

## (SURGICAL TREATMENT OF THE PRIMARY LESION OF LEPROSY

R. BOENJAMIN, M. D.  
*Central Institute for Leprosy Research*  
*Batavia*

Opinions about the existence of a primary lesion of leprosy are still divergent. The primary lesion of syphilis often presents a typical picture, clinically and otherwise; and, too, the place of penetration of the microorganisms and the locally stimulated tissue reaction are frequently observable. With leprosy, however, the relations in this respect are quite different.

In the first place, the period of incubation of leprosy may be very long—a matter of months or years. The connection between the place of infection in the skin and the local appearance of a primary symptom is, therefore, difficult to determine. Secondly, such a primary skin lesion—usually a small hypochromic macule—gives the individual no cause for complaint, as regards either sensation or outward appearance, and he is frequently unaware of its nature often mistaking it for a harmless “*panoe*” (pityriasis versicolor). The discovery of such lesions, therefore, can be expected only in careful examinations of persons who have been in contact with leprosy.

It is generally assumed that the leprosy bacillus enters the human body through the skin or the mucous membrane of the nose or tonsils, while infection via the lungs or gastrointestinal canal is considered improbable (Klingmüller). Those who assume the existence of a primary lesion (Klingmüller, Rogers, Muir, Rodriguez and others), explain its genesis as follows: Where the microorganisms enter the skin they may remain for a very long time and ultimately give rise to local, superficial changes of the skin and nerve. This primary focus is recognizable clinically as a macule with hypopigmentation (seldom hyperpigmentation) and reduced sensitivity. Histologically, this primary anesthetic macule presents no specific picture; there may be only round-cell infiltration around blood vessels and nerves, or in some cases the epithelioid and giant cells of the tuberculoid lesion. The primary focus may also manifest itself, however, as a skin nodule in which may be found the Virchow lepra cells, signifying lepromatous leprosy.

The formation of one or another kind of primary lesion of the skin depends on the reaction of the tissue at the time of the

penetration of the microorganisms. From this focus, which may remain inactive for months to years, the spread of the bacilli to other parts of the body via the lymphatics or blood-vessels occurs when the organism can no longer defend itself against them; and then there appear new lesions—anesthetic macules or lepromas according to whether the body can offer marked or slight resistance to the invasion.

In the belief that the infection may for a time be localized in the primary lesion, several investigators have tried to prevent its dissemination by chemical cauterization or surgical extirpation of the entire lesion area. Apparently successful attempts to do this have been reported by several workers.

When attention was first given to this matter in this institute, the only available information was that found in Klingmüller's book (8). According to him, Rake was the first to apply surgical treatment to "primary leprosy" lesions—although what he actually did is not said and his publications cannot be consulted—and Leloir also recommended the extirpation of primary foci. He then goes on to mention the following reports, none of which is available.

Morcano and Würtz dealt with a 4-year-old child with a small flat macular lesion of the right temple which gradually grew to 8 mm. in diameter, with anesthesia extending 5 mm. beyond the edge and without swelling of the lymph nodes. Twelve months after its appearance it was removed; bacilli and vascular changes were found in sections; there was no return, and no generalization. Sederholm reported a case in which a small, insensitive area on the forearm was removed together with the related swollen nerve, with no further evidence of the disease several years later. Sakurane, in one case, destroyed a small lesion on the wrist with potash lye, and in two other cases excised solitary macules on the forearm and wrist, with no further manifestations in any of them during a 10-year observation period. Glingani's case was that of a forceps-delivered child of a woman with nodular leprosy which, at the age of 12 months, developed small nodules with numerous bacilli at the place of injury by the forceps blade. These lepromas were excised, and 25 years afterward the individual, then grown to womanhood, was still entirely healthy. Klingmüller's own experience is briefly mentioned as the apparent cure of a case of maculoanesthetic leprosy by the excision of macular lesions, with no further manifestations in 21 years.

