

THE PHILIPPINE JOURNAL OF SCIENCE

VOL. 27

AUGUST, 1925

No. 4

THE DISTURBANCES OF CUTANEOUS SENSIBILITY IN LEPROSY¹

By JOSE N. RODRIGUEZ

Acting Chief Physician, Culion Leper Colony, Philippine Health Service

ONE TEXT FIGURE

INTRODUCTION

In a paper read before the first Leprosy Conference held at Berlin in 1897, Jeanselme² deplored the fact that, in spite of the importance of anæsthesia in the diagnosis of leprosy, this symptom had not received the attention it merited in the study of the disease. To-day, after a lapse of a quarter of a century, this remark of the French savant still holds good. In spite of the advances in the knowledge of leprosy brought about by a better understanding of the pathology and bacteriology of the disease as claimed by Macleod,³ the excellent monographs of Jeanselme and Lie⁴ still form the groundwork of our knowledge on this subject and they are still extensively quoted.

The investigations of Head and Rivers⁵ have thrown new light on the study of the cutaneous senses. After section of

¹ Published with the approval of the Director of Health and upon recommendation of the Philippine Leprosy Research Board.

² Des troubles Sensitifs dans la lépre, *Lepra Conferenz, Berlin* 3 (1897) 384.

³ A brief survey of the present state of our knowledge of the bacteriology and pathological anatomy of leprosy, *Brit. Journ. Dermatol.* 21 (1909) 309.

⁴ *Lepra maculo-anæsthetica und Lepra anæsthetica, Lepra* 5 (1904) 78. *Lepra in Rückenmark und den peripheren Nerven* (1904), cited by Macleod.

⁵ *Brain* (1908) 323, cited by W. H. Howell, *Text book of Physiology*, 6th ed., W. B. Saunders Co., Philadelphia (1918) 278.

the cutaneous nerves, these workers studied the return of the various elements of sensibility—touch, tactile discrimination, heat, cold, and pain—following the union of the cut ends. They observed that there are essentially two sets of sensory fibers which, after section and reunion of the nerves, regenerate at different times. One group, the protopathic, conveying sensations of pain and extreme changes of temperature, regenerate earlier than the second or epicritic set, which can be stimulated by small differences of temperature, ranging between 26° C. and 37° C., and by light pressure. Moreover, they demonstrated the presence of sensory fibers in the muscular branches which respond to appropriate stimuli even after the skin has been rendered completely anæsthetic by section of the cutaneous nerves. On the basis of these findings they proposed a new classification of sensory nerve fibers as follows:

Cutaneous sensory fibers:

Epicritic—

Heat, small differences.
Cold, small differences.
Touch, light pressure.
Tactile discrimination.

Protopathic—

Heat, extremes.
Cold, extremes.
Pain.

Subcutaneous or deep sensory fibers:

Pressure.
Pain.
Muscular, position.

Nonsensory afferent fibers:

From muscles, joints, etc., ending in cerebellum.

So far as I am aware, Hopkins⁶ is the only worker to consider the disturbances of sensation in leprosy in the light of this classification.

LITERATURE

Before presenting my own observations, it is desirable to survey briefly the current views in regard to the etiology of the sensory disturbances in leprosy. In spite of the extensive literature on the subject of nerve leprosy, there is no unanimity of opinion regarding even the most important points beyond the fact that the nerves may be affected anywhere along their

⁶Early manifestations of leprosy, *New Orleans Med. & Surg. Journ.* 70 (1917-1918) 56.

course—in the nerve endings, in the peripheral branches, or in the nerve trunks. Nonne⁷ says: "The nerves pay to the lepra bacillus the same tribute as do the other tissues of the body." The nerve fibers undergo a severe parenchymatous and interstitial involvement, with periarteritic and endarteritic changes of the nerve arterioles. *Lepra bacilli* have been found in the connective tissue elements of the epineurium, the perineurium, and the endoneurium, lying free in the lymph spaces or in fixed tissue cells and plasma cells. They have also been seen in the nerve fibers themselves located in the neurolemma and in the sheath of Schwann, but they have never been found within the axis cylinder. The bacilli are often seen singly and in rows, seldom in clumps. An interesting finding is the considerable number of regenerating fibers and the relatively frequent finding of the axis cylinder still persisting after the destruction of the medullary sheath.

The way in which the nervous system is invaded, and the character of the changes in the spinal cord (if any exist), variously attributed to leprosy, remain to be definitely established.

The relation of the cutaneous macules to the nerve lesion is also an unsettled question. A great deal of attention has been paid these macules. They are often, though by no means regularly, seen early in cases of nerve leprosy; when present they are manifestly closely related to the nerve changes, "in the nature of a persistent inflammatory process of the type of erythema perstans,"⁸ a belief supported mainly by many of the older workers though shared also by a number of present-day leprologists. The opposite view is held by many authorities who are of the opinion that the macules, known as "neuroleprides" among the French, are caused by the actual presence of the *lepra bacillus* in situ, at some time or other, and that they are but "microscopic images" of the ordinary lesions of skin leprosy, differing from these only in that the extension is inward into the subcutaneous layer and in that there is no marked formation of new tissue.

Due to this difference of opinion, the presence or absence of the *lepra bacillus* in these macular patches is a subject of much interest. While many workers have failed to find the organism in the neurolepride several, notably Looft,⁹ Babes,¹⁰ and Kling-

⁷ *Lehre von der Lepra anaesthetica*, *Lepra* 5 (1904) 22.

⁸ *Brit. Journ. Dermatol.* 21 (1909) 309.

⁹ *Virchow's Archiv.* (1892) 128, cited by Nonne.

¹⁰ *Lepra Conferenz* 1 (1897) 155.

müller¹¹ succeeded in finding them. The bacilli were always very few, located principally in the endothelium of the capillaries. Macleod rightly questions whether a few lepra bacilli, which organisms cause comparatively little cellular reaction, can produce such skin lesions. Furthermore, there is the possibility that the organisms may be present only incidentally, having been deposited there secondarily from the blood stream, which is obviously more or less contaminated, as it were, in leprosy. On the other hand, Darier¹² doubts if a more or less mysterious modification of the nerve influx can produce a lesion with perivascular infiltration and cellular degeneration without the superimposed or concomitant presence of the bacilli.

