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CLINICAL OBSERVATIONS WITH REFERENCE TO LEPROSY IN CHILDREN OF LEPERS¹

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In a valuable contribution to the subject Chiyuto⁽¹⁾ was, as far as we are aware, the first to describe and definitely attribute to leprosy certain rather unstriking changes not theretofore observed or regarded as leprotic. The commonest type of early change that Chiyuto found was the "hazy depigmented area." In his words, "these macules are clearly visible if observed in appropriate distance and favorable angle and light; their borders merge gradually with the surrounding skin." He also described as leprotic a minute, papulo-vesicular eruption simulating "gooseflesh" observed in 40 per cent of his cases, and "ringworm-like," or circinate lesions in some cases. A shiny, dry or ichthyotic condition of the legs, with or without flushing of these regions, was also described in all of his cases, but no comment was made as to their significance.

The first-mentioned type of lesion described by Chiyuto is different in appearance from the whitish patch, or "macula alba," described by Gomez and his co-workers⁽³⁾ as the commonest early lesion among children of lepers in Culion, which was later confirmed by Rodriguez⁽⁵⁾. This lesion was described by Gomez as whitish light fawn in color, level with the skin, with a smooth non-sealy surface

¹ Contribution from the Medical Section, under the direction of Dr. C. B. Lara, Chief Physician. Read before the 32nd annual meeting of the Philippine Islands Medical Association, December 21, 1934, and published with the approval of the Director of Health in the *Journal of the Philippine Islands Medical Association* 15 (1935) 115. Reprinted with minor changes made or approved by the authors. For lack of space the tables are not reproduced but the references to them are retained.

and irregular edges. The lesion referred to by Gomez and by Rodriguez was distinctly depigmented and showed clearly in the photographs of their cases. The hazy depigmented area described by Chiyuto is too faint to be photographed in the ordinary way; it is more easily recognized by sight than by description or photograph. It is not possible to state, from inspection, whether this area is depigmented or merely ischemic, and clinically it would seem appropriate to designate it as the "hazy pale area." This is the term that will be used in referring further to that condition.

The observations reported here were stimulated by the work of Chiyuto. After familiarizing ourselves with the appearance of the hazy pale area and the proper manner of looking for it, we have, since the latter part of 1932, undertaken all the special examinations of children that theretofore had been made by the different physicians serving on the Negative Examining Committee and by the physician in charge of the care of the children.

In presenting the following observations, the writers are aware of their limited scope and value, in that the children are constantly being removed from further observation by release to relatives or transfer to the Bureau of Public Welfare. Besides, the observations on these children are not supported by adequate histological data, owing to a general opposition to biopsies on the part of the parents. The examination was further handicapped by the fact that most of the children were too young to cooperate with the examiner. However, as there seems to be no immediate prospect of remedying these limitations, we have decided to publish our observations for what they may be worth.

Material studied.—This study comprised a group of 240 children most of whom were born of leprous fathers and mothers. Of those born in the Colony, 209 have never been outside Culion, while 8 had been released and subsequently readmitted at the request of relatives. Thirty-one children were born outside and later admitted with their leprous mothers. The cases ranged from newly born to 10 years of age; fully two-thirds of them were under 1 year of age. There were 113 males and 127 females. All children above 6 months of age had been in contact with their leprous parents for at least that length of time.

A group of 78 children (36 males and 42 females) of nonleper employees in Culion, ranging in age from 2 months to 8 years, was also examined. This group was examined only once, however.