More is said of the much-reported Hawaiian case recorded by Goodhue and McCoy in 1916 (6) and by Goodhue and Hasseltine in 1924 (5). A girl child born at the leprosy settlement of leprous parents—both neural cases—but removed to clean surroundings within 6 hours after birth, presented at the age of 19 months a slightly raised, 8 by 12 mm. lesion on the left forearm. A "moderate number" of bacilli were found in it, and its histological structure was "entirely consistent with a leprous nodule." Although she was at once returned to her parents in the settlement and stayed there, she was without symptoms of leprosy nine years after its

removal, and smears showed no bacilli. Later on Hasseltine (7) wrote that at the age of 25 she was still free from any sign of leprosy although married to an inmate with lepromatous leprosy; and still later Fennel (3) wrote that she had remained without manifestations.

Of more recent reports, one is that of Wayson (15), also from Hawaii, relating the case of a French priest aged 61 years, resident at the Kalaupapa Settlement for 8 years, who had developed three small infiltrated lesions on his forehead where he habitually rubbed with his fingertips when reading. Removed surgically they were found to be bacteriologically positive and histologically "characteristic of leprosy." There had been no further development in more than four years; and seven years later Fennel (3) said that the individual still remained without symptoms.

There has also been some interest in this matter in Argentina. Puente and Fiol (12) recommended in a meeting, extirpation of solitary lesions not situated on the face; they had had no relapses, but how many cases were involved does not appear in the abstracts published. In the discussion, Fidanza told of cases treated by him, with relapse. At the same meeting Fernandez and Schujman (4) reported a case so treated which had relapsed; but the lesion was avowedly lepromatous. Some years later Baliña and Basombrio (1) reported the surgical removal of lesions of 14 tuberculoid cases with one or a few lesions (one involving only a nerve), and the destruction of such lesions by other means (galvanocautery, electrocoagulation, CO<sub>2</sub> snow) in 7 other cases of the same kind (one of them, also, with nerve involvement). Chaulmoogra treatment was continued. Only one case has relapsed.

In the meantime there had appeared a symposium (14) on the subject, initiated because of the favorable experience of Rodriguez and Wade (13) with two cases in which solitary lesions had been excised for histological study. Fidanza favored extirpation or destruction of lesions when there are only one or two of them. Nelson Souza Campos gave details of 6 of the cases which he had so treated. Lowe tabulated the results in 19 cases, without conclusion as to the desirability of the measure. Ryrie told of cases with original solitary lesions burnt away with acid without preventing later spread, and was doubtful of the justification of surgical removal of early leprids. Lampe, in this institute, had extirpated a solitary lesion from a single case three years previously (9), and Lobel had treated a second one in that way. Giffen and Hayashi indicated doubt of the practicability of radical excision.

#### PERSONAL EXPERIENCE

Although what could be learned about the extirpation of solitary lesions at the time this work was begun was not conclusive, it seems sufficiently encouraging to justify applying the measure experimentally in this institute. Favorable material has been available, because of the system of examinations of families of actual cases which has enabled us to diagnose cases with the earliest lesions. The method has now been in use for several years, with satisfactory results so far. Although the number of cases treated is as yet too small to permit drawing any final conclusion, the results are believed to support the idea

that under certain circumstances leprosy bacilli may be harbored for some time at the portal of entry in the skin.

The indications which we have adopted for the application of this method are as follows: (a) The primary skin lesion must be solitary, and it must not cover too large an area. An anesthetic macule more than 10 cm. in diameter we regard as not suitable for this treatment, because it may be generally expected that by the time that size has been attained there will have been further dissemination of the bacilli. (b) There must not be enlargement of the associated nerves, nor swelling of the regional lymph nodes, both of which conditions signify dissemination of the bacilli from the primary focus.

Diagnosis can usually be made only clinically, because smears from primary lesions are mostly negative for bacilli and the nasal secretion also does not contain them. Diagnosis is based on the following criteria: (a) Existence of hypoesthesia and (or) disturbance of the temperature sense, although at a very early stage there is sometimes hyperesthesia. (b) Hyperchromia of the macule; rarely, hyperpigmentation may be seen. (c) Incipient atrophy of the skin, manifested by disturbances of hair growth and of sweat secretion. (d) The epidemiological data of the patient, such for example as regular contact with leprosy patients, may support the diagnosis.

