THE EARLY DIAGNOSIS OF LEPROSY[1]

THE FIRST CLINICAL FINDINGS OBSERVED IN SEGREGATED CHILDREN OF LEPROUS PARENTS

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INTRODUCTION

Among physicians who have been trained in the United States or in Europe it is the common belief that leprosy is a chronic persistent disease of the skin, in which neurological phenomena are sometimes present, and that the appearance of the patient is made loathsome by deformities and mutilations. They also consider it a disease of warm or tropical countries, one which is not easily communicated and which is cured by the administration of preparations of chaulmoogra oil.

Each of these beliefs includes fallacies which lead to a misunderstanding of the disease and its problem. The classical clinical picture—"facies leontina," nodules which are laden with the specific bacteria, ulcerations, anesthetic macules and contractures—applies to late, advanced, or neglected cases. The rather general acceptance of this concept for the identification of the disease presents a situation corresponding to that which existed a generation ago in the diagnosis of pulmonary tuberculosis. Today tuberculosis is diagnosed at a very early stage of its clinical evolution. This advance has been facilitated by experimental investigations, which are not yet possible in leprosy. However, very important contributions have also been made by repeated and prolonged observations of the children in tuberculous families, and it seems probable that such studies of the children of leprous parents will be of assistance in the earlier diagnosis of leprosy.

The practical need for earlier diagnosis becomes immediately apparent when it is realized that leprosy exists in most of the countries of the world, and is prevalent in some countries of temperate

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or cool-temperate climates, although its incidence is probably not approximately known even in countries with a well organized registration of vital statistics. Nor can its communicability be accurately predicted since, though it seems to be of rare occurrence in most parts of Europe and the United States, it is endemic in some parts of them; and it occurs in families with a frequency, under some circumstances, which is comparable to that of tuberculosis. The method of its communication from one individual to another is likewise not decided, but it has been determined that a leprous person may appear to be well and may at the same time be spreading the specific bacterium from the mucous membranes of his nose. In other words there are "carriers" of the bacterium of leprosy.

The recognition of the earlier phases of the disease may also be expected to lead to a better understanding of its pathogenesis and treatment, as well as of its epidemiology. There is no drug which may be regarded as a specific remedy. Treatment by chaulmoogra preparations has been acknowledged by some of its former advocates to lack specificity, and the therapeutic value of the preparations is not yet determined. On the other hand, spontaneous clinical quiescence or arrest frequently occurs, and even among moderately advanced cases the subsidence of activity seems to be greatly promoted by general and symptomatic medical measures which are supplemented by suitable hygiene and diet. It would appear that application of such measures to early cases in a thorough and systematic fashion might facilitate the recovery of more of them before they have reached the intractable stage.

Leprosy is not a disease of the skin alone, although lesions of the skin and its appendages are prominent among its manifestations. It is a systemic infection in which the characteristic bacterium can be demonstrated in the blood stream during different phases of the disease, and is characterized by pathological changes in the blood vessels, the nerves, and the lymph nodes, vessels, and spaces. The muscles and bones of the extremities are often affected and viscera may be involved, though the skin changes are more evident. The course of the disease is usually one of distinct advances or progressions with alternating recessions. The progressions may evolve slowly or with great rapidity and intensity, and the recessions may be transitory or may eventuate in periods of clinical quiescence or arrest which persist for periods of weeks to years.

Neurological symptoms and signs form an essential part of the clinical syndrome in practically all cases. Many lesions of the skin as well as other symptoms and findings are often of but transient duration in any stage of the disease, and are especially so in the early stages. In these early stages the skin changes frequently resemble those in which disturbances of innervation or nutrition of the area have occurred, and may mimic the appearance of those of a number of dermatological conditions. Since they are frequently evanescent, or since they may never have developed, they may be absent at the time of examination, and only some portion of the characteristic neurological syndrome may be present.