Manner of examination.—It was not possible to use the same room for the examination of all the children, as the younger ones were in the Colony proper while the older ones were segregated in the Balala Nursery. Weather changes also influenced the conditions in the examining rooms, only natural illumination having been used. We found that reflected diffuse light that was not too bright, entering from one side of the room with the patient in the path of the light and the examiner to one side, gave satisfactory results. All kinds of skin blemishes were looked for and described, but appreciation of changes in the superficial nerve trunks in infants was unsatisfactory in most of the cases. No systematic bacteriological examination was attempted, in view of the consistently negative results obtained by previous observers as regards the early pale or depigmented patches. The few laboratory examinations of definitely suspicious lesions were made by members of the Pathological Section staff. However, sections were obtained from cases coming to autopsy, from sites indicated in the clinical observations. This material is being studied by Dr. Jose O. Nolasco, of the Pathological Section. The clinical examinations were made at more or less irregular intervals of from several weeks to several months. Some of the observations were based on examinations made prior to 1932.

OBSERVATIONS

In analyzing the data for suspected skin lesions we have excluded those that were or appeared to be definitely nonleprotic, like scabies, eczematoid dermatitis, eczema, furuncles, tinea spots with the characteristic branny desquamation, insect bites, scars, etc. When there was any doubt, as in the few cases with ringworm-like lesions, these were classified as suspicious or suspected. The term "suspected lesion" is here to be understood to mean an unidentified lesion rather than one definitely suspected to be of leprotic nature. It was apparent, from the beginning of our study, that various types of known nonleprotic lesions (for example, prickly heat, eczema, dermatitis, insect bites, scabies, bruises, and other forms of injury) may, on healing, leave behind hazy pale or depigmented areas that clinically we could not distinguish from similar changes of unknown origin. A hazy pale halo was also frequently found around the blue birthmarks of young children; these halos could be recognized long after the birthmarks had faded.

Types of "suspected" lesions.—For convenience, the different types of suspected lesions were grouped into two main classes; namely, those that may be considered as resulting from direct involvement of the skin, and those that may more properly be attributed to disturbed nutrition or neurocirculatory structure and function. Suspected skin lesions included the hazy pale areas; the clear,

markedly pale or whitish depigmented areas with more or less ill-defined borders; the pale or depigmented mottlings; the rough, scaly or granular areas (including ringworm-like lesions) with varying degrees of pallor or depigmentation, with or without reddish borders or surfaces; the goose-flesh, lichenoid or follicular areas; and the clear depigmented macules with definite borders, the red and pink macules, the papules, and infiltrations, these four kinds representing the more familiar types of lesions in manifest cases of leprosy. Under neurotrophic and circulatory changes were included the shiny or glistening and apparently tense condition of the skin, with or without accompanying dryness of the superficial outer layers of the epidermis when not directly attributable to non-leprotic processes; also localized flushing, cyanosis, and clinical evidences of nerve involvement.

Case and age incidence.—The total case incidence as regards the two main classes of suspected lesions for age groups of comparable sizes is given.² Among the children of 6 months of age or less, 51 per cent were found with suspected skin lesions and 49 per cent with signs of neurotrophic and circulatory change. The incidence progressively increased in the next higher two age groups; those over 1 year of age gave 97.3 per cent and 86.8 per cent, respectively, with suspected skin lesions and with neurotrophic-circulatory changes. The corresponding figures for the children of nonlepers were 59.0 per cent and 86.0 per cent. Unfortunately, the latter group was seen but once, whereas the children of the lepers were examined repeatedly.

Type of incidence of suspected lesions.—The various types of suspected lesions were also analyzed in relation to different age groups.³ The hazy pale area was the type most commonly observed. This type, as well as the pale mottling and the rough pale area, was seen even in the youngest children (2 months of age or younger), and at this age it is not possible to exclude the causal influence of the generalized scaling of the skin in the newly born. The markedly pale or depigmented areas and the follicular, goose-flesh or lichenoid lesions were first seen in children over 2 months old.

The hazy pale area was found in about one-third of the children 6 months of age or younger, in nearly two-thirds of those from 6 to 12 months old, and in almost all of the children over 1 year of age.

² Table 1 of original publication.

³ Table 2 of original publication.