Extirpation of the skin lesion is performed under local anesthesia. The entire lesion is removed together with about 0.5 cm. of normal-appearing skin around it. The skin is removed down to the subcutaneous connective tissue.

#### REPORT OF CASES

The descriptions of the patients from whom primary skin lesions were excised, on the grounds indicated above, here follow. After extirpation none of the patients received further treatment.

CASE 1 (Skt. P. 76).—An Indonesian girl baby, born June 1936, had a small, dark-brown papule on the right cheek when she was 10 months old (Plate 13, Fig. 1). Her mother had lepromatous leprosy (L3), while her uncle and aunt both had neural leprosy (N2).<sup>1</sup> An only child, she lived with her widowed sick mother and the two other sick relatives. Clinical diagnosis: Tuberculoid leprosy.

On October 26, 1937, when the child was 16 months old, the papule was extirpated. Histopathology: Confirmation of the clinical picture of tuberculoid leprosy; positive for bacilli.

Observations: Reexamined in May 1938, there were no symptoms of

<sup>1</sup> In this report the clinical classification of the Cairo Congress is used.

leprosy and a smear from the operation scar was negative. Nothing noteworthy was found in October 1939, when her mother died, leaving her to the care of her sick aunt. Further examinations in April 1940, June 1943, April 1944—when a smear of nasal secretion was found negative—and January 1949, the girl then almost 13 years old, were all negative. She has remained free from any symptom of leprosy and in excellent general health, in spite of the fact that family reasons have made it impossible to separate her from her sick relatives. She has always been living with them.

This case was published by Lampe (9).

CASE 2 (E. P. P. 242).—A Menadonese man aged 22, born in Menado in 1916, unmarried and working as a clerk in the government office here. Coming to the leprosy institute on August 26, 1938, in excellent general health, he presented on the extensor surface of his left forearm, directly below the elbow, a single pale, anesthetic macule, smooth of surface and without scaling. He had already been treated by several physicians in Batavia without benefit. He denied leprosy in his family, or recollection of having had any association with any leprosy person. He claimed that the macule, which measured 4 by 2 cm., had existed for only 3 months. He had no complaints of itching, paresthesias, or pains in the limbs. No enlarged nerves were found. Smears from the macule and of the nasal secretion were negative. Clinical diagnosis: Leprosy, neural, first stage (N1).

On August 29, 1938, the macule was excised. Histology: Perivascular round-cell infiltration and distinct tuberculoid structure, with typical Langhans cells. Leprosy bacilli not found.<sup>2</sup>

Observations: Reexamined in August 1939, the patient's general state of health was good; there was a keloid scar at the place of operation, and it still had some hypoaesthesia; no other macule on the body. Again in August 1940, and June 1941, nothing significant was found. In 1942, during the Japanese invasion, the patient removed from Batavia. In 1947 I met him here again and he told me that no new lesions had appeared. Believing himself completely recovered, he has discontinued further examinations.

CASE 3 (Mnd. P. 490).—An Indonesian, born in Kampung Tanah Abang (Batavia) in 1913, this patient was seen during a family examination in October 1938, when it appeared that 7 of the 14 children had leprosy. Mnd. was first examined then because he was afraid that he might have been infected by his sick brother, but no leprosy lesion could be found. However, during a second family examination in October 1939, he was found to have a small, pale, smooth-surface macule, almost round in shape and about 13 mm. in diameter, on the extensor surface of the left upper arm. In this macule, which had existed for less than a year, there were distinct disturbances of sensibility, with reduction of temperature and pain sensations. Ulnar nerve not enlarged. Smears negative. General state of health excellent; no complaints whatever. Clinical diagnosis: Leprosy, neural, first stage (N1).

