Rodrigues, *et al.* Reply to Letter from Drs. Nishioka and Goulart

TO THE EDITOR:

We appreciate the comments of Drs. Nishioka and Goulart regarding the choice of controls for case-control studies on leprosy. This has been recognized as a controversial subject, especially with respect to the evaluation of a possible protective effect of BCG ([4, 5]). As a general rule, in case-control studies controls should be selected from a reference population with an opportunity of exposure similar to the cases and with the equivalent probability of having been included in the study if they develop the disease of interest. Adjustment for differences in these aspects may be done by matching cases and controls on selected variables at the design stage of the investigation or by conducting a stratified or multivariate analysis.

In our study ([3]), controls were age-, sex-, and geographically matched to cases. The selection of classmates from cases also assured that they had a similar socioeconomic background and were representative of the population at risk, from which the cases came. As far as we can anticipate, the balance of these characteristics between cases and controls is required to obtain comparable groups regarding BCG coverage and the risk of developing clinical leprosy. We agree with Drs. Nishioka and Goulart's comment that cases are likely to be more exposed to *Mycobacterium leprae* infection than controls because cases are more likely to have a household contact than controls. We would say that this difference, if not taken into account, would overestimate the protective effect of the vaccine. Some authors consider that the methodological issue about vaccine efficacy and effectiveness is not whether cases and controls have the same "amount of exposure," but if there is "comparability of exposure to infection" between vaccinated and unvaccinated individuals ([1, 2]).

We would have liked to match cases and controls with regard to having or not having a leprosy contact in the household. This would resolve the problem of opportunity to exposure to infection. Controls would have been selected either from the community or from within the case's household, depending on whether the case had or did not have a household contact. To be more exact, the clinical form of the index leprosy contact also should be taken into consideration. This turned out not to be feasible, considering the matching required on age and sex, which may also relate with the length of exposure and the 3:1 ratio between controls to cases adopted in the study. The selection of household controls other than the contacts of the cases, as suggested by Drs. Nishioka and Goulart, seems, in the same way, not feasible.

In order to control for a possible bias related to a difference in household contact among cases and controls, we carried out a stratified analysis of our data. The results indicated that among case/control sets (matched analysis) with a leprosy household contact the BCG protective effect was 90.7% (95% C.I. = 72.4%–96.9%). Among sets with no leprosy contacts, the BCG protective effect against leprosy was estimated to be 77.3% (95% C.I. = 34.3%–92.2%). There-

fore, similar levels of BCG efficacy for preventing leprosy were found when compared with 81% protection in our study ([3]).

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