Leloir¹³ in 1886, and Unna¹⁴ in 1894, came to the conclusion that these macules were of a neurological nature, caused by an involvement of the nerve trunks, because they found the trunks more involved than the smaller branches and because of the extensive atrophic changes which point to an involvement of the larger nerve trunks. Moreover, they also failed to find the lepra bacillus in these lesions. This opinion is shared, with some modifications, by Neisser,¹⁵ by Arning,¹⁶ and by Zambaco,¹⁷ who likewise believe that the atrophy is not of peripheral origin. Virchow used to teach that the process begins in the trunks, followed by descending and ascending degeneration, according to the Wallerian law. Gerlach¹⁸ and Dehio,¹⁹ however, are not in agreement with the conception of Unna and Leloir. The former claims that the earliest and most advanced changes occur at the peripheral nerve endings, with a tendency to ascend. These two workers lay stress on the fact that no definite relation apparently exists between the sup-

¹¹ *Lepra* 3 (1903) 145.

¹² *Recherches sur les taches erythemato-pigmentées de la lépre*, *Lepra* Conferenz, Berlin 3 (1897) 396.

¹³ *Traite pratique et theorique de la lépre* (1886), cited by Nonne.

¹⁴ *Histopathologie der Hautkrankheiten* (1894), cited by Nonne.

¹⁵ *Vierteljahresschrift für Dermatologie* (1883).

¹⁶ *Eine eigentümliche Veränderung an den grösseren Nervenstämmen bei einzelnen Fällen von Lepra*, *Verhandl. des VI. deutschen Dermatologen-Kongresses*.

¹⁷ *Des rapports qui existent entre la maladie de Morvan, etc., et la lépre*, *Lepra* Conferenz, Berlin 1 (1897) 21.

¹⁸ *Untersuchungen über die Unabhängigkeit der Bildung anästhetischer Flecke von der Erkrankung zugehöriger Nerven bei der Lepra anaesthetica*. *Inaug. Diss., Dorpat* (1890), cited by Nonne.

¹⁹ *Ueber die Lepra anaesthetica und den pathogenetischen Zusammenhang der Krankheitserscheinungen*, *Lepra* Conferenz, Berlin 1. (1897) 85.

posedly involved nerve trunks and the areas of anæsthesia. For these reasons, Gerlach and Dehio believe that the process begins at the peripheral nerves rather than at the trunks. Gerlach, after making serial sections of the nerves from the brachial plexus to the nerve endings in the affected skin in a case of pure nerve leprosy, found that the peripheral nerve fibers invariably showed the most-advanced lesions. He believes that the process originally begins as a round-cell infiltration around the sweat glands. The nerve endings are secondarily invaded and destroyed.

The simple scheme shown in fig. 1 illustrates the hypothesis of Gerlach and Dehio.

According to this hypothesis, the process starts as an infiltration of the skin, *sl*, which becomes anæsthetic owing to involvement of the sensory-nerve endings. Then follows an ascending nerve-fiber degeneration, beginning in the affected skin area along the peripheral cutaneous branch, *a*. When it has extended to *b*, a mixed branch from which a motor branch *c* is given off, the muscle supplied by this branch is affected. Later, when the degeneration reaches a point in a nerve trunk indicated at *d* the function of the mixed branch *e* is affected and, through its terminal cutaneous branch *f* and motor branch *g*, the skin and muscle supplied at a greater or less distance from the site of the first lesion, *sl*, will also exhibit nervous disturbances. In this manner there is a gradual extension of the affection.

Gerlach also noticed, independent of this degeneration, inflammatory proliferations involving the entire nerve trunk, localized almost wholly at certain well-known points of predilection, as along the ulnar nerve above the elbow where the trunk is exposed to external injury. At such places the motor

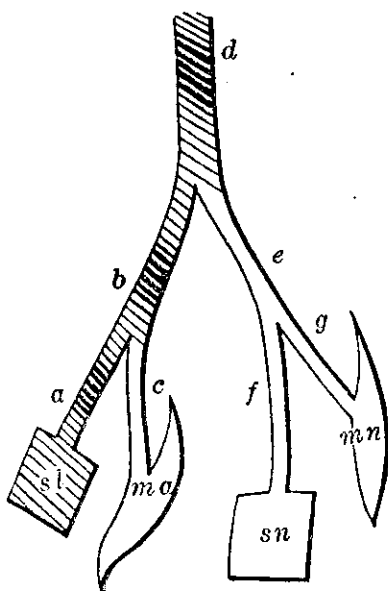


FIG. 1. Schema illustrating the Gerlach-Dehio hypothesis (from Dehio): *a*, diseased sensory-nerve branch; *b*, diseased mixed nerve; *c*, not involved muscular branch with muscle, *ma*; *d*, mixed-nerve trunk; *e*, mixed nerve; *f*, cutaneous branch to skin, *sn*; *g*, muscular branch with muscle, *mn*; *sl*, leprotic skin; *sn*, skin; *mn*, muscle.

fibers are also degenerated, if the infiltration has advanced far enough.

The finding of lepra bacilli in the macules and the work of Voit²⁰ tend to confirm the greater part of the findings of Gerlach. Voit followed the nerves step by step from the periphery toward the center, and found constantly that the skin branches were entirely degenerated in these cases, although he did not find any specific leprotic changes in the nerves. In places exposed to traumatism he found fresh inflammation, principally of the fibrous elements, in the entire cross section of the nerve trunk, producing a degeneration of the sensory nerves; but, contrary to the findings of Gerlach, the motor fibers were very slightly involved or not at all. Under skin areas that were deeply anæsthetic he found the muscle bundles still intact.

Babes, Klingmüller, and Jeanselme helped to strengthen the theory of peripheral involvement of the nerves. Jeanselme found some of the nerve endings so sclerosed and changed to solid fibrous tissue that he could hardly recognize the residuum. Klingmüller believes that an embolic process of the small vessels under the skin initiates the process, the surrounding tissue including the nerve endings being secondarily affected with gradual, ascending involvement of the larger branches.

The objections to the theory of primary peripheral involvement are many and serious. The following are some of the most important that have been raised: (a) This theory cannot be applied to the many cases in which there are no macules or in which these appear only after marked nervous manifestations are already present; (b) it does not explain why, although macular lesions are often seen in the trunk, this region is usually free from nervous manifestations; (c) neither does it explain the frequently more or less symmetrical arrangement of the anæsthesia, the macules being irregular in shape; and (d) the atrophy of the deep tissues, including the bones, in advanced cases can hardly be attributed to the degeneration of the peripheral nerve alone, and points to a central disturbance.