The other types of skin lesions were found much less frequently. The rough pale area and the pale mottling were observed with approximately the same frequency in the different age groups; and the markedly pale or depigmented areas and the goose-flesh and lichenoid lesions were found with increasing frequency in the higher age groups, as in the case of the hazy pale area.

With regard to the more familiar representative types of leprotic skin lesion, one or more suspected pink or red macules were seen in eight cases, the youngest of which was between 10 and 12 months and the oldest between 4 and 5 years old. In four of these cases the macule could not be distinguished from simple erythema or localized flushing from accidental causes; but in the other four it was somewhat suggestive of leprosy. The latter however, were all found negative for *My. leprae*. All the suspected red macules were too transitory to be regarded as definitely suspicious of leprosy. One or more papules, apparently not acutely inflamed but glistening, not tender, and more or less firm, were found in six cases (from 8 to 24 months old; of these, the papules in four cases were found positive (++) to (++++) for *My. leprae*. The bacteriologically positive cases ranged from 15 to 23 months of age, and the two negative ones were from 6 to 8 months old. Another case showed, at the age of 2 years 4 months, a bacteriologically negative papule which was later examined at Manila and identified as tuberculoid leprosy. One case showed a clinically typical leprotic, depigmented macule with clear borders, which was first noticed by the mother when the child was 3 months old. The macule was found negative for *My. leprae*, but a bacteriologically positive papule developed outside the macular area when the child was 17 months old. One case showed, at the age of 3 years, a thickened area below the left elbow which suggested an infiltration or a scar. The lesion has remained stationary for nearly a year now, however, never appeared pinkish, and was repeatedly found negative for *My. leprae*.

Among the neurotrophic and circulatory changes a shiny and apparently tense condition of the skin of the anterolateral aspect of the lower half or two-thirds of the legs was observed, even among the youngest children, occurring in 30.8 per cent of the cases 6 months of age or younger. In the higher age groups the incidence of this type of change progressively decreased, with only 1.3 per cent of the cases affected among those over 1 year of age. Dryness, with superficial fine wrinkling of the skin of the anterolateral aspect of the

legs, usually with some degree of shininess, was first noticed in children over 2 months of age, the incidence progressively increasing in the higher age groups; 59.2 per cent of the cases over 1 year of age were affected. Scaling or ichthyosis of the anterolateral aspect of the legs followed the same trend as the drying and wrinkling, though the increase in incidence occurred chiefly after the age of 1 year. Apparently the three conditions—shininess, dryness, and ichthyosis—are successive stages in the same change.

Flushing of the skin of the legs was seen in only five cases, and of the feet in one case. The youngest child showing flushing of the legs was from 8 to 10 months of age. Cyanosis, chiefly of the hands or feet, was observed in ten cases, the majority of which were over 1 year of age. Cyanotic spots on the palms and soles of very young children are not infrequently found after healing of scabies in these regions. Anesthesia was detected in one case, enlarged ulnar nerves in another case—both between 2 and 3 years of age—and contracture of the small fingers in an 8- to 9-year-old child.

Suspected lesions in children of nonlepers.—With the exception of enlarged cutaneous nerves, contracture of fingers, and flushing of the legs, all the different types of suspected lesions found among the children of lepers were also seen among the children of nonlepers: The commonest type found was, as in the former group, the hazy pale area. It was observed in all age groups, even among the youngest children (under 2 months of age), though it showed no apparent difference in incidence in the different age groups, being present in approximately 50 per cent of all cases. On the other hand, the markedly pale or depigmented areas and the goose-flesh type of lesion were found more frequently among the older than among the younger children. A shiny, dry, or finely wrinkled condition of the skin of the legs was also observed in a considerable proportion of the cases—in fact, in a greater proportion than among the children of lepers. There were relatively fewer cases, however, with ichthyotic legs or cyanotic hands and feet than among the children of lepers.⁴

Total incidence rate of suspected lesions.—The approximate total number of lesions found in all the examinations (i.e., on both groups of children) was also studied in relation to the different age groups and the number of examinations made on each group.⁵ Up to the age of 20 to 24 months the interval between

⁴ Table 3 of original publication.

