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EDITORIALS

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THE "LUCIO" AND "LAZARINE" FORMS OF LEPROSY

Recent events, beginning with the rediscovery of Latapí [1] in 1938 of a form or variety of leprosy described nearly a century ago by Lucio and Alvarado [2] as "manchada" or "lazarina," have raised the question of whether or not there is a really valid distinction between that Mexican form and those seen elsewhere. If so, there follows the question of what condition may properly be called "lazarine leprosy"—if use of that term is properly to be continued at all. There is no question about "*manchada*," for it signifies "spotted" in quite the same imprecise way as does "*tachetée*" and has no more definitive a place in leprosy terminology. An attempt is made here to review this whole matter comprehensively.

Interest has been stimulated by presentations made before two congresses last year, first the one on leprosy at Havana in April, then the joint one on tropical medicine and malaria in the following month at Washington. The organizers of the section on tropical dermatology and mycology of the latter invited Pardo Castelló of Havana to present a paper on "lazarine leprosy in Cuba," and Latapí of Mexico City to present one on "lazarine leprosy in Mexico." To the former the assignment was a

[1] LATAPÍ, F. Manifestaciones agudas de la lepra. Rev. med. **18** (1938) 526-538.

[2] LUCIO, R. and ALVARADO, I. Opúsculo sobre el Mal de San Lázaro o Elefantiasis de los Griegos. México, M. Muruguía y Cía., 1852, 53 pp.

"natural," for he and Caballero [3] had read a paper on that subject in 1930; the one which he read at Washington, written with Piñeyro,[4] is reprinted in this issue. Latapí and Chevez Zamora [5] wrote under the assigned title but probably uncomfortably, since in their earlier publications they had used the term "lazarine" only for historical identification. In one of the two papers which they read at Havana [6] the condition was referred to as "la lepra 'manchada' de Lucio," and in the other [7] simply as "la lepra de Lucio." The actual designation which Latapí has given the condition is *"lepromatosis difusa pura con brotes de vascularitis agudas necrosantes multiples* (lepra 'manchada' o 'lazarina,' Lucio y Alvarado, 1851)," [8] which is excellent as a description but a little awkward as a name for practical use.

In the article of Lucio and Alvarado, published only as a monograph but reprinted textually by Gonzalez Urueña,[9] the patients seen at the Hospital de San Lázaro in Mexico City were divided into three groups: (*a*) *tuberculosos*, (*b*) *anestésicos*, (*c*) *lazarinos* or *manchados*. Poncet, a French army medical officer who was stationed in Mexico in 1863, the year before Maximillian was made emperor, and who took advantage of the opportunity to study leprosy there, wrote with respect of Lucio and of the "remarkable memoir" published by him and Alvarado; and, although he did not think these forms were quite as peculiar as Lucio did, he nevertheless regarded the second and third as highly interesting.

It was evidently Poncet who prevented the Mexican forms from being entirely ignored in Europe, as will be seen. Latapí

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[3] PARDO CASTELLÓ, V. and CABALLERO, G. M. Lazarine leprosy; peculiar monosymtomatic form of leprosy. Arch. Derm. & Syph. **23** (1931) 1-11.

[4] PARDO CASTELLÓ, V. and PIÑEYRO, R. Lazarine leprosy. Its position in the present classification of leprosy. Proc. 4th Internat. Cong. Trop. Med. & Malaria, Dept. of State, Washington, D. C., 1948, vol. 2, pp. 1313-1317; *reprinted* in THE JOURNAL **17** (1949) p. 65.

[5] LATAPÍ, F. and CHEVEZ ZAMORA, A. Lepra lazarina en México. Proc. 4th Internat. Cong. Trop. Med. & Malaria, Dept. of State, Washington, D. C., 1948, vol. 2, pp. 1307-1312.

[6] LATAPÍ, F. and CHEVEZ ZAMORA, A. La lepra "manchada" de Lucio. Memorias V Cong. Internac. Lepra, Havana, 1949, pp. 410-413; *also*, in English translation, The "spotted" leprosy of Lucio. THE JOURNAL **16** (1948) 421-429.