In advanced cases with anæsthetic involvement of entire extremities, sometimes more or less symmetrically, this theory falls short, for these changes suggest either a segmentary involvement of the posterior gray matter, especially in cases with dissociation of the sensations similar to syringomyelia or

²⁰ Das Rückenmark, die peripheren Nerven und die Hautflecken bei der Lepra maculo-anaesthetica, *Lepra* 1 (1900) 179.

disease of the posterior roots, or possibly even a functional disturbance. However, it would seem that nothing definite in the spinal cord and the posterior roots is to be found to account for these manifestations. It is true that Babes reported the discovery of the organisms in the spinal ganglion cells and in the ganglion cells of the anterior horn, and Kalindero found them in the intervertebral ganglia nine times in twenty-two autopsies; but, on the other hand, Danielssen and Boeck failed to find characteristic lesions in the spinal cord, and many others have failed to find leprosy bacilli in the cord, even in advanced cases.

Using the Weigert-Pal stain, Babes²¹ found evidence of degeneration of the fibers in the column of Goll, in the cervical portion. Voit²² described a slight rarefaction of the fibers in the columns of Goll and Burdach in the cervical and thoracic cords, but these findings were not constant. In the blood vessels he found endothelial nuclear proliferation and diffuse thickening of the walls, all of which can be found in chronic diseases, and especially in cachexia. In the ganglion cells of the anterior and posterior horns, Voit saw slight changes of degeneration, as described by Babes, Kalindero,²³ and Looft. According to Voit, von Strumpel and Fr. Schultz, two authorities on diseases of the spinal cord, using material from their own cases as well as from those of Voit, failed to find changes in the spinal cord or in the spinal ganglia different from those seen in cachexia or secondarily following involvement of the roots.

From this incomplete survey it would seem that, in the absence of any regularly occurring lesion in the spinal cord, which should be decidedly marked in advanced cases, the central structures can practically be eliminated from consideration. The question is, then, whether the disturbance arises from a lesion of the trunk, including the smaller subdivisions, or whether it develops as a result of cutaneous involvement, which, because of some determining influence, affects the nerves as an ascending involvement instead of developing the familiar lesions of ordinary cutaneous leprosy.

While the evidence advanced by several authorities in favor of the primary peripheral involvement cannot be ignored, there

²¹ *Lepra Conferenz* 1 (1897) 155.

²² *Das Rückenmark, die peripheren Nerven und die Hautflecken bei der Lepra maculo-anaesthetica*, *Lepra* 1 (1900) 179.

²³ *Lepra Conferenz* 3 (1897) 357.

are too many commonly observed clinical features that are not explainable by this hypothesis to permit its acceptance as the only method by which neural lesions develop. It is not seen why it may not be that both processes occur in different cases.

PRESENT STUDY

The present paper, based on 800 neurological examinations on 200 cases of all types and stages of leprosy, is limited exclusively to a study of the troubles of cutaneous sensibility, particularly the anæsthesia, which characterize this disease.

I believe that the anæsthesia superimposed on the skin lesions should be distinguished from the nervous disturbances independent of the cutaneous manifestations, the "anesthésie névretique" of the French. These two types will be discussed separately.

The various phases of the sensory disturbances were studied and special attention was paid to the changes in such disturbances observed from time to time in a group of cases that were being treated with the ethyl esters of chaulmoogra oil. Such examinations, along lines suggested by the work of Head and Rivers, in correlation with other, more-usual examinations, are believed to be of importance in determining the actual degree of improvement taking place in cases under treatment.

A brief description of the method followed in making these examinations will not be out of place at this juncture.

METHOD OF EXAMINATION

In investigating the cutaneous anæsthesia of leprosy no expensive, complicated apparatus is necessary. The success of the examination depends more on the care and thoroughness with which it is done than on the elaborateness of the instruments used.

The patient should be undressed so far as possible, though undue exposure and roughness which would tend to make him—or, more particularly, her—restless or ill at ease should be avoided. The examiner should also make it a point never to hurry the patient and should make due allowances for his intelligence and mental capacity. At least two examinations are necessary, and they should preferably be made on different days. Very often among our patients a third or a fourth examination must be made, because the disturbances are often found at the second examination to have changed considerably, in both extent and quality.

To examine the temperature sense two small test tubes and a supply of warm and cold water are all that is actually necessary. Ordinarily only the protopathic sensibility need be tested, and for this purpose the temperature of the warm water may be anywhere between 40° and 60° C., and that of the cold water, between 10° and 15° C. Temperatures higher than 60° C. are not only unnecessary, but are likely to cause some injury. If it is desired to test the epicritic temperature sense, the temperature of the water must be accurately determined. It should be not more than 37° C. for the warm tube, and not less than 26° C. for the cold. In our work two basins of water were kept at the proper temperature by adding small quantities of ice water or hot water as needed, and the tubes were filled from these at very frequent intervals.

For light touch, a light camel's-hair brush or a wisp of cotton should be used. Some use the head of a pin for this purpose, but such procedure cannot be recommended as it requires care not to apply more pressure than is necessary or desirable. It is a good plan to make the patient, whose eyes should be kept closed or covered, count every time he feels the touch. Tactile discrimination is best determined with a von Frey's æsthesiometer, but an ordinary light carpenter's compass with somewhat blunted points and a scale with accurate millimeter markings will do as well. The threshold stimulus is determined with a baræsthesiometer, of which Eulenburg's is a type; but for ordinary examinations, the determination of the threshold stimulus is not essential.

In testing for the pain sense, an ordinary sharp needle is all that is necessary. The patient must be carefully instructed to distinguish between pain and pressure, as very often he claims that the prick is painful when all that he feels is mere contact or pressure. It is well to observe the facial expression or any reflex movement of the patient after a prick; in dull patients this may be the only indication available to the examiner.

ANÆSTHESIA IN THE CUTANEOUS LESION

Duhring,²⁴ Gaucher,²⁵ and Broque,²⁶ among others, hold that there is always present in the skin lesions of leprosy some de-

* Cited by de Buermann.

* *Traite des Maladies de la peau*, 2: 468, cited by de Buermann.

* *Traite* 1 (1917) 519.

gree of sensory disturbance. However, many others, notably de Buermann and Gougerot,²⁷ failed to find the anæsthesia in a certain number of cases, and therefore proved that this statement does not hold true in all cases.

In order to present more clearly the character of the nervous changes over the cutaneous lesions the different types of these skin manifestations will be discussed separately. Of the principal lesions, we distinguish three distinct types; namely, the infiltration, the nodule, and the macule. What is designated as infiltration consists of more or less diffused thickening of the cutaneous tissue which appears glistening, reddish, dark brown or coppery in color, and often hairless. The thickening may be slight or marked; often, particularly when marked, an exaggeration of the skin folds is produced.