On October 27, 1939, the macule was extirpated. Histology: Parakeratosis; papillae distinct. Limit between epidermis and cutis quite

<sup>2</sup> Report by the Department of Pathologic Anatomy, Medical College.



visible. Tissue changes, probably caused by intracellular edema. No specific changes in cutis and subcutis, except here and there infiltration of round cells and leucocytes around the blood vessels, sweat glands and hair follicles. No "free zone" visible. Negative for leprosy bacilli.<sup>2</sup>

Observations: When reexamined in August 1940 he exhibited a keloid scar but no other macules; general health good, no complaints. He had married and was living with his wife in another house in the same Tanah Abang quarter. In 1944 and again in 1947 he was still without suspicious macules.

CASE 4 (Idr. M. P. 499).—An Indonesian young boy, born in Kampung Kepuh (Batavia) in 1936, living with his healthy parents and an uncle who had moderately advanced lepromatous leprosy (L2). During a family examination in October 1939 he was found to have a small, pale, smooth-surfaced macule on the extensor surface of the left forearm (Fig. 2). This lesion was said to have existed for only one month. Temperature sense distinct, pain sense undisturbed. Ulnar nerve not thickened. Smears negative. The little patient was somewhat thin, but the state of health was satisfactory; no complaints. Clinical diagnosis: Neural leprosy (N1).

On October 31, 1939, the macule was excised. Histologically: Epidermis thin, with distinct papillae; hyperkeratosis; thinning of the stratum spinosum. Round-cell infiltration in several places. Directly under the epidermis, granulomatous accumulation with a few epithelioid cells, lymphocytes and leucocytes, arranged around the vessels and in one place reaching the epidermis. In the subcutis, more of the epithelioid-cell granuloma, distinctly delimited from the surrounding tissue, the whole resembling a tubercle. Here, too, the lesion was situated mainly around the blood vessels, sweat glands and sebaceous glands of the hairs. Leprosy bacilli not found.

Observations: Apart from a keloid cicatrix nothing noteworthy was seen during reexaminations made in December 1940, September 1941, March 1943, and February 1944, except that on that last occasion the boy, who had been rather thin, had become a little fatter. When last seen, in February 1949, he was a fine boy of 13 free from any symptoms of leprosy.

CASE 5 (Dj. P. 992).—An Indonesian woman, born in Kampung Djawa (Batavia) in 1910, married, with 7 children of whom 2 had leprosy, supposedly infected by leprous neighbors; she and her husband developed the disease afterwards. Dj. stated that she first saw her macule in June 1942, when she was 32 years old. Examined when it was supposed to be only one month old, it was a pale, smooth-surfaced, distinctly hypoesthetic macule, measuring 2.5 by 0.5 cm., located high on the left side of the neck (Fig. 3). The auricular nerve was not enlarged. The usual smears contained no leprosy bacilli. Clinical diagnosis: Neural leprosy (N1).

\* On June 19, 1942, the macule was excised. Histological picture: Atrophic epidermis, papillae not distinct; slight hyperkeratosis. In the cutis and subcutis, round-cell infiltration and leucocytes around the blood vessels, sweat glands and sebaceous glands of the hair. No "free zone." No leprosy bacilli found.

Observations: Three months later, in September, only the surgical scar was to be seen. In February 1944, a smear from the scar was found negative for bacilli. The patient continued to live with her sick husband

and children, our advice notwithstanding. In January 1949 she remained healthy and without complaints, and there were still no new macules to be seen. The sensibility of the cicatrix had become normal.

CASE 6 (Nas. P. 993).—An Indonesian woman, born in Kampung Djawa (Batavia) in 1915, married and with 3 children, one of whom had developed leprosy three years before she herself did. The source of infection was probably outside the immediate family; other leprosy cases were known among the other members of her family who lived in the same kampung. In June 1942, during the first family examination, she was found to have a hypopigmented but hyperesthetic, smooth-surfaced macule on the extensor surface of the left forearm, 4 by 1 cm. in size, said to be about a month old. The only complaint the patient had was occasional paresthetic sensations in the left hand. Ulnar nerve not enlarged. Smears negative. Clinical diagnosis: Neural leprosy, early (N1).

