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 nonleprous 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 incubation (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 nonmultiplying 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, antileprous 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.

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

culoid sera filtered and unfiltered through Millipore membranes (0.45 or 0.22 μ). All these leprous materials were inoculated in unclassical media [3,6] (and unpublished data).

4. The obtaining of coccoid microforms after filtration led to examination of the problem of their origin.

Filterable forms of mycobacteria have been the object of controversies in the past. Their existence was finally not admitted because it was never possible to obtain acid-fast bacilli after inoculation of the filtrates in nutritive media. These repeated failures were due to the inability of classical media to allow the evolution of filterable forms into classical acid-fast bacilli.

With our special media used recently and with electron microscopic studies, the stages of development of these inframicroscopic elements (called form 3) were observed until they reached first visible coccoid forms and then became acid-fast organisms (manuscript in preparation).

5. A lot of 34 acid-fast strains issued from coccoid germs were obtained. Biochemical tests provided evidences for a new mycobacterial species ([4]).

Analysis of bacterial cell walls of this species showed that mycolic acid of mycobacterial type with 22-24 carbon chains were present (manuscript in preparation).

If we consider all these facts, it appears that a life cycle characterizes the Mycobacteriaceae. To get and then to observe the characteristic stages of this life cycle, suitable media must be used.

Existence of a life cycle is also well known among various organisms: some bacteria, fungi, protozoans, etc. Numerous workers have showed that environmental variations, i.e., temperature, light, and medium composition, may induce biochemical changes and correlated morphological evolution. These different stages of the biological cycle are the expression of specific portions of the genome.

Particularly, it has been demonstrated that bacterial sporulation is under genetic control and that specific environmental factors are responsible for the activation of sporulative genes.

In mycobacteria it may be considered that inexpressed genes in classical media may be activated under peculiar conditions and thus determine the development of the different stages of the life cycle.

In conclusion, it would be useful to remember that Dr. Wade ([9]) said in 1962: "leprologists in general seem not to have taken very seriously the idea that other than familiar form of *M. leprae* may exist."

The concept of a dimorphism or better of a life cycle in the Mycobacteriaceae, may be a new and beneficial approach for further investigations and leprosy understanding.

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The Problem of Reincorporation into Society of Exleprosy Patients

TO THE EDITOR:

In the year 1944 we had the good fortune to know one of the best leprologists the world has ever seen, Dr. Ernest Muir, who was for many years Sir Leonard Roger's inseparable collaborator and who together earned enough merits in Western Europe to deserve to be called "Fathers of Leprology ROGERS and MUIR," as Danielssen and Boeck had been designated by some in Northern Europe. Together they also accumulated much information about India which has always been considered as the place with the highest prevalence of leprosy.

Muir also deserves credit for being a pioneer in the histopathology of leprosy, considering it fundamentally important in the study of each patient.

It was especially Muir who insisted repeatedly after our first contacts that we should become members of the International Leprosy Association. He naturally succeeded in his purpose, and then asked us to write a report for the IJL describing the leprosy conditions in our peninsula at that time.

The situation could not have been worse. We only knew lepromatous patients with "facies leontina" and some neural patients, terribly mutilated. Most of them were interned in the hospitals, and the few who were not segregated were hidden. We had not yet begun the leprosy campaign which was just going to be initiated by the Spanish dermatologists. Our report was published in the IJL, Volume **15** (1947) 178-182. We tried, briefly, to illustrate that even from remote times the Spanish motivation was profitable to the culture and even to the world's hygiene, always propagating far more good than bad.

At that time leprological matters were far more advanced across the Atlantic in South America than in any of the European countries and fortunately, a large commission of Spanish dermatologists the following year went to Argentina, Brazil and some of the other South American countries. They also visited Cuba, Mexico, U.S.A., Philippines, Hong Kong and so on.

We regard among our teachers Jose M. Fernandez, Guillermo Basombrio, Baliña, Argüello Pit, Castañe Decoud, Quiroga and other Argentines; the Brazilians Agricola, Rabello, Souza Lima, Souza Campos, Azulay, Bechelli and many others; the Mexicans, Latapi, Barba Rubio, Samuel, and Dra. Rodriguez; the Venezuelans, Vegas; Rodriguez, Lara, Manalang, Chiyuto and others from the Philippines. They all taught us a great many advances on leprology which, though it may seem strange after several European wars, were unknown not only to the Spaniards but to the whole of Europe. We say strange because, unless we are wrong, the first scientific knowledge of every science and also leprology awoke in our old continent. The vacuum in this knowledge, in my opinion, can only be imputed to the ominous effects that spread from every war.

The fact is that as soon as we returned from our overseas study trip, we began doing early diagnosis of leprosy, now recognizing early forms which we formerly had ignored. Then, we were fortunate enough to be among the first in obtaining the recently discovered sulfones (at that time) with which we obtained good results. Immediately afterwards, with a better organization not only of the sanitary problem but also of the social problem, we could draw to us leprosy patients and whole families who formerly hid themselves from public health actions.

It has been a long time since we first began the census of patients, relatives, and contacts, studying them in four aspects: clinical, histopathological, bacteriological and immunological. We had begun with 600 patients, and in the year 1962, with the collaboration of most of the Spanish dermatologists, we had already studied more than 7,000 patients and three times that number of relatives and contacts by the above methods.

During our annual investigations we found that many of the patients were cured and there were very few cases of reinfection.

With the collaboration of all Spanish dermatologists, the "Patronato Social Antilep-