MORPHOLOGIC CHANGES OF THE CUTANEOUS NERVES IN LEPROSY

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Danielssen and Boeck (1848) considered all of the changes of the skin and nerves, in neural leprosy as resulting from a general trophic disturbance of central origin. Virchow (1863) regarded the anatomic nerve changes as an ordinary granular atrophy, the formation of macules being caused by disturbance of nourishment resulting from the atrophy of the diseased nerves leading to the region affected. On the other hand Meissner (1883), emphasizing the fact that the characteristic peripheral growth of the skin lesions is observed only in leprosy, held that it showed these lesions to be independent of the innervation of the areas; such a trophic disturbance is not observed in any other form of neuritis. It remained uncertain why, in affections of the mixed nerve trunks, only the sensory fibers undergo degeneration at first, the motor fibers continuing to function normally for a long time. When it is considered that, with extensive affection of the peripheral sensory nerves, the central nervous system remains unaffected in the majority of the cases, and that the lesion process is of ascending character, then it is understandable why in the pathology of leprosy another view is recognized, namely, that the nerve affection spreads centripetally, starting peripherally from the most superficial cutaneous nerves.

Dehio (1890) was the first to assert categorically that in leprosy there exists a gradually developing degenerative atrophy of the nerve fibers and of whole nerve branches, progressing from the periphery toward the center. Soss (1891) also established the fact of a progressive neuritis, and expressed the opinion that it is necessary to search in the skin for the primary affection. The case of maculo-anesthetic leprosy which he observed was subjected to an accurate histologic study by Gerlach (1890-1891). In the nerve branches in the subcutaneous tissue he discovered, together with degeneration of the myelin sheaths, a small-celled leprous infiltration that affected the sheath of the nerve and

permeated its whole cross section. Within the skin lesions, he concluded, this condition increases gradually and ultimately extends beyond the limits of the nerve branches to form, in the vicinity of the sweat and sebaceous glands, "cylindrical or sausage-like tumors" within which the smallest branches of the cutaneous nerves disappear entirely. In their place there appear sausage-like accumulations of the leprous granuloma which extend to the superficial layer of the subcutaneous tissue and ramify there, as in the dermis itself. In the nerve branches, however, the new-formation does not progress centrally beyond the cutis. Thus the lesion is confined to the smallest branches of the cutaneous nerves, whereas the larger ramifications in the subcutaneous tissue are almost completely free from the leprous infiltration and the nerve trunk itself is always free.

All of this refers to the early, slightly advanced skin lesions. When, exceptionally, the leprous focus spreads into the larger branches, it is easy to prove that the condition is younger than in the more peripheral parts. He denied categorically the affection of the nerve trunks when the peripheral branches are free from leprous infiltration.

Gerlach also described the process of gradual degeneration of the peripheral cutaneous nerve branches, which ends with their fragmentation. In sections of macular lesions he observed that in the early stages of the disease the medullated nerve fibers can be followed up to the papillary layer, and that the elegant tassel-like branches become striking at the sebaceous glands. The older the disease the less frequently are unaffected nerves encountered; finally they disappear entirely and in their place appear the "nodular-cylindrical tumor columns."

Two kinds of sensory disturbances were distinguished by Gerlach: first in the region of the skin lesion and in combination with the disease process therein, and second independent of the latter, in distant regions, caused by degenerative changes progressing from the center to the periphery (descending degeneration).

According to Woit (1898), after the destruction of the cutaneous nerve connections the corresponding nerve fibers undergo ascending degeneration, which can be followed to considerable distances in the subcutaneous nerve trunks. At the first International Leprosy Conference (1897) Blaschko expressed himself in favor of this opinion. He demonstrated skin sections in which

the nerves found in the neighborhood of the vessels were affected only peripherally, and not deeper, and asserted that the anatomic findings all indicate that the skin changes, clinically and anatomically, precede the nerve involvement. The centripetal theory was also supported by Ssamgin (1898). On the other hand Unna (1897), who stood for the centrifugal viewpoint, stated that he had not succeeded in discovering peripheral degeneration of the nerves, the technique of examining peripheral nerve endings being too imperfect.

The affection of the sensory nerves in leprosy, according to Reschetillo (1904), proceeds gradually in the ascending direction, though not without interruption, so that the more superficial nerve zones are attacked earlier than the deeper ones. This he explained on the ground of transfer of the lepra bacilli in the direction of the vessels which nourish the nerves.