Nodules are firm, fairly well circumscribed growths ranging in size from a rice grain to a walnut, usually appearing late in the disease. They are divided clinically into two types, cutaneous and subcutaneous. Nodules of the latter type are deep; and the skin, which is movable over them, at least primarily, shows no discoloration or special change. Those of the common type are more superficial, the localized thickening taking place in the dermis itself; frequently fine vascular arborizations can be seen through the thin stretched epidermis.

Macules are typically found in neural or mixed leprosy. In color they range from light brown, hardly discernible on the skin of a Filipino, to pale yellowish white. These macules are usually negative on ordinary bacteriological examination. In some cases macules that are in general similar to these have slightly raised, sometimes pinkish borders; the central portion may be of the same color as the rest of the macule, or it may be darker, or it may have a pinkish tint. Such lesions are evidently active and the finding of bacilli is to be expected.

Infiltration.—In forty-four selected cases with infiltrations that were examined, the lesions were located principally on the face and extremities. They ranged in duration from two months to thirteen years. Seven of these cases, or about 16 per cent, showed no sensory changes whatever over the lesions; in four of these seven duration was between three and four years and in three, from one to two years. A group of nineteen others of similar duration (one to four years) showed changes of sensi-

²⁷ *Lepra* 9 (1909) 55.

bility over the lesions, from which it is seen that the existence of the nervous changes does not depend entirely on the duration of the infiltration.

In twenty-two of the cases with infiltrations, half of the total, the sensation of light touch was unaffected while the sensibility to pain and temperature was impaired or absent. Thus the dissociation of sensibility, as described by Jeanselme in his cases of cutaneous leprosy, is evident in this group. Hyperæsthesia, near or around the older infiltrations was not observed.

Nodules.—The firm nodules appear as a rule in rather advanced stages of the disease. They are often located on the face, at the lips, nose, and ear lobes, and especially on the extremities. As anæsthetic changes in the extremities are usually more or less extensive in such cases, it is often impossible to distinguish the nervous changes over the nodules from the general anæsthesia of the surrounding skin. In only six of thirty-two cases showing this particular variety of skin lesions were the nodules surrounded by nonanæsthetic skin. All six showed sensory impairment over the lesions; the remaining sensibility was identical in character with that mediated by the protopathic fibers.

Macules.—Thirty cases with macules, varying in duration from three months to ten years, were studied. In seven of these lepra bacilli were found in one or more patches. Of the twenty-three bacteriologically negative cases all but two showed disturbances of temperature, pain, and light touch sense; in 30 per cent there was complete loss of sensibility. The bacillus-positive macules were most interesting from the neurological viewpoint. In five of the seven hyperæsthesia was present in some portion of the macule, usually along the border or at some segment or portion of the periphery. In spite of the hyperæsthesia, however, the sense of tactile discrimination was distinctly impaired in all the cases. In the other two positive cases no hyperæsthesia was found; in these the organisms were very few. Therefore, the presence of hyperæsthesia in some part of the macule or any portion of the surrounding skin seems to indicate that the lesion is active and progressing; as a rule, it is positive for the lepra bacillus.

The results of these examinations show that in the case of the macules the earliest changes consist of the involvement of the epicritic fibers, together with those mediating pain of the protopathic set. An interesting finding in some of the macules

is the presence of the so-called paradoxical cold reaction. The sudden application of a test tube heated to 60° C. produces a sensation of cold. Head and Rivers consider this reaction characteristic of the sensibility mediated by the protopathic fibers, present only when the epicritic system has been destroyed.

In two of the bacteriologically negative cases the macules were very faint, pale brown, and hardly distinguishable from the surrounding skin. In these the cutaneous sensibility was normal.

To summarize, the macules positive for *Bacillus lepræ* were the only cutaneous lesions found in this series that showed hyperæsthesia. Ninety-three per cent of the skin lesions of this type showed disturbances of sensibility. The epicritic system is apparently involved first and there is no dissociation present. The skin over the nodules was found to be anæsthetic, or partly so. Sixteen per cent of the infiltrations showed no sensory disturbances.

ANÆSTHESIA INDEPENDENT OF CUTANEOUS LESIONS (ANESTHÉSIE NÉVRETIQUE)

Sixty-eight lepers presenting this type of anæsthesia were studied, and monthly observations were made on the changes occurring over a period of more than a year. Forty-three were males and twenty-five females; they ranged in age from 8 to 66 years, and the duration of the anæsthesia was from one month to sixteen years.

Distribution and development.—The most frequently involved portions of the body are the extremities. The distribution of the anæsthesia in the sixty-eight cases examined is shown in the following table:

TABLE 1.—*Distribution of anæsthesia.*

	Cases.
Legs	62
Dorsum, feet	58
Forearm	58
Dorsum, hands	49
Fingers	43
Thighs	42
Arms	37
Palms, hands	28
Buttocks	24
Lumbar region	11
Scapular and interscapular regions	9
Neck	7
Face	6
Abdomen	4
Scalp	4

It is seen that the legs, feet, and forearms showed the most-frequent as also the earliest involvement, with very little difference; the neck, face, scalp, and abdomen were relatively seldom involved.

Although the anæsthesia is, as a rule, unilateral at the onset, sooner or later the corresponding area on the opposite member also shows nervous changes, and in some cases the arrangement is remarkably symmetrical. The significance of this distribution of the anæsthesia has been the subject of much discussion by leprologists. Some insist that it points to some lesion in the spinal cord, although there seem to be no adequate pathological grounds for this supposition. Those who are interested in the subject are referred to the extensive monographs of Jeanselme, Lie, Nonne, le Dantec,²⁸ Dijerine,²⁹ and the comparatively recent article by Cussec,³⁰ who took advantage of a trip from Marseilles to Dakar on the hospital ship *Flandre*, to examine some of the sixty Senegalese lepers who happened to be on board the vessel.

In the lower extremities the anæsthesia began, in the majority of our cases, at the lower portion of the tibial region, and spread downward over the feet, and laterally and upward, until the entire anterolateral portion of the leg was involved. In a considerable number the anæsthesia started at the outer third of the dorsum of the feet, extending upward, or a separate focus started at this region and fused with the spreading area from the legs.

At the posteromedial surface of the leg the extension is more gradual. From this stage the anæsthesia extends upward to involve the external surface of the thighs, spreading out in the form of a fan as it ascends. Sometimes the separate spots of anæsthesia appear at the lateral surface of the thighs and at the buttocks, and these fuse with the ascending anæsthesia. The upper limits rarely reach the inguinal fold; there remains usually an area of normal sensibility over the groins, which persists even in advanced cases. Posteriorly it seldom goes above the level of the iliac crests.