[7] LATAPÍ, F. and CHEVEZ ZAMORA, A. Interpretación actual de la lepra de Lucio. Memorias V Cong. Internac. Lepra, Havana, 1949, pp. 1019-1024.

[8] "Pure diffuse lepromatosis with outbreaks of multiple necrotizing vascularitis," (etc.).

[9] GONZÁLES URUEÑA, J. La Lepra en Mexico. Buenos Aires, El Ateneo, 1941; pp. 201-231.

and others have referred to certain of his publications [10,11] as if they dealt with the particular form under discussion, whereas those references are to a twice-published article on "lepra antonina." The other forms are mentioned only briefly, and described as Lucio and Alvarado had described them:

> The leonine or tubercular (elephantiasis of the Greeks), characterized by the presence on the face, the extremities and the mucous surfaces of isolated or massed tubercles.
>
> The antonine or anesthetic, characterized by anesthesia of the face and extremities, sometimes of the trunk, and by loss of a certain number of bones of the hands and feet.
>
> The lazarine or spotted (*tachetée*), characterized by the presence on the extremities of painful spots (*manchas*) the color of blood, well delimited, which give rise to a bad kind of ulceration.

The first of those forms, he wrote, a full decade before Hansen discovered the leprosy bacillus, "has been perfectly studied." The second, as said, is the subject of the article which, Gonzalez Urueña has pointed out with regret, is incomplete in that it does not deal with the third form. Poncet published no other article in Mexico, and if he described the third form in France it was in some later publication which we have not located. However, he contributed several detailed case reports to Leloir's remarkable anthology-treatise.[12]

In Leloir, "lazarine" leprosy is dealt with repeatedly although not with notable precision, chiefly in two appendices. One, [12a] in which the writings of Lucio and Alvarado and of Poncet referred to, follows the chapter on "systematized neural leprosy" and bears the subhead: *"Q'est-ce que la lèpre tachetée et bulleuse dénominée lèpre lazarine par certains auteurs?"* There are three detailed case reports communicated by Poncet, two of them Mexican, one from Spain. Leloir clearly regarded the condition as a feature of neural leprosy; and previously he had written on the subject in connection with a study of cutaneous affections supposedly of nervous origin.[13] The other appendix,[12b] following the chapter on "mixed leprosy, bears the subhead *"Lèpre, dite lazarine Mexicaine (èrythéme pemphigoïde, ulcéreux ou escha-*

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[10] PONCET, F. Etude sur la lèpre au Mexique. Gaceta méd. Mexico **1** (1864) 49-61 and 65-77.

[11] PONCET, F. De la lépre au Mexique. Recueil Mem. de Med. Chir. Pharm. milit. **12** (1864) 306-333.

[12] LELOIR, H. Traité Pratique et Theoretique de la Lèpre. Paris, Delahage et Lecrosnier (and *Progres Médical*), 1886. (*a*) pp. 190-200; (*b*) pp. 214-220.

[13] LELOIR, H. Recherches cliniques et anatomo-pathologiques sur les affections cutanées d'origine nerveuse. Paris, 1881; chapter Lèpre. *Also*, with Déjérine, Arch. Physiol. 1881. (From Leloir, 1886.)

rotique) mélangée a la lèpre tuberculeuse," and consists of three other case reports, two of them actual Mexican cases contributed by Poncet and one of a patient from Venezuela studied in Paris by Leloir himself. The reports of the two Mexican cases in the first of these appendices, in neither of which is there mention of thickenings or nodulations of ordinary lepromatous leprosy or polyneuritic manifestations of neural leprosy, are summarized as follows:

