement of the peripheral nerves, it would not account for the lack of involvement and asymmetry referred to above.

For reasons which remain obscure, the findings reported by Scollard, *et al.* and our experience in Oxford seem to indicate that peripheral nerve involvement in the armadillo model does not invariably correlate with the extent of ultimate bacillary dissemination.

—A. Colin McDougall, M.D., F.R.C.P.

Department of Dermatology
The Churchill Hospital
Headington, Oxford OX3 7JH, U.K.

Reprint requests to: 87 Lower Radley, Near Abingdon, Oxfordshire OX14 3BA, U.K.

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Drs. Scollard, Lathrop and Truman Reply

To The Editor:

It is reassuring to learn that Dr. A. C. McDougall and his colleagues, examining a larger number of specimens in a different laboratory, made observations similar to ours concerning nerve involvement in experimental *Mycobacterium leprae* infections in the armadillo. We share his view that the reasons for the individual differences in extent and intensity of infection remain obscure. A number of factors, including the source of the bacilli, viability, variation between isolates, and individual host resistance, could all contribute and merit additional investigation. However, the question of asymmetry may be more immediately informative.

Nerve lesions in human leprosy are notably asymmetric, and the finding of similar