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EDITORIALS

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RESISTANCE IN EARLY CHILDHOOD

It seems not to be generally realized that it is now necessary to modify to some extent the generally accepted view that infants and young children are highly susceptible to leprosy, and that only adults are resistant to it. This change of view is necessitated mainly by the relatively recent recognition by Lara at Cullion, in the Philippines, of previously undescribed lesions occurring among the children of leprosy parents, especially in those below the age of three years, and also by observations of similar significance by de Souza Campos in São Paulo, Brazil.

The first published reports positively identifying the particular lesions referred to are those of Lara and de Vera in 1935,^{1,2} although some of them had been previously described by Chiyuto³ and probably by others as well. The subsequent articles

¹ LARA, C. B. & DE VERA, B. Clinical observations with reference to leprosy in children of lepers. *J. Philippine Islands Med. Assoc.* **15** (1935) 115.

² LARA, C. B. & DE VERA, B. Early leprosy in infants born of leprosy parents, with report of cases. *J. Philippine Islands Med. Assoc.* **15** (1935) 252.

³ CHIYUTO, S. Early lesions of leprosy and their importance in the transmission of disease. *Mo. Bull. Philippine Health Serv.* **14** (1934) 363.

of Lara on the Culion children,^{4,5,6} which contain further descriptions of the lesions and their course accompanied by the necessary laboratory examinations performed by J. O. Nolasco and Jose Manalang, and two special reports of histological findings by Nolasco and Lara,^{7,8} form the bulk of the available data on the subject. Because these children were separated from their parents and isolated in the Negative Children's Home, it was possible to reexamine them at frequent intervals under almost ideal conditions.

The main interest lies in the findings in the youngest children, below the age of 3 years. The lesions of the next age group, 3 to 6 years, showed distinct differences on the whole; and children older than that are again different.

Of the six varieties of lesions observed in the youngest group the most common one, comprising 45 per cent of all found, Lara designated "wheal-like papules." Bacteriologically, two-thirds of them were found to be heavily bacillated; on biopsy, three-fourths of them showed a predominantly tuberculoid structure.⁷ Most of the lesions of this type (78%) healed spontaneously without subsequent relapses.

Another variety, designated "papulo-nodular," formed 13 per cent of the total. Most of them, also, were heavily bacillated (3-plus or 4-plus); and 3 out of 4 showed undifferentiated structure, consisting of diffuse monocytic infiltration with a few ill-defined foci. These laboratory findings, taken with their clinical characteristics, would place these lesions under the "reactional" rather than the "torpid" tuberculosis sub-type, a fact which had been emphasized by Fernandez.⁹ A still larger pro-

⁴ LARA, C. B. Early leprosy in children of lepers; further observations on the early, definitely identifiable leprotic lesions. *Mo. Bull. Bu. Health (Manila)* **18** (1938) 325.

⁵ LARA, C. B. Observations on the incidence of leprosy in children of lepers. *Mo. Bull. Bu. Health (Manila)* **22** (1946) 47.

⁶ LARA, C. B. Leprosy in infancy and childhood. *Mem. V Congr. Internac. Lepra* 1948; Havana, 1949, p. 414 (*abst. I.J.L.* **16** (1948) 277).

⁷ NOLASCO, J. O. & LARA, C. B. Histopathology of early lesions in fourteen children of lepers. I. Analysis of previous skin blemishes in relation to sites of biopsies and other positive and probable lesions. *Philippine J. Sci.* **71** (1940) 321.

⁸ NOLASCO, J. O. & LARA, C. B. Histology of clinically healed "primary" lesions of leprosy in children of lepers; their clinical progression and final resolution into healed scars. Report of thirteen cases. *Mem. V Congr. Internac. Lepra* 1948; Havana, 1949, p. 545 (*abst. I.J.L.* **16** (1948) 295).

⁹ FERNANDEZ, J. M. M. *La Infeccion Leprosa en el Niño*. Editorial Rosario S. A., 1947, pp. 53-56.

portion (85%) of these lesions showed complete healing without recurrence after a follow-up of from 1 to 13 years.

Both of these types of lesions were indurated, usually markedly so, and varied in color from pink to purplish. When first seen, Lara states, they may be no larger than a pin-head, and even at their maximum development they seldom exceed 10 mm. in diameter. He insists (personal communication) that unless the clear skin is carefully examined with a hand-lens many of the smaller ones will probably be missed. Certainly it would be almost impossible to detect them if there were co-existent insect bites or lesions such as prickly heat, dermatitis, scabies or pyodermata.