⁵ Table 5 of original publication.

examinations was, on an average, two to three months. The older cases had been examined relatively less frequently in relation to their age, as many of them had been born outside. In general, it was found that the number of suspected lesions tended to increase with age, the exceptions being the age subgroups of 10 to 12 months, 12 to 16 months, 2 to 3 years, and over 3 years. In the age subgroup of 20 to 24 months, which had the greatest number of examinations and also of suspected lesions, there was found an average number of 7.9 suspected skin lesions and 10.4 neurotrophic and circulatory changes for each case. In the other age subgroups, especially the younger ones, which were examined relatively more frequently, the corresponding figures were lower. The total incidence rates for the whole group of 231 children were 3.55 (suspected skin lesions) and 5.51 (neurotrophic and circulatory changes). These findings are much lower than those reported by Chiyuto(1)— 35.25 ± 1.60 skin lesions for children of from $2\frac{1}{2}$ to 20 years of age. While it is possible that a few lesions were missed by us or excluded in the analysis—mottled spots were considered as only one lesion if grouped in the same region or area—our calculation also included duplications or even triplications, as in some cases showing transition of one type of lesion to another both the original and the transitional types were counted independently instead of only once.

The group of children of nonlepers that were examined only once showed an average number of 1.47 suspected skin lesions and 1.77 neurotrophic and circulatory changes for each case.

Regional frequency of different types of suspected lesions.—The order of frequency of the different types of suspected lesions and affected regions, from the most frequent to the least, was found to be as follows:^a

(A) For suspected skin lesions: 1. *Hazy pale area*: thigh (VI); buttock (III); face (I); leg (V); chest and back (II); abdomen and lumbar (IV); arm; forearm (VII); neck. 2. *Mottled pale area*: face (I); buttock (III); chest and back; abdomen and lumbar; neck; leg; thigh (II); forearm. 3. *Rough pale area*: face; buttock; forearm and thigh; chest and back; leg; arm. 4. *Markedly pale or depigmented area*: face (III); buttock (III); thigh (III); abdomen and lumbar (IV); chest and back (IV); forearm (and neck, II) and leg (IV); [arm (I)]. 5. *Gooseflesh, follicular, or lichenoid area*: chest and back (I); abdomen and lumbar; forearm; thigh (III); arm (II); buttock; face and leg.

(B) For neurotrophic and circulatory changes: 1. *Dry, finely wrinkled skin*: leg (I); thigh and forearm (II) and chest, abdomen and lumbar; buttocks; face. 2. *Shiny skin*: leg (I); thigh; face, chest and buttock; forearm and abdomen. 3. *Ichthyotic skin*: leg (I); forearm and thigh; arm; face, chest and abdomen.

Incidence and relation of skin diseases to suspected lesions.—Of the 240 children of lepers included in these observations all but a few of the youngest showed some kind of skin disease, or evidence

^a The figures and regions inclosed between parentheses indicate the order of regional frequency in the children of nonlepers.

of it, in one or more examinations. The most commonly encountered diseases were scabies, prickly heat with or without superimposed eczematoid dermatitis, pyodermitis, and eczema. There were also a few cases of impetigo, tinea versicolor, and mild ringworm eruptions, especially among the younger children. Insect bites, intertrigo, furuncles, bruises, and burns were also noted. Definite scars were considered in the same category with the skin disease as a class.

In many cases the scars or marks left after the subsidence of the above-mentioned skin affections, especially by those involving chiefly the superficial layers of the skin, simulated closely the appearance of the "suspected skin lesions." Because many of the examinations were made at intervals of from two to three months, it was thought possible that some of the suspected lesions were really vestiges or scars of previous nonleprotic skin eruptions. An attempt was made, therefore, to correlate the relative total regional frequency of the suspected lesions with that of the skin diseases.⁷

With the exception of the legs, where neurotrophic changes were found more frequently than any other type of lesion, skin-disease lesions were always more frequently found than suspected lesions for each corresponding region.

