

Observations on the Status of Leprosy Research

TO THE EDITOR:

In contemplating the present state of research in leprosy we can say that positive facts relative to a large amount of experimental work have been practically insignificant. The Second International Colloquium of Leprosy, held in Borstal (October, 1974) left a deep feeling of frustration because in most of the subjects discussed it was not possible to reach positive conclusions, therefore, the contributions of the session were scanty. In confirmation of this statement it is noted that there is still no exact method available for evaluating antileprosy activity of the sulfones as is evident from the discussions at the Colloquium. The following observations may help in evaluating the present state of experimental leprology.

1. The position of tuberculoid leprosy within leprosy. Tuberculoid leprosy must be totally separated from leprosy. This nosologic entity comprises a very important area of indistinctiveness and disorientation when certain factors are considered and evaluated relative to so-called lepromatous leprosy. Such factors are, for example, premunition, contagion and chemotherapy. This confusion has been the most important reason for the lack, to the present, of any exact concept of the premunition value of BCG in leprosy.

2. Value of the so-called leprosy diathesis. It is absolutely necessary to understand that *M. leprae* is unable to settle in a normal organism and, therefore, this abnormality of the organism prior to invasion by the bacillus can be called diathesis, predisposition or autooxidative disease and must be constantly borne in mind in all studies of leprology, be they related to pathogenesis, prevention, treatment or otherwise. It is important to understand that "because one is leprosy, one has Hansen's bacillus" and not "because one has Hansen's bacillus one is leprosy." This is not a play on words but a pathogenic causal ordaining.

3. Curability of lepromatous leprosy. At this stage of leprosy research it is clearly evident that lepromatous leprosy is an incurable disease. It is also evident that miraculous drugs with spectacular effects on this disease will not appear. To persist in the concept of

curability is to miss the point of a great deal of chemotherapeutic research related to this disease. A good controller of the disease must be searched for as a goal in the fight against the same.

4. Value of the lepromatous and indeterminate form in the study of leprosy. Lepromatous leprosy is a bacterial infectious complication of true leprosy disease. In other words, the patient with lepromatous leprosy presents a complex rather than a simple problem and is, therefore, not an appropriate patient in which to study the disease of leprosy. Of all the clinical forms of leprosy, the lepromatous representing as it does the final and most complicated of the leprosy process, must not be used for basic studies in leprosy. The so-called indeterminate form is, in this respect, that most closely approaching the true leprosy disease. It is the form in which leprosy is most purely represented. It represents the autooxidative disease as it has just begun to be complicated by the infectious process.

5. Value of immunology in leprosy. All parameters of immunity which are found to be related in lepromatous patients are the consequence of rather than being responsible for bacterial growth and, therefore, the findings have only a very relative value. The specific anergy of the lepromatous patient to *M. leprae* is the consequence of and not the cause of the growth of *M. leprae*. It is difficult to comprehend and admit that nature provides diseases or alterations definitive for specific bacterial pathogens. It must be borne in mind that autooxidative disease—the biochemical basis of the leprosy diathesis—precedes the growth of *M. leprae* and can of itself depress the so-called mechanisms of immunity.

6. Effects of the "chemotherapeutic" treatment of leprosy. It is absolutely necessary to understand that any specific treatment of leprosy must act on the autooxidative disease (the leprosy diathesis) and not on *M. leprae*. Because of this diathesis there is no value in "killing" Hansen's bacillus with respect to definitive improvement of the disease. This is shown by the impossibility of rendering lepromatous patients' bacilli negative despite prolonged and intensive treat-

ment with drugs of extraordinary bactericidal activity, such as rifampicin. If the problem of leprosy treatment were "to kill" *M. leprae*, then questions have to be asked such as: "Where does the disease reside?" and "Why does *M. leprae* develop in the host?"

7. Metabolic disturbance in leprosy patients. Leprosy patients fundamentally have a disease of their lipid metabolic system, at the level of autooxidation processes of lipids. As a result, other systemic diseases such as cancer, atherosclerosis, diabetes, rheumatism, pigmentary disorders, etc., must show differences in incidence, evolution and pathologic characteristics when they appear in

leprosy patients as compared with their manifestations in nonleprosy persons.

8. Action of sulfones in leprosy. Thorough pharmacologic and toxicologic studies of the sulfones in normal animals can provide data of great value for the understanding of the pathogenesis of leprosy. Autooxidative disease is simply a manifestation opposite to that which sulfones provoke in normal animals.

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Comments on Dr. Chatterjee's Correspondence

TO THE EDITOR:

In his very interesting correspondence (IJL 45 [1977] 294-296), Dr. Chatterjee called attention to some forgotten or neglected bacteriological observations in leprosy research.

Pioneers as well as several modern workers thought that cyanophil germs obtained in attempts to cultivate *M. leprae* might be related to the Hansen bacillus. Concepts of dimorphism or hypotheses regarding a life cycle were early considered. Thinking that this hypothesis afforded an explanation of some clinical features in leprosy we adopted it at the beginning of our work.

Patients with the tuberculoid form of leprosy frequently develop lesions wherever even a few acid-fast bacilli are observed. This small number of germs cannot explain the intensity of the lesions. It seemed rational to suppose that *M. leprae* may exist in another form than as classical bacilli, this form being not observable by routine investigations.

Assays were performed to verify the hypothesis of a life cycle for *M. leprae* and other mycobacteria. Results obtained were the following:

1. Prolonged incubation of bacillary suspensions obtained from lepromas have not enabled us to obtain direct cultures of acid-fast bacilli. In the more propitious cases, bacilli elongation or limited multiplication (X 10, X 20) were observed (⁵).

2. In numerous assays prolonged incuba-

tion (6-12 months) of bacillary suspensions from lepromas or of banal mycobacteria brought forth some peculiar elements (called form 2) possessing bacillary morphology and able to undergo sporulation (^{1,2}).

These microorganisms were regarded by some workers with scepticism and criticism. However, assays in this way were carried on and new results were obtained.

First, it is possible, by using specific media, to induce with various mycobacteria, a rapid and abundant appearance of form 2. Delays of two to six weeks were sufficient whereas in our previous assays 6-12 months were necessary before observing few non-multiplying form 2 organisms (report in preparation).

Second, the successive stages by which sporulated form 2 undergo transformation to acid-fast bacilli were observed with various mycobacteria, in numerous assays (⁸). Furthermore, form 2 types of several mycobacteria reacted respectively to antibiotics, anti-leprosy drugs, as well as to phosphate bromides in the same way as acid-fast bacilli of these mycobacterial species (⁷).

3. With other assays we obtained coccoids only evidenced as cyanophil forms by the Ziehl-Gram technic and further becoming blue-stainable with the Ziehl-Neelsen method.

Cocoid germs were obtained from bacillary suspensions derived from lepromas, crushed leprids, and lepromatous and tuber-