Two less frequently observed varieties are the "pebbled" or "micropapulate" one (5.4 per cent) and the "indurated scarlike" one (3.8 per cent). These are regarded as probably modified or subsiding papules or wheals.

These four kinds of lesions, taken together, constituted about 67 per cent, or two-thirds, of all that were found in these very young children. As a group they are characterized by a papulate condition which, during the active stage, are bacteriologically positive yet show a tuberculoid histology, and have a distinctly self-limited course leading to the formation of scarlike lesions or, more characteristically, real atrophic scars. The predominance of this papulate class of lesions affords strong evidence of a relatively high degree of natural resistance in these very young children.

The remaining one-third of the lesions found were of two kinds, both macular. One, the "slightly raised macule," forming 20 per cent of all lesions in the youngest group (as against 27 per cent in the 3-to-6-years group), is different in certain important respects from those already described and cannot be properly classed with them. They are larger, usually pinkish and hypopigmented, and only rarely are they distinctly indurated. Bacteriologically, 50 per cent of them were negative, and those found positive were only slightly to moderately so. Histologically, the perivascular round cell architecture predominated. As for clinical course, 77 per cent of them either relapsed or became progressive. This type of early childhood lesion was responsible for most of the cases becoming lepromatous within a few years after the onset.

These slightly raised macules appear to be the same as the

"pink macules" reported by Rodriguez⁹ in 1926 as seen among older Culion children. Of 68 who showed early manifestations of leprosy, 22 per cent showed such macules. They are more commonly known as "erythematous macules" among other leprosy workers.

Finally, Lara described "flat depigmented areas," constituting 12 per cent of the lesions in the younger children but 48 per cent of those in the next age group. Histologically, they showed either perivascular round cell infiltration or an undifferentiated structure. Bacteriologically, they were either negative or only slightly to moderately positive. Most lesions of this kind do not show evidence of self-limitation. As a whole, therefore, they seem to indicate lack of resistance to the disease on the part of the patient.

These lesions are apparently the same as those found among 50 per cent of children between the ages of 3 to 7 years, by Nicolas and by the writer,¹⁰ and called by us the "pale macule." It is also variously known as the "simple macule," or the "hypopigmented flat macule."

The macule lesions of childhood leprosy were recognized very much earlier than the papular ones and have been thoroughly studied by many investigators. Notable contributions in this field have been made by Muir, Lowe and Cochrane in India; Souza Campos and Souza Lima in Brazil; Fernandez in Argentina and Lampe in Dutch Guiana.

This macular type of lesion has acquired an established place in the symptomatology of leprosy, it being the typical one of the so-called uncharacteristic form of the disease. As is generally known, there are erythematohypopigmented macules which exhibit the characteristics of both the pink and the pale ones. It is also a well-established fact that many of these simple macules become lepromatous, others show a turn to the tuberculoid type, some persist as of the simple form with little change from year to year, and some may fade away completely.

Among still older Culion children, i.e., from 6 to 15 years old, the writer found the first observable lesions to be very variable. It is during this period of late childhood that acroteric anesthesias, muscular atrophies and contractures are first met with. We begin to see also advanced lepromatous lesions on the buttocks, ear-lobes, extremities, and elsewhere. On the other hand, the typical torpid tuberculoid lesions become more mani-

¹⁰ RODRIGUEZ, J. N. Studies on early leprosy in children of lepers. *Philippine J. Sci.* **31** (1926) 115.

fest. In other words, the lesions appearing at this more advanced age approach the adult types.

To summarize the somewhat complicated data on the lesions among Culsion children who had been exposed to infection at least several months before being isolated, the following observations emerge:

1. Leprosy lesions found among such children less than 6 years old are either papular or macular. The papular lesions appear to indicate high resistance to the disease, whereas the macular ones indicate relatively low resistance.

2. The papular lesions predominate among the children less than 3 years of age (67%), while the macules are more common among those between 3 and 6 years (75%, against only 32% in the younger group). Therefore, more of the younger children appear to show resistance than the older ones within this range. These findings are indeed unexpected for most leprosy workers.

Independently, and very early too (1937-1938), the first studies of Souza Campos were published.^{11, 12, 13} These important articles are not directly available to the writer, but one can do no better than to quote Fernandez,¹³ who is himself an authority on the matter.