This neurological syndrome is one of a multiple peripheral neuritis in which the motor fibers of the mixed nerves are less frequently or less severely involved than the sensory and "trophic" fibers, and in which there is frequently if not always evidence that the sympathetic nerves are damaged. The clinical aspects of the neuritis are characterized by the following features:

1. An outstanding selectivity in the involvement of single or multiple twigs, branches or trunks of the superficial nerves, among which the facial, auricular, ulnar and peroneal nerves are very commonly affected.

2. Disturbances in superficial sensibility, which are frequently and prominently manifested in the areas to which these latter nerves are distributed, as well as in other areas.

3. Enlargement or thickening of various portions of the affected nerves, which are occasionally tender or accompanied by pain (Plate 35, Figs. 1 and 2).

4. Trophic changes in both the skin and muscles. In the latter, the atony or atrophy develops with a rapidity and to a degree which seems out of proportion to the loss of function, and resembles that occurring in some of the neuro-muscular atrophies rather than that of the toxic neuritides or of poliomyelitis (Plate 35, Fig. 4 and Plate 36, Figs. 5 and 6).

5. Vascular disturbances rather constantly accompany these other changes and may or may not correspond in distribution to the anatomical arrangement of the nerves, and are further distinctive in that the areas in which they occur are generally warm to the touch rather than cool (Figures 5 and 6).

Though these various changes may develop with comparative rapidity and become extensive in the early stages of the disease, it

is decidedly more common during this period to find them restricted to the parts supplied by certain single twigs or branches of the nerves. Thus the muscle fibers which close the lower eyelid and those which elevate the upper angle of the mouth are quite frequently the only muscles of the face which are paretic or paralyzed (Fig. 3); and one or more muscles of the first interosseous space, and of the hypothenar and thenar eminences of the hand, are most often those lowered in tone, atrophied or paretic (Figs. 4 and 5).

One portion of the skin of a finger, such as the fifth, may be anesthetic and the remainder relatively normal; and one finger, such as the third or middle, may be cyanotic and the others normal in appearance; or patches of normal-appearing skin may be left as islands in areas of vascular changes (Figs. 4 and 6). The gradations of sensibility to touch, temperature or pain may range from a hyperesthesia to an anesthesia. The circulatory changes may vary in degree and extent from a blanched or reddened finger tip to cyanosis of an entire limb; and the trophic changes from a dry, glossy or scaly patch or finger to a diffuse edema of an entire extremity.

The skin lesions which sometimes accompany these neurological changes in children have been studied and described in particular by Gomez et als (1), Rodriguez (2), and Chiyuto (3). They often appear as one or more circumscribed pale macules or patches. However, the color change may be a mere blanching or a complete loss of the normal color (white), or on the other hand the lesions may be pink, dull red, bluish-red, copper color, salmon color or brownish. In size they may range from 2 or 3 mm. to 5 cm. or more in one or another diameter. They may be slightly edematous, with a border whose edge is only perceptibly elevated above the surrounding skin, or so raised as to resemble an urticarial wheal or even an erysipelatous cellulitis. On the other hand they may be dry and scaly, with papular borders simulating in appearance either an eczematoid dermatitis or a dermaphytosis. These lesions may be evident during only a few weeks. Sensation may be definitely altered in them, or they may be apparently normal.

Attempts to demonstrate the specific bacterium in the lesions described are usually fruitless, whether histological or bacteriological methods are employed. However, it may sometimes be demonstrated in a preparation made by gently scraping the mucous membrane of

the nose of the patient, though it has not been found in his skin.[2] Less frequently, in the early stages, the skin lesions may become infiltrated and thickened and assume the characteristics of the typical myxedematous plaques, papules or nodules in which the bacterium can usually be readily demonstrated.

PRESENT STUDY

A study of the ages on admission of patients entering the hospital for the treatment of leprosy in Hawaii shows that a definite percentage of them have contracted the infection in early life, often after short exposure, the disease apparently manifesting itself first at or about the time of puberty. In order to pursue this study further, but particularly to observe the changes which may be recognized earliest, and the subsequent development of these changes, a group of 108 children who were born of leprous parents have been examined several times during the past three years. Nearly all of these children had been separated from their parents at birth or soon thereafter, and were admitted to a government institution in which they had remained either without having subsequently any known contact with leprous persons or with only casual contact. Their ages ranged from a few months to sixteen years. Their racial origins were Hawaiian, mixed Hawaiian, Chinese, Japanese, Filipino and Portuguese. All of them had been under medical supervision, and had received good general care during this period.

