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LAZARINE LEPROSY ITS POSITION IN THE PRESENT CLASSIFICATION OF LEPROSY¹

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REVIEW OF THE LITERATURE

In a paper read at the annual meeting of the American Dermatological Association in 1930, Pardo Castello and Caballero (1) presented the subject of lazarine leprosy with a report based on the study of 23 cases, reviewing the literature up to that time. Since then lazarine leprosy has been the subject of much controversy and varied interpretations.

It seems that the term "lazarine leprosy" was first used by Lucio and Alvarado of Mexico (2) in 1852 to designate a diffuse, bullous, hemorrhagic, and necrotic form of this disease, and therefore their publication antedated that of Zambaco Pachá (3), which we thought was the earliest bibliographic reference.

In 1935 Rodriguez (4) of Manila wrote on lazarine leprosy and stated that the distinguishing features of this variety of leprosy were a rapid and sometimes sudden development, often in the early stages of the disease, with the formation of blisters and blebs which start from erythematous patches, solitary nodules or pachydermic edema of the extremities; the rupture of the bullae is followed by rapidly spreading ulcers or areas of necrosis which may disorganize cutaneous tissues, muscles, tendons, and open the joints, ending in tremendous tissue destruction and deformities. To this point Rodriguez's descrip-

¹ Reprinted, with permission, from the *Proceedings of the Fourth International Congress on Tropical Medicine and Malaria*, Washington, D. C., Department of State, 1948, Vol. 2, pp. 1313-1317. Apart from the correction of the spelling of one person's name no changes have been made in the text, but the list of references has been made to conform more with the authors' original manuscript and two additions have been made in brackets.—EDITOR.

tion of lazarine leprosy tallies exactly with that of Pardo Castello and Caballero in 1930. Histologically, Rodriguez states, the structure was typically tuberculoid, but contrary to the usual scantiness of *M. leprae* in tuberculoid leprosy, these organisms were found in large numbers in lazarine leprosy lesions. Rodriguez believes that this peculiar phenomenon in tuberculoid leprosy is due to allergy and extreme irritability of the tissues towards the invading organisms, resulting in violent efforts to limit the invasion and to eliminate the organisms. Rodriguez also gives the possible explanation that the rapid destructive course of the infection in lazarine leprosy may be due also to the utter lack of resistance on the part of the host, to extreme invasive powers of a particular strain of the bacillus, or to the coexistence of another infection.

The phenomenon of bleb formation in leprosy, followed by gangrene of the skin, has been known in Latin-American countries for many years and has been called vejigón blanco and vejigón negro (white bladder and black bladder), as reported by Barrera and Peña Chavarría (5) in 1927.

Cases of ulcerative or sloughing tuberculoid leprosy were reported in 1938 by Ryrie (6), but in his 20 cases the condition presented no bullae, but started with rapid exfoliation and sloughing of the tissues followed by ulceration and final distorted scars.

In 1939 Vespoli (7) refers to lazarine leprosy as a bullous and ulcerative condition beginning on an erythematous macule and progressing rapidly to destruction of tissue; mention is made of the tuberculoid structure with the usual feature of numerous bacilli in the necrotic areas.

In 1940 Rodriguez and Wade (8) reviewed again the subject of lazarine leprosy and commented on the formation of bullae in tuberculoid leprosy, in lepromatous leprosy, and during acute tuberculoid reaction, reporting a case similar to the cases reported by Pardo Castello and Caballero in Cuba, in which tuberculoid structure was the prominent histologic picture.

In 1941 Burks and Brunsting (9) reported a case of bullous formations in a young Mexican patient suffering from lepromatous leprosy, which resembled the cases described by Lucio and Alvarado and later by Latapí and others in Mexico.

In 1941 Fernandez Vautrai (10) considered lazarine leprosy in a critical article and commented on the Lucio type seen in Mexico, the cases reported by Rodriguez and Wade, and those reported by the Cuban authors, and concluded that the term

"lazarine leprosy" should not be employed to designate a special clinical form of leprosy.

Bechelli, Rotberg and Maurano (11) in their clinical description of leprosy in the excellent treatise on leprosy published by the Brazilian Public Health Service, mention leprous pemphigus in cases of tuberculoid leprosy, and their description tallies with that of lazarine leprosy, although they do not employ this designation.

FURTHER EXPERIENCE WITH LAZARINE LEPROSY IN CUBA

One case of Lucio's diffuse bullous leprosy seen by us in Mexico in 1947 and a few cases with the same features observed in the San Lazaro Hospital in Havana were entirely different from those first reported by Pardo Castello and Caballero in 1930 as observed in Cuba. The Mexican patients are typically lepromatous and in them the formation of bullae, superficial necrotic areas and telangiectases, followed by hemorrhage, crust formation, and scarring with pigmentation, are the prominent features. These lesions, however, are always superficial, very numerous, and never cause the deep-seated ulcers and mutilations seen in the Cuban cases and in the cases reported and pictured by Zambaco's illustrations. Their histologic structure is that of lepromatous tissue with vascular lesions predominating, ending in necrosis; the bullae are flat, flaccid, sometimes amounting to just a separation of the corneous layer of the skin by scanty serohemorrhagic fluid.