On the upper extremities the first lesions appear at the ulnar surface of the forearms at a variable distance from the wrist, sometimes as far up as the lower third of the arm. Or they may start at the external margin of the hands, involving at the very onset the small finger and soon afterward the ring

²⁸ *Pieces de pathologie exotique* (1911).

²⁹ *Semeiologie nerveuse* (1919), cited by Cussec.

³⁰ *Archives de Médecine et Pharmacie Navales* 111 (1921) 303-312.

finger. From these points the anæsthesia spreads upward, the arms being involved first on the extensor surfaces. The axillary space is not involved.

In three cases of advanced mixed leprosy of over fifteen years duration the anæsthesia was practically generalized, the only sensitive portions of the body being the axillary and inguinal regions, the cubital spaces, part of the scalp, the lower portion of the abdomen, and a narrow strip with skin along the spine and over the sternum.

The changes of cutaneous sensibility on the external generative organs of eighty-four male patients, about 85 per cent of whom have leprosy of the mixed type, were also studied; no observations were made on females.

In forty-five of these men, 53 per cent, no anæsthesia was found; in twelve, or 14 per cent, there was thermo-anæsthesia and analgesia at the scrotum alone; and in the rest, twenty-seven, or 32 per cent, the prepuce and scrotum together presented such changes.

In making such examination, it is important to bear in mind that the glans penis possesses only protopathic sensibility. I have heard of workers describing cases of mixed leprosy in which the sensory changes, consisting of partial anæsthesia, were found at the glans only. It seems very likely that there was no anæsthesia at all in these patients.

Naturally the enjoyment of the sexual act was said to be markedly diminished in the majority of the cases having anæsthesia over the external genitals. However, a few claimed an almost undiminished enjoyment in spite of the presence of practically complete anæsthesia of the penis and scrotum; several of these were still productive.

CHARACTER OF THE SENSORY DISTURBANCES

The anæsthesia of leprosy is variable in quality and extent, not only in different patients presenting similar degrees of advancement, but also in the same patient. The character and extent may even change from day to day. Jeanselme divides the anæsthetic area into two distinct zones; a fixed inner area, probably produced by material lesions in the nerves involved; and a more-mobile and unstable outer fringe based on a simple functional trouble of the cutaneous sensations. Although this arrangement of the anæsthesia was not found in all our patients, it was present in a considerable percentage of the cases.

This border-line fringe is of interest because, after attempts at treatment, perhaps through the influence of suggestion, this area is reduced to a minimum and an improvement may be assumed when actually no permanent benefit has been produced. It is certain that the psychic factor plays an important rôle in influencing the extent or even the character of the anæsthesia and, in order to define its true limits, repeated examination is necessary in most cases. One is often at a loss how to evaluate or interpret modifications or changes observed.

The disturbances of the various elements of cutaneous sensibility will be taken up separately.

Temperature.—Of the cutaneous senses, the earliest to be involved is that of temperature. In 85 per cent of the sixty-eight cases examined for “anesthésie névretique” it showed the most-extensive and the most-marked disturbance. It is also the most variable and the most unstable. As a general rule, the heat perception is affected earlier than the cold. In the more-advanced cases, the difference in extent between the areas showing epicritic impairment of the temperature sense and those showing disturbance of the protopathic system is not often remarkable. Complete loss of the temperature sense is the rule in advanced cases, so that a burn severe enough to cause a blister is not perceived by the patient. In this way blisters and bullæ may frequently be found, especially at the ankles, legs, hands, forearms, and feet, which may be taken as some trophic manifestation of the disease itself.

The heat and cold spots were also investigated at the border of the anæsthetic areas. The spots were found to become less numerous as we examined toward the anæsthetic portion. In some areas only few of such spots remained, separated by skin devoid of any temperature sensibility.

Pain.—Next to temperature, the pain sense is the earliest and the most extensively affected. In the older cases the loss is so complete that a pin prick gives the sensation of mere pressure. At the borders of the completely analgesic areas a deep prick will give the sensation of pain, but the sensation is delayed. The fact that sensation of pain, though mediated by protopathic fibers, is lost early in leprosy shows that the involvement of the peripheral nerves does not follow the ordinary epicritic-protopathic sequence observed in simple section of the nerves. Instead, an imperfect dissociation of the cutaneous senses is effected. This finding suggests a lesion in the cord

or the presence of some selective affinity by the morbid processes for certain nerve fibers; namely, those for pain and temperature.

Light touch.—This is lost comparatively late and often is the least extensive. In unfavorable cases, taking a rapid course, the area of absent or impaired light touch extends rapidly, sometimes outgrowing the area of analgesia. In cases responding favorably to treatment the sensation of light touch returns somewhat more rapidly than do the others. It would seem that the fibers conveying the sense of light touch are not ordinarily as deeply involved as those mediating the other cutaneous senses.

Tactile discrimination.—If the affected area is compared with a healthy portion of the skin near by, or on the opposite side, the dissimilarity is seldom marked, the usual difference being from 3 to 5 millimeters. Sometimes there is impairment of tactile discrimination, indicated by the æsthesiometer, although the sense of light touch is still intact.

Subcutaneous sensibility.—The sensation of pressure, pain, and muscular position are often retained, even in the late stages. In deeply anæsthetic areas the application of a hot body, or a piece of ice, or a pin prick, will cause a sensation of simple pressure due to stimulation of the deep sensory fibers. The sensation of pain is lost much earlier than the other two.

Although the initial site of the anæsthesia does not correspond with any particular nerve distribution, it is usually located within the area supplied by certain cutaneous nerves. In the upper extremities, for example, the anæsthesia usually starts within the area supplied by the ulnar and the median cutaneous nerves, and on the legs within the distribution of the sural and the superficial peroneal. In children it is very common to see the initial patch within the area supplied by the last thoracic and the first lumbar spinal nerves, but this is very unusual in older persons.

Hyperæsthesia.—Hyperæsthetic and paræsthetic symptoms are frequently noticed at the onset of the disease, though they may reappear at any stage of the malady. The most-frequent complaint noticed was numbness; this was reported by 71 per cent of those who felt paræsthetic symptoms at the prodromal stage. The numbness is invariably limited to the extremities, sometimes felt only on one side, but usually bilateral. This numb sensation is most marked toward the latter part of the day, or at night before bedtime. Oftentimes it is accompanied

by tingling or prickling, usually at night, when the affected limb may also feel peculiarly weak and heavy.