Thirty-five of the group were found to exhibit one or more of the changes above outlined, at the time of one or another examination. All of these examinations were made by two or more trained observers independently, and the results were regarded as valid only when there was unanimous agreement among them. This precaution was taken since the findings are often of such mild degree that one hesitates to accept them as definitely abnormal. This applies particularly to the determination of slight enlargement of the trunk of the great auricular nerve, of the ulnar nerve at or immediately above the notch between the olecranon and the condyle, and of the peroneal nerve at the neck of the fibula.

[2] These preparations should be made under direct inspection with a good light. The mucous membrane of the septum or lower turbinate may be scraped without undue discomfort to the patient by the use of a semi-sharp narrow blade, such as that of a Frear submucous elevator. In doing this the induction of bleeding should be avoided.

Unilateral paresis of the lower eyelid and of the elevators of the angle of the upper lip may be apparent only when the patient is composed and the facial muscles are relatively at rest. The affected eye then presents a rounder eye-slit and a broader margin of sclera between the cornea and the edge of the lower eyelid than that seen in the other eye (Fig. 3). Paresis of the upper lip may be indicated by a little flattening or pouting of the edge of the vermilion border of the lip on the affected side, which can be determined only by contrasting the configuration of the two sides (Figs. 3 and 4). An attempt to make these changes more pronounced by attracting the patient's attention, or by his smiling or grimacing, often serves to make them more difficult of detection.

It is exceedingly difficult, if not impossible, to be assured of slight enlargement of nerve trunks or paresis of the facial muscles if these changes are bilateral. A definite conclusion is often reached only in retrospect, when the process has persisted and advanced to a degree which is unmistakable. In fact, the detection of many of the slight neurological changes is only accomplished by a most thorough and detailed examination, which may need to be repeated in order properly to evaluate the observations.

The demonstration of tactile anesthesia in children can be accomplished readily by touching the area to be tested with a camel's hair brush or a wisp of cotton. The determination of lowered or increased tactile sensibility is much more difficult, since the child is often confused in the differentiation of the degree of sensation felt. Thermic dysesthesias, which are demonstrated customarily by the application to the skin of tubes of cold and warm water (0° C. and 50° C.), may also be difficult to determine, but frequently they can be elicited before tactile disturbances of seemingly greater intensity can be established. The patient confuses the cold and heat sensations, but though he may be able to tell that the brush has touched him, he is unable to tell whether he feels it better or less well than in normal areas. In making these tests it is self-evident that the confidence and cooperation of the patient are absolutely necessary. Both patience and experience are required of the examiner, and even a willingness to make a game of the procedures. This latter approach is sometimes very successful in examining one in a group of children. The test of tactile sensibility by pecking the skin with a pin point, or alternately with point and head, is a procedure which often yields little or misleading information, since even if the child is not men-

tally confused the sense of pressure, which is seldom disturbed, is mistaken for the superficial or "epicritical" sensation.

The circulatory changes which so frequently accompany these slight neurological findings may not be striking, and are commonly those of capillary stasis. The skin may be mottled, or the fingers and toes a deep red or bluish-red, or there may be a patch of bluish- or brownish-red color (Fig. 6). On the other hand, one or more finger tips may be blanched. Disturbances in the secretion of sweat are frequently found in small areas, as on the palmar surface of a finger or a hand (Figs. 5 and 6).

Bone and joint changes which are manifested in the pointing or sharpening of a terminal phalanx of a finger (Figs. 5 and 7), or the development of a flat foot (pes valgus), have occasionally been found among our patients whose clinical leprosy was known to be of relatively short duration, though ordinarily they are considered to be indicative of more advanced stages. The pes valgus has developed invariably in a limb in which there were neurological changes. X-ray pictures are sometimes helpful in detecting the early pathology in the cartilages and bones.