The studies of Souza Campos constitute one of the most valuable contributions on this subject of early infantile leprosy. Placed in an unexcelled position to observe, since he is in charge of the children of leprosy parents isolated in the preventoria of the Department of Leprosy Prophylaxis of the State of São Paulo, this author was the first to establish concretely the clinical, immunological, and evolutive characteristics of the infantile tuberculoid type which constitutes the most frequent and earliest form of infection observed in these children in Brazil and in our country [Argentina] in the first five years of life. In a series of publications Souza Campos describes with precision the clinical manifestations of this type of leprosy, demonstrates their close relationship with a frank state of sensitivity to lepromin, expounds his etio-pathologic interpretation, and demonstrates the benignity of this type of infection. . . . We only wish to point out here that the papules and nodules described by this author as the specific clinical expression of this modality of leprosy, as well as their sequela the residual cicatrix, coincide with the manifestations described by Chiyuto and Lara. . . .

Our opinion concerning the early semiology of infantile leprosy . . . is that the lesions least subject to mistake as early manifestations of the disease are the nodular ones of the tuberculoid type which are accompanied

¹¹ SOUZA CAMPOS, N. Aspects cliniques de la lèpre tuberculoïde chez l'enfant. *Rev. brasileira Leprol.* 5. (1937), Special Number, p. 99.

¹² SOUZA CAMPOS, N. Evolução rara dois casos de lepra na infância. *Rev. Uruguaya Dermat. Sifil.* 9 (1938) 114.

¹³ SOUZA CAMPOS, N. Resultado do "leprolin test" nos preventorios de filhos de leprosy. *Rev. brasileira Leprol.* 6 (1938) 31.

by a positive lepromin reaction and are observed in children of leprous parents during infancy, as pointed out by Chiyuto and Lara and definitely individualized by Souza Campos. Its frequent sequel is a very typical residual cicatrix, to which I called attention on another occasion.¹⁴ It is true that, from the pathological point of view, these lesions cannot be considered as the real first manifestation of the infection, since it already reflects a state of sensitization of the organism which logically should have been preceded by an earlier morbid stage. But from the practical viewpoint we insist that they constitute the most concrete expression of the early semiology of the disease.

With regard to the last point mentioned by Fernandez, it seems reasonable to ask if it is not possible for a mother to transmit to her child a passing sensitization—and, presumably, also immunity—so that, until that condition is lost, the child at its first contact reacts as if it had received a previous sensitizing dose, with the production of the tuberculoid lesions which have been discussed.

An alternative possibility is that the infecting organisms first introduced, before the appearance of any outward manifestation, may serve as a sensitizing antigen so that when lesions do appear they are of the tissue-reactive (i.e., tuberculoid) type.

From all that has been said it seems justifiable to arrive at the general statement that, before the age of 3 years, most children born of leprous parents who show manifest evidence of infection present lesions which signify high resistance to the disease; that between the ages of 3 and 6 years the most common lesions observed indicate, as a whole, relatively low resistance; and that above the age of 6 years the lesions approach the adult types.

This general rule has not been definitely proved to be true, however. Children showing the different types of lesions in infancy and childhood must be followed up for many years before it can be established whether or not they are really and permanently resistant, and there are many other points to be clarified. But there can be no doubt about the occurrence of apparently self-limiting tuberculoid lesions, which are to be considered indications of a relatively high degree of natural or individual resistance in children below 3 years of age, a period heretofore believed to be the one of highest susceptibility.

Finally, prolonged follow-up investigations of these interesting cases may prove which of the following possibilities is the most nearly right:

1. That most infants (of leprous parents) are born with a

¹⁴ FERNANDEZ, J. M. M. Cicatrix residual da lepra tuberculoide infantil. *Rev. brasileira Leprol.* 9 (1941) 357.

high degree of natural resistance to leprosy which is rapidly lost between the second and third year of life, giving way to a marked susceptibility which in turn is again gradually replaced by the relative resistance of adult age; or:

2. That some individuals have an inborn natural resistance, accompanied by a capacity to offer an allergic response to the infective agent of leprosy, so that, if and when an infection takes place, self-limiting tuberculoid lesions are produced in them irrespective of the age at exposure; or:

3. That, at whatever age, the primary lesion in leprosy is essentially tuberculoid in nature, or at least passes early through such a stage although the lesions of this phase are usually so insignificant as to size and so fleeting in course that they are often missed. Later, other types of lesions, more readily detected and more persistent, may develop.

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