Prickling as if with many needles, without numbness, had been noticed by nine patients, and unexplained weakness without any other symptoms, by five. Two complained of sensation of cold, originating at the tips of the fingers and coursing toward the elbows. Three had tearing and stabbing pains along the legs or arms, sometimes so severe that they "became almost crazy with the pain," as one of them expressed it. Two others felt vague pains along the legs on walking, another two had cramps, one had rheumatoid pains, and five suffered from persistent itching which was not relieved by scratching. The paræsthetic symptoms may precede the initial lesions by a period of several months, or they may develop at the same time as or shortly after the appearance of the skin manifestations.

At irregular intervals during the course of a case of nerve or mixed leprosy, the patient may suffer from acute accesses of neuralgic pains of varying intensity. In some instances these attacks accompany the phenomenon known as "lepra fever." The pain is sometimes very severe, persisting for days, during which time the patient may suffer immeasurable anguish, and sleep is impossible.

The paroxysms are accompanied by exquisite hyperæsthesia of the affected parts, though the sensations of light touch and tactile discrimination remain impaired. Following the neuritic paroxysm, or an attack of lepra fever, the anæsthesia is often found to have extended. In many instances, however, it eventually tends to recede and may become less extensive than previously, or may even disappear completely without treatment.

With sudden changes in the weather, some lepers complain of persistent pain in the soles of the feet and along the extremities, accompanied by severe chills, although there is no rise of temperature. In those cases, the autonomic and general nervous systems seem to be on the very verge of disorganization.

Perversion of the cutaneous senses.—This is found with frequency at the margin of the anæsthetic areas. The sensation of light touch may show the phenomenon of "sommation,"³¹ which is said to be present if an area previously not sensible to touch is repeatedly touched with a fine camel's-hair brush or a wisp of cotton, and the sensation reappears after some

³¹ See Cussec, *Archives de Médecine et Pharmacie Navales* 111 (1921) 303-312.

time. In two cases the patients invariably pointed about 4 centimeters below the point touched. As to the temperature sense, the application of a hot test tube may give rise to a sensation of cold, or vice versa. A retardation of the sensation is also observed in leprosy, though not so frequent or marked as in the atrophic type of beriberi.

EFFECT OF ETHYL ESTER TREATMENT ON THE ANÆSTHESIA

The sensory changes observed in thirty-six cases of mixed leprosy receiving ethyl esters of chaulmoogra oil regularly for a period of six months, in average doses of 7 cubic centimeters a week, were compared with the improvement noticed in the cutaneous lesions. The data obtained are given in Table 2.

TABLE 2.—*Effect of ethyl ester treatment on the cutaneous lesions and on the anæsthesia.*

Type of lesion.	Moderately improved.		Slightly improved.		Total improved.	
	Cases.	Per cent.	Cases.	Per cent.	Cases.	Per cent.
Cutaneous (nodular, infiltrations, macules)	6	16.6	16	44.4	22	61
Anæsthesia:						
Tactile anæsthesia	3	8.3	12	33.3	15	41.6
Analgesia	0	0	14	38.8	14	38.8
Thermoanæsthesia	3	8.3	7	19.4	10	27.7
Total	6	5.5	33	30.5	39	86.1

Type of lesion.	Stationary.		Worse.	
	Cases.	Per cent.	Cases.	Per cent.
Cutaneous (nodular, infiltrations, macules)	12	33.3	2	5.5
Anæsthesia:				
Tactile anæsthesia	14	38.8	7	19.4
Analgesia	14	38.8	8	22.2
Thermoanæsthesia	14	38.8	12	33.3
Total	42	38.8	27	25.0

The skin manifestations became moderately improved in six cases, or 16.6 per cent; slightly improved in sixteen, or 44.4 per cent; they remained stationary in twelve, or 33.3 per cent; and in only two did they become slightly worse.

As regards the anæsthesia, only 5.5 per cent were moderately improved; 30.5 per cent were slightly improved; 36.1 per cent remained stationary; and 25 per cent were found to have become worse. Of the different elements of cutaneous sensibility, the tactile sense showed the greatest total improvement, 41.6

per cent, followed by the pain and temperature senses in the order named.

The undoubted benefit of the treatment was also demonstrated in a few cases which had to be dropped during the course of the experiment, due to complications. In three of these the joint and neuritic pains, which had disappeared during the entire period of treatment, were again felt as soon as the injections were discontinued.

To summarize, it may be said that the ethyl ester treatment improves the anæsthesia, although this improvement is not as marked as and is brought about more slowly than the changes in the cutaneous lesions. The sensibility of light touch, pain, and temperature are improved in the reverse order in which they become involved.

DIAGNOSIS

Anæsthesia plays an important rôle in the diagnosis of leprosy, particularly in the neural or maculo-anæsthetic type, in which the bacilli are seldom found. In some instances the presence or absence of sensory disturbances may be the determining factor in arriving at a clinical diagnosis.

The following are important points in the diagnosis of leprosy:

Paræsthesia.—This symptom was observed in the prodromal stage in 50 per cent of my cases. I have seen in the dispensary of the Philippine General Hospital three lepers (who are now in Cullion) whose condition was diagnosed as the rudimentary form of beriberi, and who were treated for that condition for months. One was admitted to the medical ward, and another was referred to the physical department for galvano-faradic treatment; but in neither case was the true nature of the affection even suspected, until they finally developed frank cutaneous manifestations of leprosy.

Anæsthesia.—Anæsthesia, particularly to pain and temperature, is a very early sign of leprosy. Its usual location, extent, mode of progress, and character have already been fully described.

Thickening of the superficial nerve trunks.—Even in the earliest stages, one or both ulnar nerves are frequently thickened, oftentimes irregularly. Occasionally, the great auricular and superficial peroneal nerves are also thickened and palpable.

Pigmentation (macules).—This may be noticed either prior or subsequent to the nervous symptoms; it is commonly observed

in cases of early leprosy among Cullion children.³² Pale patches or macules are also found in syphilis and certain skin diseases such as tinea versicolor, commonly seen among Filipinos. Usually, however, the macular lesions of leprosy have a wider distribution, are less scaly, and present more regular borders than does tinea. In some instances it may be impossible to distinguish between the two, both *Bacillus lepræ* and the fungus *Microsporon furfur* being found in the same area. The presence of anæsthesia and the absence of sweat after the pilocarpin test reveal the leprotic character of the lesion.

Localized erythematous patches or infiltrations.—These are sometimes the first cutaneous manifestation of the disease.

Painless enlargement of the superficial lymphatic glands.—Such enlargement, particularly of the inguinal, epitrochlear, axillary, and cervical glands, is a suspicious sign.