On June 19, 1942, extirpation of the macule. Histological picture: Epidermis thick, with acanthosis and hyperkeratosis; papillae not distinct; here and there spongiosis; in several places the epidermis contained small abscesses. The limit between epidermis and cutis was distinct except where the abscesses were situated. Cutis: nonspecific granulomatous accumulation and perivascular round-cell infiltration. Subcutis: less round-cell infiltration around the blood vessels and sweat glands. A "free zone" visible. Leprosy bacilli not found.

Observations: In September there was nothing of note other than the keloid scar; the paresthesia of the left hand had disappeared. In February 1944, a smear from the old cicatrix was negative. In January 1949 the patient, expectant, was in excellent general condition with no suspicious macule. The sensibility of the old cicatrix had become normal.

CASE 7 (T. N. K. P. 1057).—A Chinese young man, unmarried born in China in 1918, had come to Java in 1936. Since then he had lived in Batavia with his elder brother who had had advanced lepromatous (L3) leprosy for years, and had worked with him as a shop assistant. When examined in August 1942 we found on his back, on the point of the left scapula, a small macule, hypopigmented, hypoesthetic and smooth-surfaced, said to be 3 months old. General condition good; no complaints. No enlargement of nerves. Smears contained no leprosy bacilli. Clinical diagnosis: Neural leprosy, early (N1).

On August 21, 1942, the macule was excised. Histological picture: Hyperkeratosis and intercellular edema of the epidermis. In the cutis, round-cell infiltration and leucocytes, mainly around the blood vessels. No "free zone" visible.

Observations: Seen once after the operation, in February 1944, the general condition was good and there were no signs of leprosy.

#### DISCUSSION

Of these seven cases in which the primary lesions were extirpated, the examination for bacilli gave positive findings in only one (Case 1). In the six others the diagnosis had to be made on clinical grounds exclusively. Negative bacteriological findings in cases with primary macules of leprosy do not constitute a contraindication of excision of the primary lesion.

It is well known that the first skin symptom of leprosy is usually a hypopigmented macule, in which the sensibility is disturbed at an early stage. Seen early enough, there may even be hyperesthesia; later there are hypoesthesia and disturbances of the temperature sense. In this "macular stage" of leprosy the tissue reaction produces a histologically nonspecific picture, a banal inflammatory condition of perivascular infiltration of round cells. Acid-fast bacilli are hardly ever found in smears from these lesions, or in the nasal secretion, or even in the histologic sections.

The first lesion is not, however, always an anesthetic macule. In some cases it is a small, dark-brown papule, with or without disturbance of sensibility, which bacteriological and histological examinations show to be either tuberculoid or typical lepromatous. In these cases, with clinically distinct infiltration of the skin—but, as with the anesthetic macular lesions, no subjective complaints at all—acid-fast bacilli are found rather often. In the clinically tuberculoid form they are few and isolated; in the lepromas, on the other hand, they are many and with typical globi.

Because of the great rarity of a solitary leproma as a primary lesion, it is not unlikely that it may be held that such a lesion is always preceded by a macular stage of the usual kind. According to Rodriguez the incipient, anesthetic macular lesion without acid-fast bacilli may become bacillus-positive within 3 or 4 years if a leproma arises from the macule, the histological picture then being that of a typical lepra-cell granuloma. However, it is not intended here to go further into this hypothesis.

What will be considered here are the experiences of investigators in other countries regarding the histological picture of primary leprosy lesions of the anesthetic macular kind.

Manalang (10), who has made an extensive study of the histologic picture of primary lesions of leprosy, has described his findings in 33 cases, of whom 18 were over fifteen years old and 15 were under that age. Most of them had anesthetic macules and were suffering from tuberculoid leprosy; most of them were negative for bacilli, and the diagnosis was therefore made on clinical grounds. The histologic picture was round-cell infiltration with or without tuberculoid changes, and without acid-fast bacilli. He expressed the opinion that the initial stage of leprosy, in which there is found only one macular lesion with disturbed sensation and with the nonspecific round-cell histological picture is usually negative for bacilli.