OBSERVATION LI (p. 196).—Mexican female, aged 48 years, duration six years. First symptoms noticed: falling of hair (frontal and temporal), eyebrows (outer ends) and eyelashes. A year later, after three days of fever with pains, the first "spots" (*taches*) appeared; very painful to touch, some simple livid plaques, others with vesicles which gave rise to ulcers. Since then the disease had followed its ordinary course. Examined by Poncet July 10, 1863. (Numerous details, including loss of hair, and deformation of nose.) Skin of face, neck and trunk normal; that of the extremities presented a melange of wine-red violaceous spots and white cicatricial plaques surrounded by coffee-brown skin. On that day she had intense fever which lasted three days, and new 1-2 cm. spots appeared on the hands and arms. (A description of this new eruption and the accompanying symptoms was recorded on July 25.) Ulcers had developed by July 31; by September 3rd they had nearly all healed. (Nothing new at the last observation, September 24th.)

OBSERVATION LII (p. 198).—Mexican female, 44 years old; duration seven years. Onset ascribed to exposure to cold (snow); a little fever then, and joint pains, and some time later the appearance of spots which have continued to appear at varied intervals in small flocks, 3 or 4 a time, not always accompanied by fever. They were dry (i.e., not bullous) but produced ulcerations which lasted about two months. The intervals had become shorter, so that at the first examination by Poncet July 13, 1863, the duration of some of the ulcers present was one or two months, of others fifteen days, of still others eight days, while some had appeared only the day before. The patient had been kept awake for the past two nights by an acute and painful swelling of the left hand, with lesions of one finger which went on to gangrene and loss of the phalanx. On the arms, much more on the external than on the internal surfaces, there were spots of various ages in greater intensity, with ulcers which gave off "a special, infected odor in spite of the use of charcoal and powdered Peruvian bark." Sensation was intact in this patient; the nose was deformed (loss of the cartilage), but the voice was clear. (Other notes, the last made on September 3rd, contribute nothing to the general picture.)

Subsequent European literature reflects the general idea that "lazarine leprosy" is a bullous and ulcerative condition in cases of the neural type. Hansen and Looft [14] did not use the term, nor did they describe anything more significant than eruptions in maculoanesthetic leprosy of pemphigoid bullae (always bac-

[14] HANSEN, G. A. and LOOFT, C. Leprosy in its Clinical and Pathological Aspects. Bristol, John Wright & Co., 1895.

teriologically negative) regarded as tropic, which might occur early in the disease but more often later on, "both accompanying the patches and in the stage of anesthesia and mutilation." Zambaco,[15] often cited in this connection, described "lèpre ulcéreuse ou lazarine" as one of the most widespread forms of leprosy but subject to frequent errors of diagnosis, and presented two case reports with drawings of deeply ulcerated lesions; but there is neither reference nor similarity to the Mexican condition. Later,[16] without saying anything of the condition in Turkey, he spoke briefly of reports by Poncet of the "lazarine or ulcerous" form, much more common in Mexico than elsewhere. Sauton,[17] to whom there was one essential "leprosis" with a great variety of skin lesions (all "leprides") which made up the different ensembles or forms which actually succeed each other, transform one to another, and occur in combination (*"se succèdent, se transforment, se combinent"*), saw in this way the production of "lazarine leprosy in company with tubercular leprosy." And:

> "As for the *lazarine leprosis,* if the ravages which it produces do not lead to the death of the subject, one sees it transform to the tubercular leprosis and often to the nervous leprosis; it is, then, only a stage, a transitory period of the disease." Regarding the pathology of the blood vessels, he said that Poncet de Cluny and Lucio and Alvarado had also seen in the arteries the same kind of changes as Gluck had described for the veins, to the point of filling up the vessels and causing a kind of thrombosis. (We have been unable, as yet, to locate any such records with respect to the Mexican condition.)

Skipping the next thirty years or so, one finds in Klingmüller [18] a definition of *lepra lazarina as* "neural leprosy with macules and bullae in which for a long time the pemphigus may be the only symptom." The condition itself is dealt with in a single page between the lengthy sections on *lepra nervosa* and *lepra mixta.*

In Jeanselme's treatise [19] there is mention of the reports of Lucio and Alvarado and of Poncet, and a description of "macular (*tachetée*) and bullous leprosy, called by certain authors lazarine leprosy," which may well have been taken from one of those

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[15] ZAMBACO PACHA, D. A. Les Lépreux ambulants de Constantinople. Paris, Masson et Cie, 1897; chapter VIII, pp. 261-277.