On the face and buttocks, suspected skin lesions and skin diseases were found in about the same frequency, but elsewhere there was no such correspondence. The greatest disproportion in the frequency of these two general types of lesions occurred in the legs, forearms and hands, arms, chest and back, abdomen and lumbar region, and thigh, in the order given.

The relative order or regional frequency of suspected skin lesions from the most to the least frequently affected region was: face, buttock, thigh, chest and back, leg, abdomen and lumbar, forearm and hand, arm and neck. For skin diseases the sequence was: leg, forearm and hand, chest and back, arm, thigh, abdomen and lumbar, face, buttock, and neck.

The frequency of skin-disease lesions tended to increase up to the age of 12 months, after which it gradually decreased. Suspected skin lesions also tended to increase up to 2 years of age, beyond which a tendency to decrease was noted.

Scabies was the most frequent skin affection of the extremities, especially of the distal portions, the trunk being involved rather less frequently. On the other hand, prickly heat and eczematoid dermatitis were more frequently seen on the face and trunk, and were apt to be severe in the latter region. Traumatic and other accidental lesions—scratches, bruises, insect bites—were seen mostly on the more exposed regions, like the face, hands, buttocks and legs. The

⁷ Table 5 of original publication.

commoner skin diseases were apt to be extensive and generalized in the very young children, while they were more discrete in the older cases.

From the above analysis it is not possible to establish any definite relationship between the occurrence of skin diseases and the incidence of suspected lesions. It may perhaps be stated that scabies is not an important etiological factor; but it can not likewise be stated that other skin diseases are of little or no importance in the causation of suspected skin lesions.

Inconstant character of suspected lesions.—Many previous observers have already noted the tendency to spontaneous subsidence and subsequent recurrence or reactivation of the more manifest leprotic lesions. Chiyuto has also observed similar changes in the early, unstriking lesions. He has given a clear account of the transition from the gooseflesh areas to ringworm-like or circinate lesions, and from these to the hazy or clear depigmented areas. We have also frequently noted disappearance or fading away of the hazy pale area, with or without subsequent reappearance; also, in a few cases, the transition from the hazy pale area to the gooseflesh or lichenoid type of lesion and from this back to the hazy pale area or simply disappearance of the transitional type. The markedly pale or depigmented areas and the pale mottlings were usually more persistent; but even these were at times clearer and at other times less well defined. The same was true of the shiny, dry, and ichthyotic condition of the legs. We have not so far seen a transition from the hazy pale area to the well-defined depigmented or pink leprotic macule in any of the children included in this study.

Histological picture of the suspected skin lesions.—We have no data under this category to present. However, Dr. J. O. Nolasco, of the Pathological Section, who has been obtaining sections from our cases that came to autopsy, has kindly allowed us to quote him to the effect that he has not seen any abnormal findings in the few cases with suspected pale areas that he has so far studied.

COMMENT

Significance of the observed suspected changes.—Chiyuto's concept that the hazy pale or depigmented areas observed by him in children of lepers are of leprotic nature is presumably based on the following evidence: (1) Their constant occurrence in these children; (2) the constant finding of perivascular round-cell infiltration in

sections made from these lesions; (3) the observed occasional transition of this type of lesion into the gooseflesh type, and the more commonly observed transition of the latter type into the ringworm-like or circinate lesion which he frequently found histologically to show definite tuberculoid changes, with the further transition of the ringworm-like lesion into the depigmented macule; and (4) his finding of the existence of a close correspondence between the number and distribution of the depigmented or pale macules in children and those of the well-developed leprotic lesions in positive lepers.

