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EDITORIALS

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BCG-INDUCED ACTIVATIONS

I. Last year, Jonquieres, of Buenos Aires, told in a letter [THE JOURNAL **27** (1959) 268] about reactions occurring in arrested lepromatous cases which had been given BCG vaccination for the purpose of establishing lepromin positivity and so of consolidating recovery and lessening the danger of relapse. In 5 of the 36 cases, reactivations of rather unusual kinds occurred after periods such as to suggest that they had been induced by the vaccination.

According to his letter (modified by a later one published in this issue), two patients —in spite of continued sulfone treatment—had abrupt flare-ups of rosy macular spots which were bacteriologically negative on first examination but were found positive later. Another two had reactivations with, besides acute spots, very small lepromas, one found bacteriologically positive at once, the other on repeat examination. Finally, there was a case regarded as of opposite significance, in a Mitsuda-negative man who had had residual neural changes. He developed evanescent, bacteriologically negative, circinate macules after vaccination and also became lepromin positive, so it was held that this patient had benefited from the reaction.

Jonquieres asked, in effect: (1) Have others observed such reactions after BCG vaccination of arrested, bacteriologically-negative, lepromatous cases? (2) Does the supposed benefit of lepromin positivity in such cases justify the attempt to induce that condition by means of BCG vaccination, in view of the risk of reactivating the disease? (3) The third question would seem to assume that, ordinarily,

apparently-cured lepromin-negative cases would be continued on sulfone treatment indefinitely unless they should change to positive, in which case the treatment might be discontinued. On that basis it is asked whether one should at some time attempt to prove cure by some measure which might induce reactivation.

Montestruc, of Martinique, contributes to this matter in the *Correspondence* section of this issue. He answers the first question by saying that he has done the same thing with lepromatous cases that Jonquieres tells about and has seen the same reactions. Because reactions may sometimes be severe and cannot always be controlled, he holds that the answer to the second question is no, that vaccination is not justified.

II. Montestruc then goes into the matter of precipitation of tuberculoid skin lesions, in others than actual (or recognized) cases, as a result of BCG vaccination. In his own experience[1] there was a young girl who first showed skin lesions a month after vaccination; but neural changes indicated that when vaccinated she had already had the disease in pure neuritic form. He recalls that Floch[2] had reported the development of tuberculoid skin lesions in several schoolchildren in French Guiana 1 to 3 months after general BCG vaccination, and that Bechelli and Quagliato[3] had done so previously. The last-named authors believed that the vaccination had not protected against infection, whereas Montestruc believes—as Floch does—that the individuals had actually been infected before the vaccination but (this being obviously implied) had developed manifestations after the increase of tissue reactivity resulting from the vaccination.

From both the theoretical and practical—or potentially practical—points of view, we would suggest, this question merits further consideration. From the outset, and especially since Igarashi and Hayashi[4] reported that the outcome with individuals of Mitsuda's original cases who had been lepromin positive had been relatively good (80% not relapsed in 10 years), there has been general acceptance of the idea that lepromin positivity, which results from tissue reactivity, indicates resistance and is of favorable significance. The present discussion involves the further question—the answer as yet unproved, but widely believed to be affirmative—whether or not there is a similar advantage

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[1] MONTESTRUC, E., BERDONNEAU, R. and BENOIST, J. Réaction tuberculoïde dans la lèpre après administration de B.C.G. *Arch. Inst. Pasteur Martinique* **11** (1958) 108-110. [Abstract in THE JOURNAL **27** (1959) 400.]

[2] FLOCH, H. and MAILLOUX, M. Relations entre l'apparition rapide de plusieurs cas de lèpre tuberculoïde et la vaccination par B.C.G. intradermique chez des enfants en pays d'endémicité lépreuse. *Bull. Soc. Path. exot.* **51** (1958) 353-359 (abstract in this issue).

[3] BECHELLI, L. M. and QUAGLIATO, R. Dados epidemiológicos iniciais sôbre a possivel ação premunitoria do B.C.G. em comunicantes de lepra. *Rev. brasileira Leprol.* **24** (1956) 23-36.

[4] IGARASHI, M. and HAYASHI, F. Observation of patients with atypical Mitsuda reactions, after an interval of ten years. *Internat. J. Leprosy* **8** (1940) 457-464.

in lepromin positivity induced by BCG vaccination, and if so how great that advantage may be—whether or not it will serve to prevent relapses.

From this point of view Jonquieres' second question may be elaborated as follows: Considering the known undependability of discharged patients in the matter of continuing their after-treatment, and also the known frequency of relapse, is it justified to attempt to reinforce resistance by inducing lepromin reactivity in Mitsuda-negative arrested lepromatous cases by means of BCG vaccination, or is the risk of reactivating the disease too great to justify that measure?

A sound answer would require comparative evaluation of the frequencies, and also the consequences as regards damage, of reactivation of the disease in the two circumstances, i.e., spontaneous or natural relapse on the one hand, and on the other hand reactivation induced by the vaccination. There is needed an experiment on a relatively large scale, carried out on a sustained basis over a period of years, whether in one large institution or in several cooperating institutions under centralized direction. From time to time as lepromatous patients under treatment are declared bacteriologically negative and therefore candidates for future parole, they would be tested with lepromin and tuberculin. Lepromin negatives would be divided into vaccination and control groups, under rules set up by competent statisticians. The numbers of cases would be added to periodically until the total involved in the experiment is sufficiently large; how long the follow-up observations should be carried would have to be determined. One wonders about the prospects of such an experiment being undertaken.

In the meantime, of course, observation of precipitation of leprosy lesions in apparently healthy persons should be continued. No one knows what may have happened in heavily endemic areas like, for example, India, where mass BCG vaccination against tuberculosis has been carried out, for the people vaccinated are not observed very long. Leprologists in such countries might be alerted to make such observations where possible.

—H. W. Wade