In the large nerve trunks one can readily establish in the living patient the presence of thickenings and nodules. In occasional cutaneous nerve endings Babes (1901) discovered such thickenings in carefully made preparations. Later in the disease these thickened yellow regions of the nerve trunk are less frequently encountered because, through sclerosis, they are converted into thin hard bundles. The histopathologic process is a development of a local leprous infiltration around the invading bacilli, which are at first deposited around the nutritive vessels of the nerves (Virchow, 1869), afterward to penetrate into the interior of the nerve fibers. Because of pressure the nerve sheath disappears, and ultimately even the axis cylinder. As a result of proliferation of the connective tissue, at the end of the process one can hardly recognize remnants of nerve fibers, and these in time disappear completely. Frequently atrophy occurs as a result of the pressure; then, between the atrophied fibers, there remain interstices filled by lepra bacilli (Babes, 1901), and myelin layers that are colored black by osmic acid (Jeanselme).

In the sheaths and nerve fibers themselves one observes accumulations of small round cells, and later elongated cells. Lepra bacilli are also present, either lying free in the intercellular spaces, or in elongate cells on the surface or in Henle's sheath, which cells Babes regarded as belonging to the sheaths of Schwann and Henle. Marked thickening of the endoneurium and epineurium is observed, due to the proliferation of large round and elliptical cells containing large numbers of bacilli. Kelley observed

bacilli in the lymph spaces along the nerves, occurring either individually or in groups.

According to Lebedew (1923) the nerves, both trunks and branches, which occur within the leprous infiltration (composed of lymphocytes and plasma cells) are penetrated by it, in time resulting in fibrosis and destruction of the nerve fibers. Bacilli can often be demonstrated between the infiltrating cells. Remaining to be mentioned is the work of Doi Schoichi, who discovered fragmentation, degeneration and atrophy of the small nerve branches in the skin.

With regard to the terminal apparatus of the nerves, Samblin (1871) stated that he never found Meissner's corpuscles in this disease, but it is not certain whether that was due to the disease itself or depended upon unsatisfactory methods of staining. C. and F. E. Hoggan (1882-3) asserted that the endings may perish rapidly, early in the disease, or on the other hand may persist long after the destruction of the nerves. They found that the Vater-Pacinian bodies in lepra-cell infiltrations along the blood vessels may not be damaged. In several cases these corpuscles still remained unaffected for years—up to 15 years—after the degeneration and destruction of the nerve fibers related to them. However, in other cases with destruction of the fibers there were also present degenerative changes in the corpuscles: the cellular lamellae became thickened and vacuolated, and finally a group of lepra cells remained in the place of the body.

In two cases of mixed leprosy Ssudakewitsch (1887) examined over fifty Vater-Pacinian corpuscles, finding marked disorder in the layers of both damaged and undamaged corpuscles in the skin of the palmar surface of the hand and fingers. One or two corpuscles were entirely normal, but many were markedly abnormal. According to the character of the affection he divided them into two groups:

(1) Atrophied corpuscles with slight changes, in which not only the lamellae and interstitial layers are affected, but also the nerve fibers which approach them and those that are in the central cavities. He did not succeed in demonstrating the approaching fibers, but the central ones were markedly thinned and without sharp double contours, which appearance was often completely lacking. The cavity of the corpuscle is contracted, the corpuscle appearing to be shrunken together, with the lamellae lying close to each other and with an extraordinarily small number of nuclei. In the absence of lepra bacilli changes of this kind can only be explained on the ground of the degeneration of the nerves.

(2) In contrast are corpuscles that are one and one-half to two times

larger than normal. The approaching nerves are degenerated and contain here and there a greater or lesser number of bacilli, and in some of them these nerves are entirely absent. In the former stage individual lepra bacilli are found between the lamellae and along the blood vessels. Later they penetrate, not only all of the interstices between the lamellae but even the central cavity, whereupon they give rise to accumulations of granulation elements composed almost exclusively of lymphocytes, without giant cells. This infiltration compresses the central fibers and leads to their destruction, regardless of whether the infiltrating elements are found in the central cavity or in the interlamellar interstices. In large infiltrations bacilli appear in globular accumulations, at times in the cells and at times free between the lamellae. The borders of the individual lamellae are lost, their concentrated structure disappearing, the whole corpuscle being dispersing. Often, however, as the Hoggans stated, there is complete destruction of the corpuscle, in the place of which there remains only a small collection of leprous cells.