As previously stated, it is frequently the case that the macules of these early clinical phases of leprosy are relatively evanescent, and they may be very difficult to distinguish at one or another examination. It is essential to their detection that the examination of the skin of the entire body be made under very favorable lighting, including that which strikes the surfaces at a tangent.

A number of the changes which we have found in these children have disappeared. This has taken place more often at or about the time of the physiological changes incident to puberty—which, on the other hand, is also the time at which the disease is apt to "blossom out." In view of experience with other cases, it seems reasonable to believe that the resolution or subsidence of these manifestations may have been facilitated by the care given the children. However, it must be understood that both the disappearance and reappearance of thickening of nerve trunks, pareses, paralyses, sensory disturbances and skin lesions take place in even moderately advanced cases.

Twenty-five of the group of 35 patients who showed suggestive changes have thus far failed to develop any sensory disturbances, or any combination of changes which would justify a definite diagnosis of leprosy, but 10 have developed such changes.

One of the ten, a boy 9 years of age, was first seen when he had an eruption of bluish-red macules on the body, arms and legs which resembled those usually classified as erythema multiforme. His face, ears, hands and feet were also slightly swollen. On the ulnar side of the palm of each hand there was a definite but poorly defined bluish-red area, and the finger tips and toes were bluish-red. There was loss of tone and slight atrophy in some of the small muscles of the hands. The trunks of the great auricular nerves seemed larger than normal, and that of one ulnar nerve was thickened. On the lateral surface of the right wrist and forearm there was an area 3 to 4 cm. in diameter in which there was thermal and tactile anesthesia, though the definite skin lesions were apparently of normal sensibility. Typical bacteria were found in preparations from the ear lobes and the nose. The nursing attendant who supervised the daily bathing of this boy stated that the eruption had been present only a few days, and was prominent only after a hot bath.

This case is one in which the first recognizable manifestations may have been a relatively rapid development of an eruption of the skin. The nature of the individual lesions and of the diffuse edema and vascular disturbances, as well as of that of the neurological changes, are such as occur in acute exacerbations in established cases. However, it is quite possible that an earlier examination may have revealed the presence of neurological disturbances. .

Among the remaining nine cases the following clinical findings have been obtained, either at the first examination or subsequently, in the numbers of patients indicated: Lagophthalmos, 8; droop of an angle of the upper lip, 6; atony or slight atrophy of the muscles of the interosseous spaces or of the thenar or hypothenar eminences, 6; paresis or paralysis of the lumbrical or interosseous muscles of the hand, 1; thickened nerve trunks or branches, auricular, ulnar, or peroneal or (in one case) supraclavicular, 9; trophic disturbances, dryness or anhydrosis, scaliness, glossiness or wrinkling, in one or more areas of the skin other than in definitive lesions, 5; sensory disturbances in one or more areas of the skin without definitive lesions, 5; circumscribed or definitive skin lesions (macules), 4; sensory changes in one or more macules, 4.

The diagnosis was made in all these cases only when there was a combination of findings which included sensory disturbances. In four of the nine the typical bacteria were demonstrated after several unsuccessful attempts, either from the skin or the nose. In one of these cases the positive bacteriological result was first obtained eight months after the initial trials were made, and two years after in two others, though several examinations were made during this period.

A better comprehension of the clinical picture observed, and some indication of the course of its development, may be obtained from the following rough, abbreviated notes made at different examinations of three of the nine cases.

CASE 1.—Boy, age 11 years, Chinese-Hawaiian.

December, 1932. No abnormalities of note.

March, 1933. Enlargement of left ulnar nerve and atrophy of left hypothenar muscles suggested.

June, 1933. Right lower eyelid and right angle of mouth drooped. Left auricular nerve seems larger than right. Both easily palpated. Left hand, first interosseous and hypothenar muscle groups atrophied.