The first two parts of the evidence may be accepted as a valid argument only if the hazy, pale or depigmented areas are constantly or frequently found only in children of lepers and not in those of nonlepers not exposed to infection but otherwise brought up under very similar conditions, and if these lesions can be constantly shown clinically and histologically to develop into unequivocal leprotic lesions. Chiyuto found tuberculoid changes only once in 27 sections from hazy depigmented areas or depigmented macules, and only perivascular round-cell infiltration in the rest; the latter finding was also observed in sections from apparently normal as well as from anesthetic skin areas. It is generally recognized that perivascular round-cell infiltration is not a specific tissue reaction peculiar to one or a few affections.

Our finding of hazy pale areas in 50 per cent of an unselected group of children of nonleprous parents suggests that not all of these areas, found in children of lepers, are of leprotic nature. However, clinical and histological demonstration of the evolution of these lesions requires time and continued observation; for the present, it seems, proof is not available.

The above considerations may to a certain extent be applied in the case of the gooseflesh, lichenoid or follicular lesions, which were also observed in children of nonlepers with a frequency comparable to their incidence in the children of lepers. The finding by Chiyuto of tuberculoid changes in this type of lesion in the few cases biopsied, and his rather constant finding of similar changes in the ringworm-like and circinate lesions, do indicate the necessity of searching for and suspecting such lesions when one is examining for leprosy. However, it should be borne in mind that lesions of the same or similar clinical appearance are frequently produced by nonleprotic affections of the skin, and a definite opinion regarding their nature in

eases with no history of exposure or without other leprous stigmata should not be given except on undoubted microscopic evidence.

As regards the alleged close correspondence between the number and distribution of suspicious lesions in children of lepers and those of the more manifest lesions in bacteriologically positive lepers, there is a possibility that such correspondence might have been merely fortuitous. The finding would be considered significant if we could assume that all early leprotic foci in children are always manifested by some recognizable skin lesion, or that all such skin lesions as those found in children of lepers are of leprotic nature; and also that all such foci, besides the well-developed leprotic lesions, have been recognized and recorded in the case of the positive lepers. Since presumably only the more familiar types of leprotic lesions were recorded for the positive lepers, whereas most or all of the unstriking or less-characteristic changes—the hazy depigmented or pale areas, the goose-flesh and the circinate lesions, as described by Chiyuto in children—had been missed or had not been recorded, it is evident that the average total number of lesions for the positive lepers would have been found greater than that for the children. Thus, Chiyuto explained the relatively fewer lesions found in some of the positive lepers, compared with those found in the children, on the ground that the hazy, depigmented or pale macules are easily missed when examining frank cases of leprosy. What has been said above regarding the hazy pale area and the goose-flesh type of lesion may similarly be applied to the other types of suspected skin lesions.

The well-defined, depigmented and pink macules, with or without marked sensory disturbances, have already been accorded an established place in the symptomatology of early leprosy and are too familiar to require comment. However, the early appearance of bacteriologically positive leprotic papules, with or without other suggestive leprotic changes, has heretofore not been given the attention that it deserves. In the last seven years this type of lesion has been found to be the earliest unequivocal lesion in the majority of the children that have become declared, or bacteriologically positive, lepers⁽⁴⁾ in Cullion.

As regards the suspected neurotrophic and circulatory changes, we can not glean from our observations any definite indication of their proper significance. The shiny and dry condition of the skin of the legs was observed even more frequently in children of nonlepers than in children of lepers. Its occurrence was apparently unrelated

to the general state of nutrition of the patient; in fact, it was chiefly encountered in apparently well-nourished children. Ichthyosis of the legs, however, was found more frequently and in a more advanced state in children of lepers than in the children of nonlepers. Flushing of the legs was found in only five cases among the children of lepers, and of these only one so far has become a positive leper. Rodriguez⁽⁶⁾ has stated that all the children under his observation who showed a flushed, tense, glistening appearance of the skin of the anterior aspect of the legs (Nicolas' sign) with, later, dryness and ichthyosis of the same regions during infancy, became lepers later on.