In the cases reported from Cuba the bullae are rarely multiple, more often solitary, usually arising on an erythematous patch, and they are the most prominent early feature of the condition. They spread rapidly and break down, leaving a moist surface which soon undergoes necrosis, extending deeply into the tissues, affecting the subcutaneous structures, fascia, muscles, tendons, and bones, resulting in deep, destructive ulcers. The histologic structure is that of tuberculoid leprosy with a central necrotic core. Bacilli are very numerous in the necrotic areas but few or absent in the surrounding tissues. The lepromin test is constantly positive in these patients and the condition tends to spontaneous recovery in the majority of cases.

Of 23 cases reported by the Cuban authors in 1930, only three have been located in the past 2 years. One showed the atrophic anesthetic scars of the healed ulcers but had no signs or symptoms of active leprosy on the skin or peripheral nerves. A second patient had also extensive scarring of both legs and

areas of anesthesia in the upper and lower extremities but no signs of active lesions of leprosy. Still a third case developed occasional blisters, and, besides the old scars of the lesions seen many years before, this patient presented smaller ones to a total of about 30. No bacilli were found in these cases.

Of three more cases seen by us since 1930, one patient, a 44-year-old man, a native of Syria, was followed by us from 1940 to 1945, and during that time bullous lesions ending in necrotic and ulcerating areas were constantly forming in the upper and lower extremities as well as in the buttocks and lumbar region. Acid-fast bacilli were found in large numbers in the pus and necrotic material, but not in the sections made of biopsies performed on the nonnecrotic affected skin. After the necrotic mass was eliminated, no more acid-fast bacilli could be demonstrated. In this case the inoculation of infected material into guinea-pigs, intradermally, subcutaneously, and intraperitoneally in 1941 gave consistently negative results. Histologically there was tuberculoid structure, marked dilatation of blood vessels with perivascular lymphocytic infiltration, and towards the necrotic area there were massive accumulations of polymorphonuclears. The lepromin test was repeatedly positive. Lepromin test made with an antigen prepared with tissue of the patient also gave positive results.² The histologic study of the nodule caused by this lepromin test showed the usual tuberculoid changes. At no time did this patient present any other symptoms of leprosy on the skin or peripheral nerves. In recent lesions the only organism found was an acid-fast bacillus with all the appearances of *M. leprae*; later, secondary infection set in and pyogenic organisms were present in abundant numbers. The erythro sedimentation rate was always moderately increased between 28 and 80 millimeters. All attempts to cultivate this acid-fast bacillus failed. We are indebted for the bacteriologic studies to Drs. Arturo Curbelo, professor of bacteriology of the University of Havana Medical School, and J. A. Martinez Cruz, of the bacteriologic department of the University Hospital "Calixto Garcia."

² This test was made with an antigen made in the same manner as the ordinary lepromin, but with tissue taken from the affected part at the same time as a biopsy was done, which tissue showed no bacilli in sections. The result of the test was positive since there developed, at the site of injection, a papule which lasted for some time. The lepromin test, made with an antigen from a case of lepromatous leprosy, was done at the same time and with identical results.

THE PRESENT STATUS OF LAZARINE LEPROSY

There seems to be no doubt that there are a number of patients with leprosy whose predominating lesions are bullous and necrotic. These lesions may occur in lepromatous cases, as in the cases reported by Lucio and Alvarado and later by Latapí and Chevez Zamora (12) in Mexico, or they may occur in the tuberculoid type of the disease, as in the cases reported in Cuba and the one reported by Rodriguez in the Philippines. We are entirely in accord with Rodriguez that in the tuberculoid cases the condition is the result of exalted sensitivity of the naturally reactive condition of the tuberculoid tissue. Conversely, we believe that in the lepromatous types the condition may be the result, as Rodriguez states, of "the utter lack of resistance on the part of the host." The cases of Lucio's diffuse leprosy as seen in Mexico, as well as those recognized as such in the San Lazaro Hospital in Cuba, have been lepromatous cases with negative lepromin and progressive degenerative manifestations. Latapí and Chevez Zamora (13) believe that the type of bullous leprosy developed in lepromatous patients (Lucio's type) is the result of the Shwartzman phenomenon spontaneously produced in these patients as a result of a synergic sensitization to *M. leprae* and to different "cocci" present in foci of infection or as secondary invaders. We are not in a position to analyze this interpretation, but we believe that further investigations are needed before final judgment is passed on the causation of this phenomenon.

We agree that there is no reason to create a lazarine type of leprosy, but that the bullous or lazarine phenomenon should be noted when reporting cases of either of the two polar types of leprosy, lepromatous, and tuberculoid.

CONCLUSIONS

We may conclude that there is no specific form of leprosy that can be called "lazarine," but that this term may be used as a synonym for predominating bullous and necrotic lesions, which may occur in either of two polar types of the classification of leprosy, lepromatous and tuberculoid. The condition differs in its clinical aspects, the lazarine lepromatous lesions being widespread, multiple, and superficial, while those of the tuberculoid type are limited, few in number, and deep-seated. With this interpretation, we believe one can help to clarify the confusion created around the term "lazarine leprosy."