July, 1934. Droop of right lower eyelid and lip. Auricular nerves easily palpated. Entire left hand seems atrophied, particularly the first interosseus and the hypothenar muscles. Grip of this hand is much weaker than that of right. Skin of palm rough and dry. Color of the fingers paler than on the right hand. The lateral borders of fifth finger on each hand seem to have some impairment of sensation, and that of the fifth finger of the right hand seems anesthetic. The diameter of the right thigh is less than that of the left. Bacteria not found.

October, 1934. There is impairment of sensation (touch and temperature) of the lateral borders of the fifth fingers of both hands, and anesthesia of most of the fifth finger of the right hand. Other findings of July confirmed. Bacteria not found.

CASE 2.—Boy, age 9 years, part Hawaiian.

December, 1932. Pale pink, papular spot on the right cheek.

March, 1933. Irregular pale scaly patches on the left cheek. Right cheek clear. Left ulnar nerve possibly enlarged.

June, 1933. Patches on the cheeks dry and inclined to be scaly. Slightly hypopigmented dry area on the right forearm, extensor surface. Palms very dry. Suggested droop of the right lower eyelid and upper lip. Both ulnar nerves enlarged. Some confusion of tactile and thermal sensation in the area on the right forearm. Bacteria not found.

September, 1933. Pale spot 1 cm. in diameter over upper angle of left scapula. Confusion of tactile and thermal sensation on posterior surfaces of both forearms.

November, 1933. Findings of June and September confirmed. Left hypothenar eminence definitely softened. No spot on shoulder.

July, 1934. On the posterior surfaces of the forearms there are large, scaly, hypopigmented and poorly defined areas over which there is marked impairment of sensation to touch and temperature. The skin of the palms is dry, and the index fingers are pointed. There seems to be a decrease in the acuteness of sensation to touch and temperature in the finger tips, more especially in that of the middle finger of the left hand. The left auricular nerve is much larger than the right. Mastoidectomy scar present. The right ulnar nerve seems larger than the left, but neither seems abnormally large. The left hypothenar muscles are softer than the right and slightly atrophied. Bacteria not found.

October, 1934. Previous findings confirmed.

December, 1934. In addition to the changes noted in July, there are on the left cheek three slightly raised, brown, circumscribed areas, two 1 cm. in diameter and one 2 cm.; these are surrounded by a halo. On the lateral surface of the left arm within the scaly area there is a slightly infiltrated, circumscribed, brown area. Bacteria demonstrated from the nasal mucous membrane, from one of the areas on the face, and from that on the arm.

CASE 3.—Boy, age 7 years, Hawaiian-Chinese.

December, 1932. No abnormalities of note.

March, 1933. Slight droop of right lower eyelid. Pale, poorly defined macules on right epigastrium, right and left flanks, right upper arm, posterior right thigh. Left ulnar nerve large. Palm of left hand dry and scaling; there are a number of small wounds on this hand. There is diminished sensation on the palm of the left hand, over the extensor surface of forearm, and in some of the macules. Bacteria not found.

November, 1933. New macules are developing over upper thighs anteriorly and posteriorly, approximately 1.5 cm. in diameter. On the left knee there is a macule of 2.5 cm. in diameter. All are pale pink centrally, with redder borders; little edema. Both palms are dry, scaling and fissuring, both legs dry and scaly, this condition extending up the right thigh. Sensation to touch and temperature is lost over the entire left hand and lateral aspect of the forearm, diminished over the extensor surface. There is also similar anesthesia or hypoesthesia over the right thigh (lower two-thirds), the right leg and foot, and the sole of the left foot. The ulnar nerves and right auricular are definitely thickened. The edge of the right ear lobe is infiltrated and slightly reddened. Bacteria demonstrated from this lesion.