For this reason he has concluded that it is not the acid-fast bacillus which transmits the infection in the first instance, but probably a nonacid-fast "virus" form of the microorganism. This nonacid-fast form, he holds, enters the human organism and sooner or later changes into acid-fast bacilli if conditions are favorable. However, we do not intend to expatiate



on this hypothesis, for it lies entirely beyond the scope of this article. Manalang's inquiries are important to us because his experience in the field of histopathology agrees with what we have observed here.

Chiyuto (2) studied 40 children, born of leprous parents, who presented early lesions. It appears that in 39 of these incipient cases the diagnosis was made on clinical grounds alone, and that because of the presence of anesthetic macules. In only one child—that one with clinically tuberculoid leprosy—acid-fast rod-shaped bacilli were found in the histologic preparations. In this positive case, however, there was not just a solitary tuberculoid papule, but anesthetic macular lesions as well.

From 9 of the 40 children biopsy specimens were taken for histological examination. In four cases tuberculoid structure was found; in one there was round-cell perivascular infiltration as well as tuberculoid changes; in the other four there was only perivascular infiltration of round cells. In one tuberculoid specimen a few leprosy bacilli were found (3 isolated rods in the endothelium of a blood vessel); the other eight specimens were negative for bacilli.

Nolasco and Lara (11) related their postmortem findings in a child 17 months of age, born at the Culion colony of leprous parents (L1 N1) and living with them from birth. For a time the child showed only the scars of scabies, but two months before its death there had developed on the right knee a papule, 5 by 6 mm., which upon examination turned out to be a leproma. It was positive in smears for bacilli and globi, and histologically it showed the characteristic Virchow lepra cells in which groups of acid-fast bacilli were found.

In the autopsy all the major internal organs were examined, and also the peripheral nerves and lymph nodes. Histologically everything was negative for bacilli except for the regional lymph nodes in the right groin. It was concluded that the papule (leproma) on the right knee was a primary lesion, and that dissemination of the leprosy bacilli had taken place via the lymphatics to the regional lymph nodes but, so far as could be detected, not beyond them.

Our own experience, related here, confirms the view that at a very early stage leprosy may show only an anesthetic macule, typically without acid-fast bacilli in smears. Our experience also confirms that of those who advocate extirpation treatment of such lesions, and we shall apply the measure to every willing patient whom we think suitable. Although for the time being we cannot support a fixed opinion on the basis of our seven cases, the results so far incline us to recommend the extirpation of such primary lesions.

#### SUMMARY

1. During the years 1937 to 1942, in part to study the histology of the primary skin lesion of leprosy but more particularly to determine the results of their treatment by surgery, we have excised solitary lesions of that kind from seven leprosy patients at the Leprosy Institute.

2. One of these patients had a distinct, solitary tuberculoid

papule on the cheek, whereas the lesions of the six others were smooth-surfaced, hypopigmented macules with obvious disturbance of the temperature and pain senses. A few bacilli were found in smears from the tuberculoid papule, while those from the six macules were negative, as was the nasal secretion in all of the cases.

3. None of the patients had nerve enlargement or swelling of the regional lymph nodes, signifying leprosy involvement. They had no complaints, and their small leprotic macules were mostly discovered by us during examinations of contacts.

4. In only one instance was the probable source of infection not evident. In the other six cases long-established contact could be determined.

5. The histological picture of the papular lesion of the cheek was tuberculoid, with some acid-fast rod-shaped bacilli present. Tuberculoid structure was also present in one other lesion, but no bacilli. The five other anesthetic macules showed only perivascular round-cell infiltration, with no bacilli.

6. None of the seven patients treated by extirpation of their primary lesions has as yet shown any further symptoms of leprosy, after observation periods ranging from three to twelve years.

#### CONCLUSIONS

On account of our own experience and the findings of other investigators, it is held probable that under certain circumstances the leprosy infection of the skin can remain localized for some time. This primary focus in the skin (primary lesion) may exist for some years before further dissemination of the bacilli occurs.

In undertaking the treatment of a patient with a solitary, primary lesion without thickened nerve or swelling of the regional lymph nodes, the extirpation of the lesion to prevent further development and dissemination of the leprosy infection should be contemplated.

