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EDITORIALS

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THE UNKNOWN FACTOR IN LEPROSY

In a disease about which we know so little as we do about leprosy it may seem presumptuous to speak of the unknown factor in its etiology but among all its obscurities there is one that is outstanding. Anyone who has studied leprosy knows well what happens when the patient's health deteriorates—how there generally follows an exacerbation of the disease. We associate leprosy with malnutrition, predisposing diseases and everything which weakens the constitution. But while we know that all this is true, and that improving the general health is the most important element in combating leprosy, we cannot but feel that it is not the whole truth. We have seen the strong and healthy suffering from the severe lepromatous form of the disease, while the unhealthy weakling, exposed to the same infection and perhaps living in the same family, escaped unscathed or with only a mild neural lesion. Undoubtedly resistance to leprosy does not depend entirely on the state of the general health, important though that certainly is. There is another, unknown factor which determines resistance. What is it?

Rotberg[1] hypothesizes an "N factor" which is present at

[1]Rotberg, A. Some aspects of immunity in leprosy and their importance in epidemiology, pathogenesis and classification of the forms of the disease; based on 1529 lepromin tested cases. *Revista Brasileira de Leprologia* **55** (1937) Spec. No. 45-95.

birth in most infants, but not in all. Those possessing it become allergized on first contact with leprous infection, and thereafter remain resistant to leprosy throughout life. If, later, they are further exposed to infection they are likely to escape without the disease developing, but if it does develop as the result of repeated or severe infections they at least escape the lepromatous form and have, at worst, the neural type with tuberculoid lesions. He bases this hypothesis chiefly on the Mitsuda (lepromin) skin test. Persons in whom the test is positive retain their positivity for life, and a positive result is seldom or never found in a lepromatous case. Thus those who give a positive lepromin test, whether they show signs of leprosy or not, are unlikely ever in future to become lepromatous cases, or to be in a position to infect others. Rotberg is opposed to the idea of racial immunity. His observations seem to show that immunity cuts right across racial and family groups.

This hypothesis, if substantiated, would be a satisfying one. To prove or disprove it, further careful investigation is necessary. The lepromin test must be applied in large numbers of cases, not only in endemic but also in nonendemic countries. It must be applied at all ages from the new-born infant up to adult life, and must be repeated as the child grows up. If it were found that the great majority of the population are guarded at birth against the worst form of leprosy, the form that is probably entirely responsible for perpetuating the disease, then the problem of leprosy control would be considerably simplified. Prophylaxis would then consist of separating out and registering the unprotected minority and preventing their contact with infectious lepers. How this would be accomplished would still remain a problem, but it would be a much simpler one if only a small fraction of the population had to be dealt with.

Recent successes in animal inoculation with human leprosy material tend to confirm the hypothesis that among members of a community similar as regards general health, a minority are much more susceptible to human leprosy than are the others. Two workers (Adler and Burnet) have already published successful results of inoculation of hamsters, and further confirmation of their results may be expected soon. It has to be remarked regarding these experiments that only in a minority of the

hamsters inoculated are the results positive, but in these the bacilli are found in large numbers. There is no progressive gradation between negatives and positives. This would seem to show that only a minority of hamsters are susceptible to human leprosy. If this were proved to be so, it would support the hypothesis that only a minority of human beings are susceptible to leprosy, or at least to its worst forms.

What is this unknown factor in leprosy? Is it present at birth or does it develop as the subject grows up? There is evidence that resistance to leprosy is higher among females than among males, but that this difference does not exist during the earlier years of life. This would tend to show that resistance is related to the secretions of internal glands which develop towards puberty. Is individual resistance also dependent on differences in the endocrine make-up?

Oberdoerffer has suggested that resistance to leprosy is bound up with the functions of the adrenals. The fact that in climates which have annual variations between cold and excessive heat leprosy tends to be worst at the end of the hot weather, when the strain on the heat regulating functions of the adrenals and other endocrine glands is greatest, tends to confirm that theory. Oberdoerffer also advances the theory that dysfunction of the adrenals is caused by sapotoxins from certain plants which form an important constant or seasonal article in the diet of certain peoples, their susceptibility to leprosy thereby being increased.

Whatever the cause and nature of this unknown factor in leprosy, whether it is present at birth or comes into action later, there can be little doubt of its existence and of its importance. The Mitsuda (lepromin) test seems to be one of the most useful aids in trying to elucidate this question. This test alone gives reliable evidence of resistance to leprosy. We cannot yet obtain bacilli from cultures uncontaminated by leproma tissue. But in spite of this disadvantage the test can still be carried out with accurate enough results. It is difficult to standardize a suspension consisting of bacilli and broken down tissue materials; but this need not seriously interfere with the accuracy of results, as it has been shown by various workers that the specific reaction is not appreciably affected by the presence of contaminating material, and that the reaction to lepromin is not greatly affected by the concentration of bacilli

in the suspension, a weak suspension giving almost as strong a reaction as one of ten times the strength.

This investigation would require the collaboration of leprologists all over the world. The test itself is simple to carry out, but the supply of standard lepromin is difficult to insure. It would be an advantage if lepromin of standard strength could be issued from one center to all throughout the world qualified and prepared to use it, either in the form of dry powder sent out with instructions, or as a suspension already made up in ampules.

—E. MUIR