October, 1934. All macules are gradually assuming the color of the normal skin, and many of them have either disappeared or are distinguishable with difficulty. The infiltration of the ear lobe has cleared. The palms continue to be dry, but are not as scaly as formerly and are less prone to fissure, and small injuries heal more quickly. Paronychia is present on two fingers of the left hand, and there is a slight flexor contraction in the fourth and fifth fingers of this hand. Some atrophy of the small muscles of both hands, more particularly the left hypothenar group. The ulnar and right auricular nerves do not seem as large as formerly. The sensory disturbances have apparently changed but little in the past year. The arch of the right foot has flattened and a definite pes valgus has developed. The right peroneal group of muscles shows definite atrophy. The last seven bacteriological examinations, taken between July and November, have been negative. Patient's general condition seems considerably improved and the leprous process is apparently stationary or improving.

In summarizing, it should be especially noted that only five of the ten patients who have developed the syndrome of leprosy have thus far displayed definitive or inflammatory lesions of the skin. Some of these lesions have been very insignificant in appearance and were not at all pathognomonic. Some disappeared entirely. In nine of the cases the neurological phenomena were the prominent, or only,

changes present for some time. These developed gradually and extended in several of the cases, but in some there has been a definite recession or disappearance of some of these findings. Practically all of the changes were of very minor degree when first noted, and could be regarded only as definitely significant when considered in relation to others present. It seems important to emphasize the fact that early cases of leprosy may show only neurological changes, and that the lesions in the skin vary in appearance and may not be typical of those of later stages of the disease. In fact, the exhibition of definitive and persistent skin lesions appears to be a comparatively late manifestation in a significant proportion of cases.

SUMMARY

A discussion is presented of the desirability of the early diagnosis of leprosy, in which (a) it is pointed out that the incidence and communicability of the disease have not been determined, and (b) it is suggested that the knowledge of its epidemiology, pathogenesis and treatment may be advanced by the recognition and study of its earlier phases.

The clinical findings of early cases are outlined, and emphasis is placed on the fact that in the early stages of the disease there may be only minor neurological findings, and that the skin lesions which may or may not be evident in these stages are often of short duration and cannot be regarded as specific to leprosy.

One hundred and eight children born of leprous parents, and subsequently maintained in an institution segregated from contact with leprous persons, were observed for a period of three years. Ten of these children have developed leprosy. The first clinical findings noted and the subsequent evolution of the disease are indicated, and are exemplified by notes of three cases.

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DESCRIPTION OF PLATES

The photographs here shown illustrate only the more advanced of the processes discussed, since it is exceedingly difficult to demonstrate in such pictures the minor changes observed clinically.

PLATE 35

FIG. 1. A moderately advanced case of leprosy, showing thickened auricular and transverse cervical nerves. Leucodermic macules may be seen on the face, neck, and outer surface of the left arm just below the shoulder.

FIG. 2. A moderately advanced case illustrating thickened branches of the peroneal nerve. Trophic changes may be noted in the skin of the lower portion of the leg, shown by the high light on the glossy skin.

FIG. 3. Early leprosy. Definite lagophthalmos of the right eye. Note the roundness of the eye-slit and the border of white sclera showing below the iris. There is a suggestion of flattening of the cheek fold and of the border of the upper lip on the same side.

FIG. 4. Moderately advanced leprosy. Flattening or slight rolling in of the upper lip, and rolling out of the lower lip on the right side. Marked atrophy of the interosseus muscles of the left hand, trophic changes of the skin, and contractures of the fingers.