The present trend in classification is toward simplicity,

trying to set the unusual and atypical cases in the nearest possible position, without creating too many clinical forms.

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DISCUSSION

[Preceding the foregoing paper by Drs. Pardo Castelló and Piñeyro in the program, and also in the published Proceedings, is one by Drs. Fernando Latapí and Agustín Chevez Zamora entitled "Lepra lazarina in Mexico," which differed in presentation from those which had been presented at the Havana Congress (one of which was published in the preceding issue of the JOURNAL). The two papers were to be discussed together. Included here are, slightly condensed, the only remarks which appeared in the Proceedings, though they pertain only to the Lucio phenomenon as seen mainly in Mexico.—EDITOR.]

DR. HARRY L. ARNOLD, JR. (*Hawaii*): While in Mexico recently I had the privilege of seeing with Dr. Latapí a considerable number of cases of the interesting "Lucio phenomenon." I had just seen a single example of it in Los Angeles and had been completely puzzled because it resembled nothing that we have seen in Honolulu. The vivid, red, sharply outlined, irregular macules in cases I saw displayed very little tendency to vesicle formation; and what is said about bullous reaction should not be taken to mean that these lesions are conspicuously bullous.

Dr. Latapí's work is important and significant because it brings out evidence of a reaction to the leprosy bacillus which is entirely different from anything we have seen. We have been accustomed to think of the possible reactions to the bacillus in terms of two alternatives. One alternative—which is a mistake, of course—is that it is treated simply as an innocent and harmless foreign body, with the establishment of the lepromas, which are not inflammatory and merely increase slowly in size over the years. The other alternative is that the infected economy fights against the infection so vigorously that most of the bacilli are destroyed, and the tissue in which this process is going on gives rise to the tuberculoid type of leprosy. Important discoveries may be expected from the study of the lepromin reaction in conjunction with the sensitivity test of Medina.

Although this form of leprosy is apparently quite uncommon except in this area, where it is the commonest one, I have seen one case in a native of Los Angeles and one in Guatemala in a native of that country. Dr. Davison, of South Africa, has told me that this phenomenon was by no means unusual in South Africa.

[ADDENDUM: In a personal communication Dr. Arnold says that the case seen by him in Los Angeles has been reported in a paper by M. E. Obermayer, S. C. Bonar and R. Rosenquist in the April 1949 issue of the *Journal of Investigative Dermatology*. He also states that one unquestionable case of Lucio leprosy had been seen in Honolulu in a Portuguese-Hawaiian woman. There was a clear history of lepromatous leprosy without any lepromas whatever at any time, and with perfectly characteristic nummular scars of the legs. The lepromin test was not done.—EDITOR.]

DESCRIPTION OF PLATE

PLATE 7

FIG. 1. Broken down bullae, necrotic sloughing tissues and pachydermic edema.

FIG. 2. Granulating ulcer after elimination of slough.

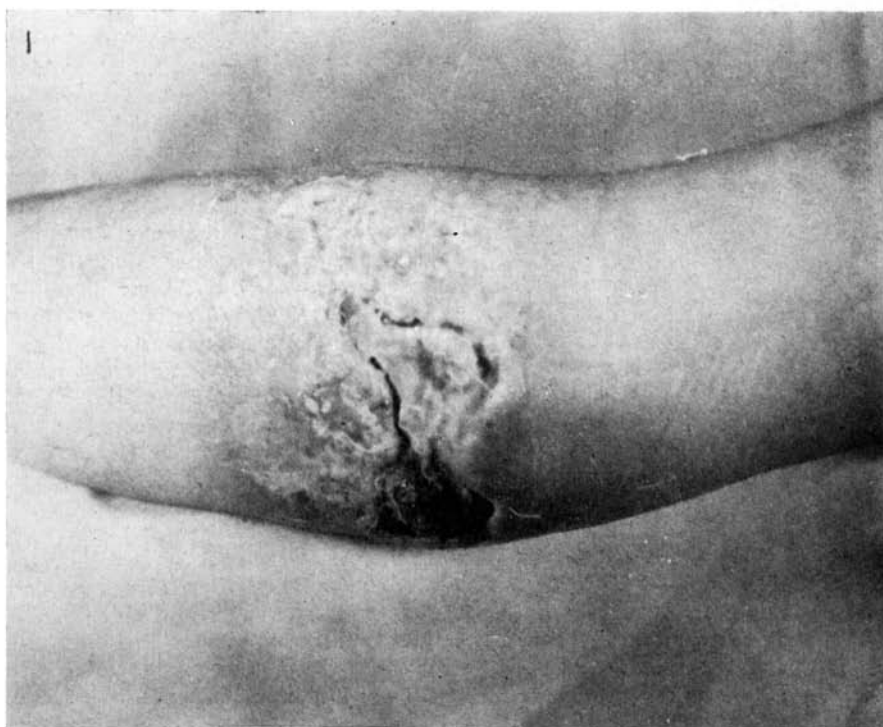


PLATE 7.