SUMMARY AND CONCLUSIONS

A group of 240 children born of leprous parents, ranging in age from newly born to 8 years, has been observed with the object of detecting the earliest clinically recognizable changes that may be attributed to leprosy. A group of 78 children of nonleprous parents was also examined once, for comparison.

The observations were for the most part clinical, microscopic examination of smears having been made only for definitely suspicious lesions; sections could not be obtained except from cases that came to autopsy.

The commonest type of suspected (that is unidentified) skin lesion found that could not be attributed directly to known nonleprotic skin affections was the hazy pale area first described by Chiyuto. Its incidence was found to increase with age, and it was observed in 96 per cent of all the children of lepers above one year of age.

Of much less frequent occurrence were the rough, scaly or granular pale areas and the pale mottlings which showed no definite relation to age, the markedly pale or depigmented areas without definite borders, and the gooseflesh, follicular, or lichenoid areas which were found more frequently in the older than in the younger age groups.

Suspicious reddish macules were found in a few cases, but these were transitory and were found negative for *My. leprae*. A definitely depigmented macule with clear borders, typical of the whitish macule of leprosy, also negative for *My. leprae*, was found in one case. Suspicious papules were found in seven cases, in four of which *My. leprae* was obtained from the lesion in smears, while in one instance the bacteriologically negative lesion was later identified as tuberculoid leprosy.

Also frequently observed were the shiny, tense, glistening but not flushed appearance of the skin of the anterolateral aspect of the legs in the youngest age group; the dry, finely wrinkled skin of the same regions in the slightly older children; and the ichthyotic condition of the legs in still older children. These changes apparently were different stages in the same condition. An associated flushing of the skin of the legs was observed in only five cases. Enlarged cutaneous nerves, anesthesia, and other evidences of nerve involvement were found in only a few cases, mostly in older children.

With the exception of enlarged cutaneous nerves, contracture of fingers, and flushing of the legs, all the different types of suspected lesions found among the children of lepers were also seen among the children of nonlepers. In the latter group the hazy pale area was also the type most frequently seen, being present in 50 per cent of the cases, regardless of age. The depigmented and the gooseflesh types of lesion and the neurotrophic changes in the children of nonlepers were found to occur with a relation to age similar to that in the case of the children of lepers. Neurotrophic changes, as a whole, were observed in a greater proportion among the children of nonlepers than among the others, but a markedly ichthyotic condition of the legs was more frequently found in the children of lepers.

The above observations, considered together with those previously reported by others, suggest that, while many of the early unstriking changes seen in children of lepers are probably of leprotic nature, not all such changes can be regarded as of that nature.

The total incidence rate of suspected lesions among the children of lepers comprised in this study was found to be much lower than that reported by Chiyuto for a group of older children. In general, it was also found that the number of suspected lesions tended to increase with age. This may be adduced as evidence that the development of the early leprotic changes, like that of the more manifest leprotic lesions, is as a rule gradual and not simultaneous.

The relative order of regional frequency of suspected skin lesions from the most to the least frequently affected region was: face, buttock, thigh, chest and back, leg, abdomen and lumbar region, forearm and hand, arm and neck. An attempt to determine whether or not there exists a correlation between the occurrence of nonleprotic skin diseases and that of the suspected skin lesions failed to show such relation except in the total regional frequency of the two classes

of lesions for the facial and the gluteal regions. However, whereas these regions ranked first and second in relation to suspected skin lesions, they occupied the seventh and eighth places, respectively, as regards skin diseases. The great frequency of scabies in the distal portions of the extremities, considered with the relatively much less frequent occurrence of suspected skin lesions in these regions, may indicate that scabies is not an important factor in the causation of the latter. The same can not be said for other skin diseases.

The inconstant character of the early suspected changes previously reported by other observers has been confirmed by our observations.

Evidence from the very meager histological material derived from our cases is too insignificant to permit of any interpretation.

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