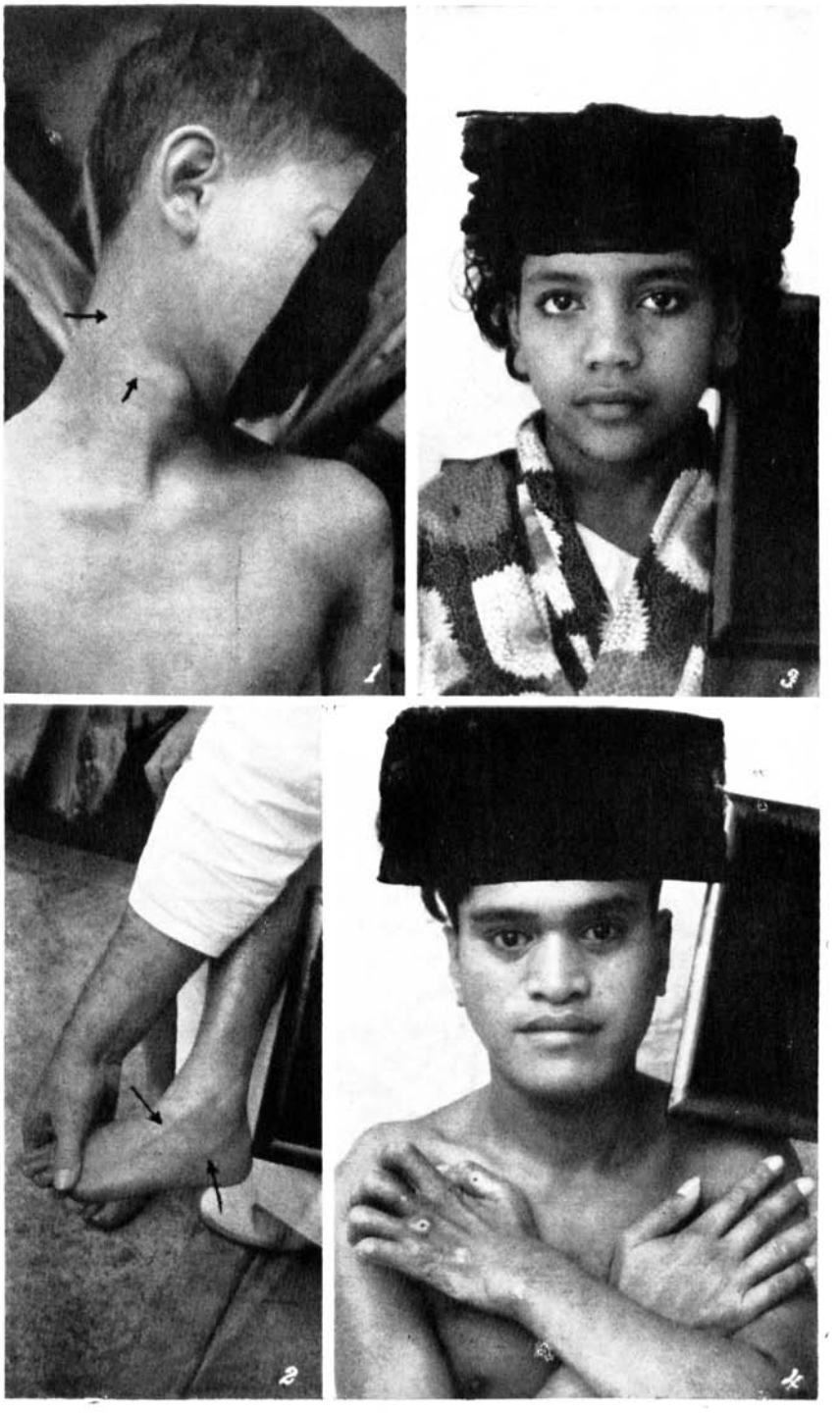

PLATE 35

PLATE 36

FIG. 5. A moderately advanced case illustrating the dry palm with the beginning of "tipping" of the fifth finger, and definite atrophy of the hypothenar and thenar muscle groups with outward rotation of the thumb.

FIG. 6. Early leprosy. Hands of Case 3, illustrating the dry fingers and vascular disturbances which are most definite at the arrow points. There is also beginning atrophy of the hypothenar eminence of the right hand.

FIG. 7. Moderately advanced leprosy, illustrating marked tipping of the terminal phalanx of the fifth finger. There is also beginning contracture of the third and fourth fingers.

FIG. 8. Advanced leprosy, illustrating the dry hands, atrophy of the thenar and hypothenar muscles of the left hand, and very definite vascular disturbances as shown by areas of discolorization. In this case there are also marked trophic disturbances which may be seen on the tips of the index and middle fingers of the right hand and on the tip of the middle finger of the left hand. Note the islands of comparatively normal skin in the right palm.