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## DESCRIPTION OF PLATE

## PLATE 13.

FIG. 1. Papular lesion of cheek, Case 1, found bacteriologically positive and histologically tuberculoid.

FIG. 2. Anesthetic macule on forearm, Case 4.

FIG. 3. Anesthetic macule on neck, Case 5.

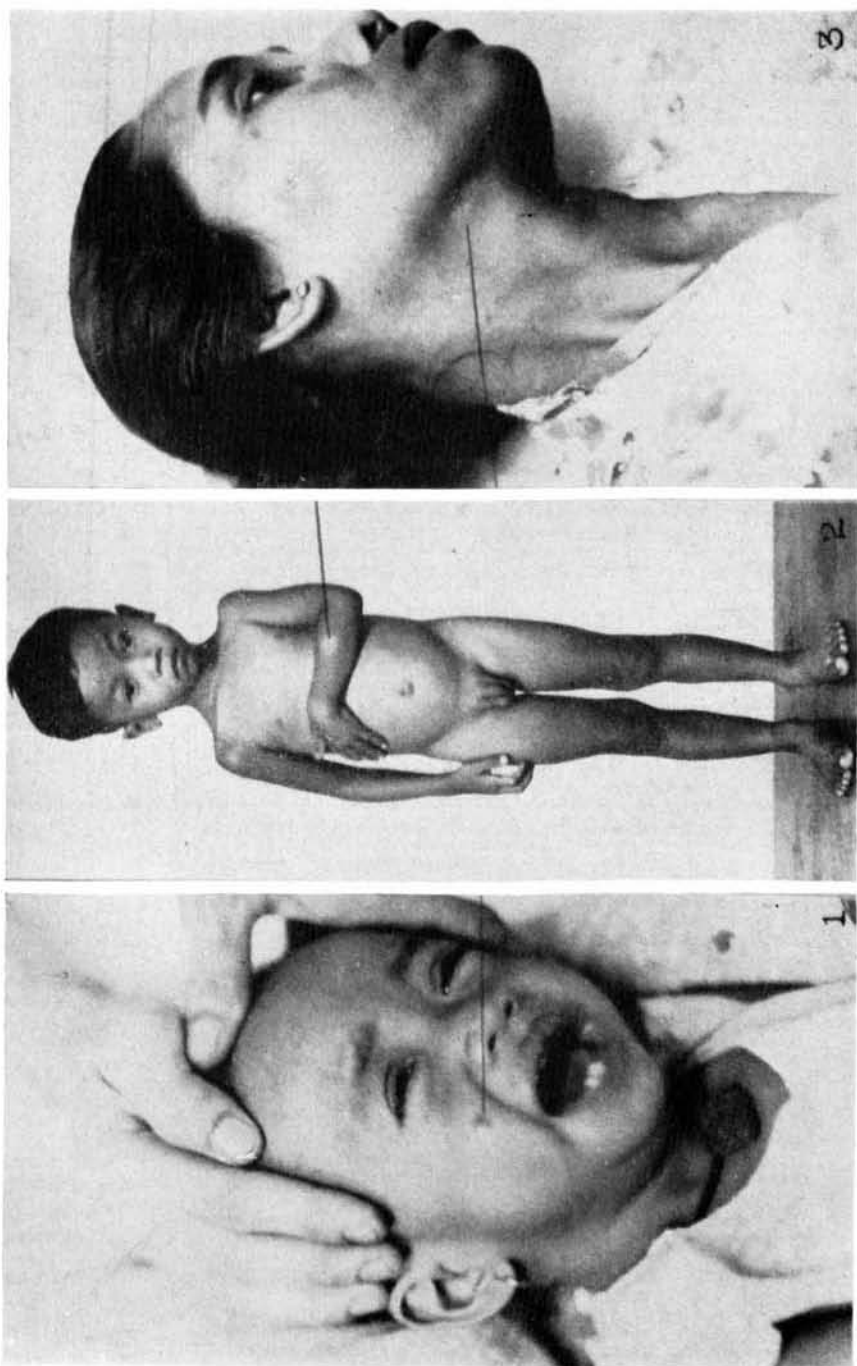


PLATE 13