Ssudakewitsch regarded the changes of the second group as resulting from a direct spread of the leprous process from the surrounding skin and subcutaneous tissue into the corpuscle itself by way of the blood vessel, which permeates from outside through the lamellae, where it ramifies. He also pointed out the possibility of the participation of two factors in the production of such changes—degeneration of the nerve fiber as well as the leprotic infiltration.

Bernucci (1923) investigated the histologic changes of the terminal apparatus of the cutaneous nerves, after making preliminary examinations of the sensory functions for the purpose of establishing the relationships between anatomical and functional changes. In lepra anesthetica he did not find the nerve endings and fibers. In advanced mixed cases those structures were represented only by very scanty remnants of nerve fibers. In nodular leprosy the nerve apparatus of the skin was unchanged, which corresponds to the absence of sensory disturbances in this form. But in apparently unchanged regions of the skin surface in these forms of the disease, even in advanced cases, neither absence nor degeneration of the nerves was observed. In the finger pulp there were found small numbers of Meissner's and Pacinian corpuscles or free intrapapillary ends; the fibers present were changed, thickened, clublike, compact. This kind of degeneration of the nerve endings was also observed at the base of the papillae. In other cases the nerve endings had disappeared; on the other hand, in the less severe forms of nodular leprosy no pathologic nerve changes were found.

Sajo and Takino (1929) observed in the Meissner's corpuscles primary and secondary changes that existed simultaneously in

different degrees, the former more marked than the latter. The degeneration of the axis cylinder in the portion transitional to the body was more developed than in the body itself. In the presence of globi that touched and pressed upon the transitional portion, there had occurred atrophy of the axis cylinder which began here and spread peripherally. The most marked changes of these corpuscles were where they were in immediate contact with the globi, or when globi were present in the corpuscle. But even when all corpuscles were filled with globi, not all of the fibers had disappeared.

Hashimoto (1933), in examining small pieces of leprous granuloma and also of macular lesions, found degeneration of the free ends of the nerve fibers. The investigators Sakurane, Kinoshita (1936), and also Bernucci, touch upon the question of changes of the cutaneous nerve fibers, but they do not contribute any new findings regarding the morphologic changes of the nerve ends.

PERSONAL INVESTIGATION

For the study of the morphologic changes of the cutaneous nerves in leprosy here reported I employed the method of silver impregnation described (in Russian) in the *Archiv der pathologischen Anatomie* 2 (1938) No. 2. For the material placed at my disposal for this study I express my thanks to Dr. S. N. Rugtschenko, of the Astrachan leprosarium.

CASE 1.—Specimen of a leprous granuloma on the upper arm. General histology: Epidermis atrophic, with unimportant hyperkeratosis. Interpapillary protuberances flattened, so that the lower border of the epidermis appears as a slightly undulating line. In the reticular layer are large centers of perivascular infiltration, which frequently merge and appear diffused in the compressed connective tissue. The infiltrate consists of lymphocytes of different sizes, lepra cells, giant cells with five to ten nuclei, together with a few polymorphonuclear leucocytes, hypertrophic fibroblasts with abundant protoplasm, and occasional mast cells. Lumens of the blood vessels are markedly reduced on account of proliferation of the endothelium. Hair follicles and sweat glands in the areas of infiltration are undergoing destruction. Along the blood vessels and the sweat ducts the infiltration extends from the deeper layers to the epidermis.

Nerve structures.—There are few nerve fibers in the superficial layers, more numerous ones deeper, near the large infiltrations, where frequently they are markedly changed or fragmented. They undoubtedly extend from the cutis to the epidermis, but it is absolutely impossible to follow them between the epithelial cells because of the large numbers of star-shaped, argentophil cells in the lower portion of the epidermis. In the subpapillary layer

the number of fibers is very small, but it increases at the border of the reticular layer, where they present marked changes. They are most numerous in the cord-like infiltrations, where they are often encircled by coarse, compact connective-tissue sheaths.