[16] ZAMBACO PACHA, D. A. La Lèpre a Travers Les Siècles et les Contrées. Paris, Masson et Cie, 1914.

[17] SAUTON, D. La Lèprose. Paris, Masson et Cie, 1901.

[18] KLINGMUELLER, V. Die Lepra. Handb. Haut- u. Geschlechtsgr. X/2. Berlin, V. Julius Springer, 1930; pp. 312 and 333-334.

[19] JEANSELME, ED. La Lèpre. Paris, G. Doin & Cie, 1934.

authors, of Leloir. Neither here nor in previous writings is there any nonsense about the nature of the underlying lesion.

In that period, however, a somewhat different slant on the subject developed. In Cuba, in 1931, Pardo Castelló and Caballero [3] presented a study of lazarine leprosy as seen in 23 cases, describing it as a monosymptomatic form of leprosy characterized by the sudden appearance of bullous eruptions, sometimes with fever, followed by rapidly sloughing ulcerations, strongly positive for bacilli, which may extend even to the tendons and bones and which take months to heal—much as described by Zambaco. This condition may occur early, in the absence of other symptoms except for the anesthesia which is present, and sometimes it leads to death from septicemia or to amputations to save life.

It is of interest, with respect to recognition, that at a later meeting at which a case of lazarine leprosy was presented and discussed [20] Pardo Castelló said that when Caballero [21] had first presented cases of that form he, himself, had refused to accept the diagnosis, believing the condition to be a chronic phagedenic ulceration. But Klingmüller diagnosed leprosy from sections, in which he found acid-fast bacilli in the nerves, and cultures and animal inoculations made at the Harvard Medical School gave negative results. Hopkins, of New Orleans, remarked that at Carville he had not seen a similar condition, with ulcerations occurring early and in the absence of well-marked lesions in other parts of the body. Howard Fox also commented that he had never seen anything like it in his travels, and said—as Hopkins had—that he could not have diagnosed the case as leprosy.

From the Philippines, in 1935, Rodriguez [22] described and pictured a case with unusual ulcerations resulting from rapid breaking down of macular lesions, with or without a phase of vesiculation, the case not typical lazarine leprosy as described by Pardo and others but the nearest to it which he had seen. In this report, for the first time, it is stated that a biopsy specimen had been found to be tuberculoid, with numerous bacilli —although it may be suspected that at least some of the cases of Pardo Castelló and Caballero were tuberculoid.

From Malaya, in 1938, Ryrie [23] described an extraordinarily severe ulcerating and scarring condition in Chinese patients,

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[20] GRAU, J.; also PARDO CASTELLÓ, V. *and others.* (Case reports and discussion.) Arch. Dermat. & Syph. **26** (1932) 924-926.

[21] CABALLERO, G. M. Sobre algunos casos de lepra desconocida entre nosotros y sobre la naturaleza de la Choppa descrita en Cuba. Vida Nueva **21** (1928) 63.

[22] RODRIGUEZ, J. Lazarine leprosy. Lep. India **7** (1935) 152-155.

[23] RYRIE, G. A. Acute ulcerating or sloughing tuberculoid leprosy. THE JOURNAL **6** (1938) 153-160.

but that was a frank if peculiar reactional tuberculoid phenomenon and certainly very different from the monosymptomatic condition, difficult to diagnose, which the Cuban workers had described. The same is to be said of the case reported in 1940 by Rodriguez and Wade.[24]