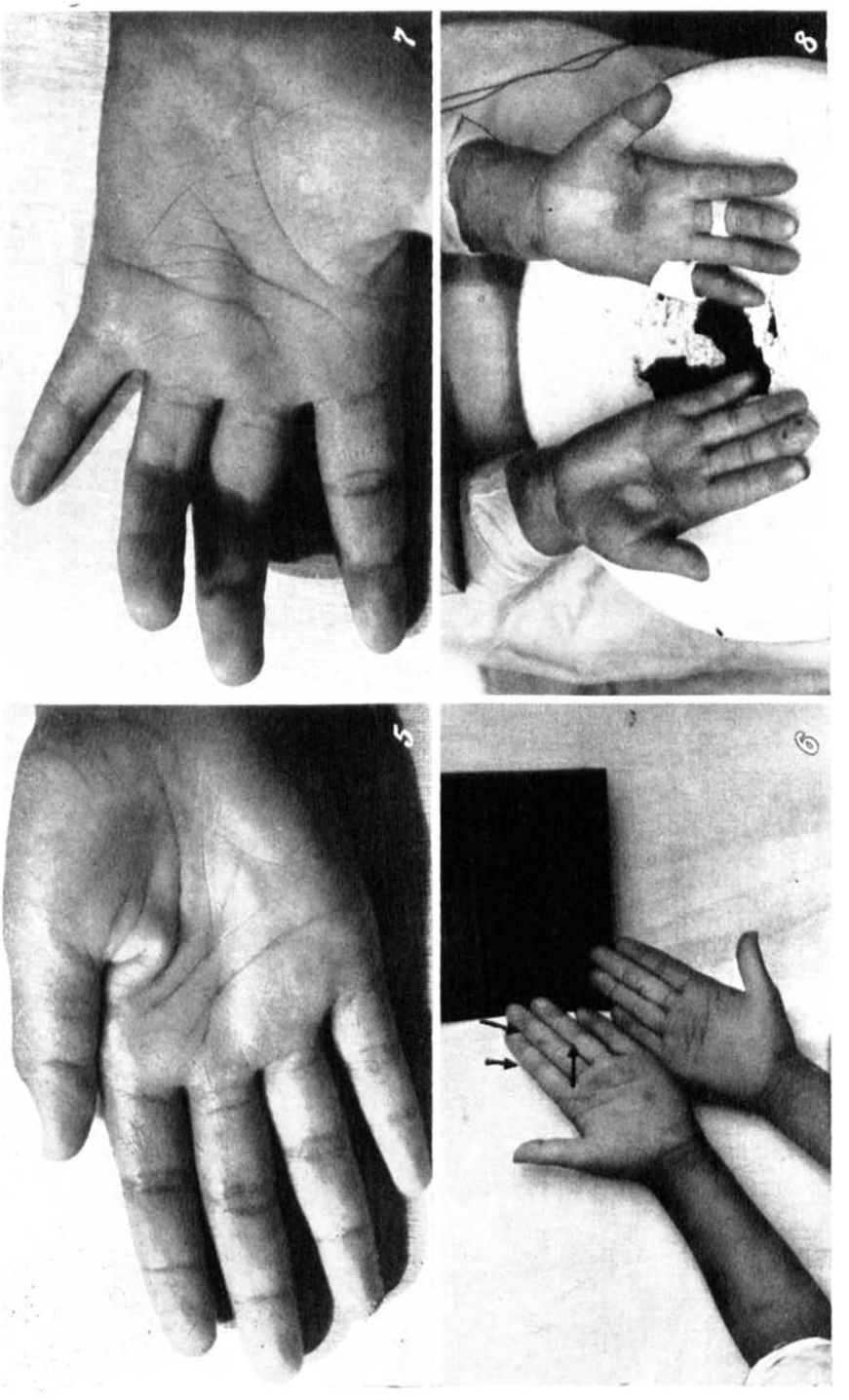

PLATE 36