"Parchment" skin (parakeratosis).—This is characteristic of nerve leprosy, often seen on the anterior and lateral aspects of the legs.

Atrophies and contractures.—As a rule, the small and ring fingers contract first in leprosy. These contractures are accompanied by a slow but progressive atrophy of the lumbricals and other short muscles of the hands.

Trophic ulcers.—Trophic ulcers should be especially searched for.

Ulceration of the nasal septum.—This is not infrequently seen, even early, at the onset of the disease.

Knee jerks.—The knee jerks should not be forgotten. Even with marked neural involvement, the knee jerks often remain unchanged. In a few cases, this symptom may be diminished or entirely abolished.

It need hardly be said that thorough bacteriological examination should be made in every suspicious case.

DIFFERENTIAL DIAGNOSIS

Discussion of the differential diagnosis will be limited in this paper to consideration of the diseases that may present symptoms simulating the neural manifestations of leprosy; namely, anæsthesia and trophic changes. These will be taken up separately.

³² Gomez, L., J. Avellana Basa, and C. Nicolas, Early lesions and the development and incidence of leprosy in children of lepers, Philip. Journ. Sci. 21 (1922) 233.

ANÆSTHESIA

Beriberi.—An early case of nerve leprosy can easily be confused with beriberi, unless the possibility of the former disease is borne in mind in all cases presenting symptoms of anæsthesia and paræsthesia. Unfortunately, such error prevents the prompt segregation and treatment of the patient, to the detriment of himself and the public.

The difference between the nerve symptoms of the two diseases can be better appreciated if it is kept in mind that in leprosy the muscular fibers in the affected nerves are not as deeply involved as are the sensory fibers, whereas in beriberi the reverse is the case, and signs of muscular paralysis appear early. Even in advanced lepers with distortion and absorption of the fingers, the grasp is still retained and the knee jerk is only diminished and may even be exaggerated. Furthermore, in leprosy the development of these changes is very slow, whereas in beriberi it is comparatively rapid.

As for the character of the anæsthesia itself, there are certain distinctive features which more or less characterize each disease. The anæsthesia in beriberi is never as complete as in leprosy. Retardation of sensation is a characteristic feature of beriberi; I have found it in all the cases I have examined so far. As long as five seconds may elapse from the time a hot test tube is applied to the anæsthetic part before the patient feels the sensation. In leprosy retardation is only occasionally observed. The sense of light touch, in relation to the other cutaneous senses, is involved much earlier in beriberi than in leprosy, so that there is no dissociation, the epicritic fibers being involved first.

In distribution, the anæsthesia is likely to be patchy at the onset in both diseases, and the same degree of symmetry may later be found in both. In beriberi, however, the anæsthesia is more likely to start at the radial half of the dorsum of the hands, whereas in leprosy the ulnar portion is more likely to be involved. A ring of anæsthesia around the mouth, without paralysis, is indicative of beriberi, for in leprosy it occurs only in very long-standing cases with paralysis of the orbicularis oris muscle.

Syringomyelia.—Late in the last century, particularly during the period between the International Congress of Dermatology and Syphilology held in Vienna in 1892 and the First Lepra

Conference at Berlin in 1897, the similarity between syringomyelia and leprosy was the subject of much discussion among the leading leprologists of Europe. Some, notably Zambaco Pasha, maintained that the two diseases were identical. Later Zambaco modified his views and came to consider syringomyelia, as well as such diseases as scleroderma, Morvan's disease, sclerodactylia, Reynaud's disease, ainhum, and the progressive muscular atrophy of Aran-Duchenne, as attenuated or aberrant forms of leprosy which manifest themselves in those countries where the conditions do not favor its proper development. He compared these diseases to the pure hereditary manifestations of syphilis. This view has not gained general acceptance, principally because the bacillus of Hansen has never been found in those conditions.

Syringomyelia is now regarded, according to Osler,²³ as a "gliosis, a development of embryonal neuroglial tissue in which hemorrhage or degeneration takes place with formation of cavities." So far as I am aware, this condition has never been reported in the Philippines.

The following are the distinguishing features between the two diseases:

In favor of syringomyelia:

- The complete dissociation of the cutaneous senses.
- Integrity of the superficial muscles of the face.
- Absence of discolorations on the skin.
- Nonenlargement of the ulnar nerves or the lymphatic glands.
- Integrity of the hair.
- Deviation of the vertebral column.
- Absence of *Bacillus lepræ*.

In favor of leprosy:

- Presence of discolorations or infiltrations on the skin.
- Enlargement of the ulnar, peroneal, or the great auricular nerves, and of the superficial lymphatic glands.
- Loss of hair over affected parts.
- Spontaneous absorption of the fingers and toes.
- Atrophy and paresis of the superficial muscles of the face.
- Presence of *Bacillus lepræ*.

Morvan's disease is a type of syringomyelia with pronounced trophic disturbances, characterized by cutaneous anæsthesia, neuralgic pains, and the formation of painless destructive whit-

²³ The Principles and Practice of Medicine, 8th ed. D. Appleton & Co., New York (1917) 964.

lows. Such whitlows are sometimes seen in cases of cutaneous or mixed leprosy.

Neuritis.—Of the various kinds of neuritis that need be considered, the most important is alcoholic neuritis. The distribution of the anæsthetic areas may simulate that of leprosy. The diagnosis is based on the history and the presence of the characteristic general tremulousness in chronic alcoholism. Arsenical neuritis can be eliminated by the presence of diarrhœa and abdominal pain, and lead paralysis by colic and the blue lines on the gums.

Sometimes anæsthesia of functional origin may be found in hysteria. The anæsthesia usually involves half of the body and it may be transferred to the other side by suggestion.

There are many cases seen in hospital and private practice in the Tropics that cannot be grouped under beriberi or under any of the more commonly recognized cases of specific etiology. It is my belief that many of these are probably cases of early leprosy, most of which may be expected to develop frank manifestation of the disease.

CONTRACTURES

Yaws.—Cases of tertiary yaws have repeatedly been diagnosed as leprosy and brought to the Cullion Leper Colony because of the ulcerations and marked deformities that are sometimes seen late in this disease. These mutilations are produced by necroses and ulcers, involving the bones, which on healing produce marked deformity of the parts affected. As a result the fingers may be contracted or bent at various angles, the legs may become shortened and twisted, and the face may be disfigured by permanent changes in its bony structure, particularly the nose and the forehead. The pleomorphic skin lesions of yaws and syphilis may be mistaken for leprosy, but the history and the usual absence of nervous manifestations over the lesions, together with the laboratory examination, render the diagnosis fairly easy.