These reports and certain others, including one of a Mexican patient with lepromatous leprosy seen in the United States whose condition resembled that described by the Mexican authors,[25] are reviewed briefly by Pardo Castelló and Piñeyro [4] before they recount their further experience with lazarine leprosy. Three more cases had been seen, and one is described briefly: In the period 1940-1945 bullous lesions were constantly appearing and leading to ulcerations which discharged abundant bacilli although none were found in sections of nonulcerated lesions, which were tuberculoid; some of that tuberculoid tissue was made into an antigen which, like the regular lepromin, gave rise to a positive Mitsuda reaction lesion. In the meantime one case of the diffuse Lucio form had been seen in Mexico, and a few had been seen in the San Lazaro Hospital in Havana (Rincon). That condition was "entirely different" from the lazarine one with which they had dealt, for it occurs in lepromatous cases and the ulcerations are always numerous and superficial, never causing deep-seated ulcerations and mutilations. The three patients of the 1930 report who had been located were still not lepromatous.

That the Lucio form of leprosy seen in Mexico—and also in Costa Rica, as is evidenced by the article by Romero *et al.* which appears in this issue [26]—is peculiar as evidenced not only by the published descriptions but also by testimony of men who have seen cases of it, as shown in the Correspondence section of this issue. Dharmendra, who went to Mexico to see it, did not see the same thing in other countries visited later and, what is more important, he does not know it in India—where there occur "diffuse" lepromatous cases which would be passed over as quite normal by most leprologists. Arnold, who also visited Mexico, has seen in Los Angeles, a Lucio case in a Mexican born in the

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[24] RODRIGUEZ, J. N. and WADE, H. W. Bullous tuberculoid leprosy; report of a case, with a discussion of lazarine leprosy. THE JOURNAL **8** (1940) 333-344.

[25] BURKS, J. M. and BRUNSTING, L. A. Lazarine (pemphigoid) leprosy; report of a case. Proc. Staff Meet., Mayo Clinic **16** (1941) 488-492. (Cit. by Pardo Castelló and Piñeyro.)

[26] ROMERO, A., BRENES IBARRA, A. and FALLOS, M. Clinical study of lepromatous leprosy in Costa Rica. THE JOURNAL **17** (1949) p. 27.

United States, said to have been reported by Obermayer *et al.*[27] and another in Honolulu in a woman of Hawaiian-Portuguese derivation. Fiol states that he happened to see a case at Carville in a young man of Central American origin, and was able to say that the typical Lucio condition is not seen in Argentina.

However inclined one may be to agree with Pardo Castelló that it is not desirable to multiply named forms or varieties of leprosy, the fact remains that there are more or less distinctive variations from the norms of the established types and that it is useful to name such forms. It seems beyond dispute that in both neural and lepromatous leprosy there are variants characterized by the formation of bullae or vesicles followed by ulceration, and that, considering the fundamental differences which exist between those types of the disease, and the differences among the cases themselves, one cannot lump all of them together under any common designation.

In lepromatous leprosy as it occurs especially in Mexico and elsewhere in that region there is evidently a diffuse form which might easily be overlooked until the eyebrows are lost, and which is prone to eruptions of small hemorrhagic lesions which become shallow ulcerations. The ulcerating phase is now known as the "Lucio phenomenon," and since that name is appropriate it will likely continue to be used; and it is also probable the name "Lucio leprosy" which Latapí and others have applied to the form as a whole will also continue to be used in that way. To designate the condition merely as "diffuse leprosy" is obviously inadequate and confusing.

The naming of the condition described by Lucio and Alvarado being thus taken care of, the term "lazarine"—which apparently they were the first to use[28]—is no longer needed in that connection, nor would it be suitable now. Since it has so long been employed to signify a bullous-ulcerating condition (or conditions) in neural leprosy, and since some general term for that condition (or conditions) in that type of leprosy is needed, it seems but logical to continue to use it in that way—and to admit the transfer. —H. W. W.

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[27] OBERMAYER, M. E., BONAR, S. C. and ROSENQUIST, R. Diffuse lepra. J. Investig. Dermat. **12** (1949) 243.

[28] Search of the introductory and historical section of Danielssen and Boeck's treatise (1848) has failed to reveal evidence of any such adjectival use of the word before their review was prepared.