Aran-Duchenne.—The disease known as the Aran-Duchenne type of progressive muscular atrophy is characterized by a contraction of the flexor muscles of the hand and extreme atrophy of the thumb muscles, the interossei, and the lumbricals, producing the characteristic claw hand (*main-en-griffe*), the counterpart of which is commonly seen in leprosy. The absence of anæsthesia and absorption of bones, the fibrillary contractions,

the absence of trophic ulcers, and the characteristic electrical reaction in this disease should make the differentiation not difficult.

Ainhum.—This disease is characterized by linear strangulation and ultimate spontaneous amputation of one or more toes or fingers. It is frequently confined to the toes, usually the small toe, the process taking many years to develop and not progressing beyond this stage. It has been found only among negroes in Africa.

SUMMARY

Though studies have been made on the anæsthesia of leprosy, particularly by the older writers, the manner of its development is not satisfactorily established, and its nature has not been studied in the light of modern knowledge of nerve function.

The work of Head and Rivers offers a new basis for the study of this disturbance. These workers, after studying the loss of sensation following the section of cutaneous nerves, have proposed a new classification of the cutaneous senses, based on the order in which they return after the cut ends are united. They also distinguish between the cutaneous sensibility of the skin proper and the deep or subcutaneous sensibility which is conveyed by sensory fibers contained in the muscular branches. The true cutaneous sensations are mediated by two systems of fibers which regenerate at different times when the cut ends are reunited; namely, a set conveying sensations of extreme changes of temperature and pain which regenerate early, in which the sensibility is low and imperfectly localized, and which is known as protopathic sensibility; the other system, regenerating later than the protopathic, mediates the senses of light touch, tactile discrimination, and small differences of temperature. This classification was, so far as I am aware, first applied in leprosy by Hopkins, but his results are not conclusive.

The cutaneous sensibility of two hundred cases of all types and stages of leprosy have been examined repeatedly with the view to studying the nature and the behavior of the anæsthesia under various conditions. The nervous changes were found to be most variable and fickle in many of the cases, sometimes even varying from day to day in the same individual.

Anæsthesia in the cutaneous lesions was examined separately from that in skin free from skin eruptions. In 16 per cent of all the infiltrations examined, there were no sensory changes whatever over the skin lesions. This is contrary to the general

idea that anæsthesia is invariably present in the cutaneous lesions. Over the rest (84 per cent) of the infiltrated areas dissociation of the cutaneous senses was present. The hard nodules, which generally appear late in the disease, were usually surrounded by anæsthetic skin. In the case of the macules the anæsthesia was complete in 30 per cent of the total number of thirty cases. The remaining sensibility in the rest belongs to the protopathic type of Head and Rivers; there was no dissociation. In macules positive for *Bacillus lepræ*, there was hyperæsthesia at the borders.

In the anæsthesia independent of the skin lesions the senses of temperature and pain were the earliest and the most intensively involved. The sensation of light touch and tactile discrimination were affected comparatively late, so that a dissociation of the syringomyelic type is suggested.

The legs, dorsum of the feet, forearms, hands, and fingers, in the order named, are the most-frequent sites of the anæsthesia. As a rule, the anæsthesia is at first unilateral but, sooner or later, a more or less symmetrical arrangement is effected in the majority of the cases.

During or after an attack of lepra fever or a paroxysm of neuralgic pains, the anæsthesia may show surprising changes; the areas may extend rapidly, or there may be a rearrangement or transformation of the senses of touch, pain, and temperature. After the disappearance of the acute symptoms, the anæsthetic areas may retain their new borders, they may return to their former limits, they may recede to a smaller area than the original, or they may disappear.

The differentiation of the anæsthesia in beriberi from the nervous changes of leprosy is not always easy. In the former disease the process is much more acute and the anæsthesia is never as complete and seldom as extensive as in leprosy and is early accompanied by signs of motor involvement, such as absent knee jerk or the presence of wrist or foot drop. The retardation of sensibility is another characteristic feature of the anæsthesia in beriberi; it is rarely present in leprosy. If in a case of nerve or mixed leprosy signs of rapid muscular weakness develop with loss of the knee jerk, and rapid development of wrist or foot drop, dry beriberi is to be strongly suspected. In some cases, the voice may suddenly become aphonic and high-pitched. Wet beriberi is less difficult to distinguish.

In thirty-six cases of mixed leprosy under ethyl ester treatment, the anæsthesia was found to have improved in 36 per cent, although the improvement is not as marked as in the skin

lesions. Of the cutaneous senses, that of light touch showed the highest percentage of general improvement and, since it is also the last to be affected, it is probably the least involved.

CONCLUSIONS

1. Not all the cutaneous lesions of leprosy are anæsthetic: Sixteen per cent of infiltrations do not show any disturbance of the cutaneous senses.

2. The anæsthesia of leprosy is fickle and variable; several examinations are necessary to determine its real extent and character.

3. Distinction should be made between the sensory disturbances in the skin lesions and those independent of all cutaneous manifestations.

4. The character of the anæsthesia depends on whether it is located in a macule, an infiltration, or a skin free from lesions. In macules there is, as a rule, early loss of epicritic sensibility; in nodules and infiltrations the anæsthesia is very variable; and in a skin free from eruptions a partial dissociation of the syringomyelic type is effected. These differences suggest the possibility that the cutaneous nerves may be involved in various ways, depending on the character of the overlying skin lesion.

5. The anæsthesia shows definite improvement under ethyl ester treatment although, as is to be expected, it is not as well marked as the improvement in the cutaneous lesions.

6. In countries where leprosy is endemic, the possibility of this disease should always be considered in every case presenting symptoms of paræsthesia such as numbness, prickling, formication, etc.

7. Although the absence of anæsthesia does not exclude leprosy, the touchstone in doubtful cases, from the clinical standpoint, is its presence in some cutaneous lesion or in some skin area.

8. The final confirmation of the diagnosis is the presence of the specific organism in the lesions or on the nasal septum.

ILLUSTRATION

TEXT FIGURE

FIG. 1. Schema illustrating the Gerlach-Dehio hypothesis (from Dehio); *a*, diseased sensory-nerve branch; *b*, diseased mixed nerve; *c*, not involved muscular branch with muscle, *ma*; *d*, mixed-nerve trunk; *e*, mixed nerve; *f*, cutaneous branch to skin, *sn*; *g*, muscular branch with muscle, *mn*; *sl*, leprotic skin; *sn*, skin; *mn*, muscle.