The following conditions attract attention: (*a*) The marked impregnation of the fibers, which are intense black and sharply contoured. (*b*) Decided thickening of almost all fibers, which as a result are somewhat coarse. (*c*) The presence of clear, well-developed fragmentation of fibers, resulting in their decomposition into quite large parts of irregular length and pronounced cylindrical form. (*d*) The frequently very uneven contours, with many irregular thickenings and indefinite outgrowths or protuberances and contractions, of variable density; these changes are seen especially clearly in the fragments of decomposed fibers. (*e*) The fragments of the decomposed fibers frequently have the appearance of strangely joined nodules in which there are present many eyes, as of needles, or loops, knotted together, and different kinds of curvatures. (*f*) Such fragments and irregular compact portions are sometimes as much as ten times as thick in diameter as the fibers, giving one the impression of a shapeless clump from which, at both ends, two coarse, thick nerve fibers go out as short protuberances. (*g*) At times these fragments look like simple thick chips with serrated splintered free ends. (*h*) In several instances, along the path of former fibers, there were seen large, quite shapeless lumps of an argentophil substance, as well as the fragments described. (*i*) In the deepest portions of the reticular layer, in the neighborhood of the large centers of infiltration, the nerve fibers break up into small, black, elliptical pieces which follow one another closely. (*j*) Frequently to be seen are completely destroyed fibers, the paths of which can be followed by means of quite broad stripes of the finest argentophil dust.

In tangential sections of the large nerve bundles which course deep at the border of the subcutaneous cellular tissue, and are composed of 30 to 60 sheathed nerve filaments, may be seen well the markedly thickened perineurium, which is separated by some distance from the nerve-fiber bundle. The space so produced, as also the sheath itself, is invaded by infiltrative elements. In several longitudinal sections such bundles undergo branching, and here it can be seen convincingly that they are composed of two kinds of fibers: ordinary black ones, somewhat thick, and others that are thicker but of yellowish-brown or dark brown color and semitransparent.

The nerve apparatus in the places of the sweat glands and hair follicles that are quite destroyed because of the leprous infiltration, is partly preserved but markedly changed. The delicate basket-like plexus of the circular and palisade fibers cannot be seen, only coarse and irregular thickening of the fibers, with large deepenings or outgrowths, and often a greater or lesser degree of fragmentation. Some of them are characterized by extraordinary thickness and coarseness, and an appearance of compression or compactness and a brownish color. Several coarse, slightly crooked filaments can be found among the smooth-muscle bundles, the errectores pilorum.

Portions of the nerve bundles which accompany the sweat-glands in the leprous granuloma are composed of five to fifteen coarse, thickened fibers which are uneven but only slightly curved. Their connective tissue sheaths are condensed, thickened and permeated by lymphocytes.

Two or three of the lower rows of cells of the epidermis, often indeed one-half of it, contain numerous cells in the form of rounded sacs in which are small round granules of argentophil substance. The lower part, at the level of the basal layer and one or two layers of the prickle cells, are diffuse black; the more superficial layers have a smaller number of black granules.

In the papillary and subpapillary layer of the cutis no argentophil lumps or nuclei are found. Occasionally in the deepest parts of the hair follicles, in the epithelial sheath, there are one to three well-developed ramified cells which, however, do not show any nuclei and are almost diffusely black. In the epithelial sheaths of some follicles there are deposited round agglomerations of argentophil cells, extending from the superficial epithelium to a considerable depth, where they gradually disappear.

CASE 2.—Lepra mixta. Specimen of a slightly infiltrated macule. General histology: The picture is similar to that of the foregoing case, except that it is of less degree. The perivascular infiltrations, that only here and there merge together, are superficially located.

Nerve structures.—The number of the nerve elements is evidently greater than in the preceeding case, and they present only slight changes. There are fewer thickened, black nerve fibers running irregularly in different directions along the subpapillary layer, reaching the epidermis and often penetrating it to become lost in the mass of argentophil substance. More often there are encountered, in the superficially located infiltrations, isolated fibers and bundles of five to ten of them, curved or al-

most straight, encircled by their connective-tissue sheaths. Outside of a slight increase of their cross section, the fibers themselves do not present any particular change; in individual filaments that enter into the composition of the bundle there are compacted portions of indefinite form and of different sizes. In the dense connective tissue there are often seen fragmented nerve fibers, broken up into short cylinders or small oval pieces of intense black color. Here and there they retain their straight position; often they are crooked; frequently, however, they are scattered in disorder, so that one can guess with little probability at the course of the former nerve filaments. The impression is gained that the leprous infiltration is located mainly around the large nerve bundles, from where it penetrates their connective tissue sheaths.

The condition of the nerve apparatus of the sweat and sebaceous glands is variable. In some instances, where there is no surrounding infiltration, it is completely normal. In the other glands, more or less affected by the infiltration, the fibers are thickened and coarse, often markedly twisted, with tumefactions of different forms and sizes; and at times they are fragmented into black, short or longish cylindrical lumps or granules. In the neighborhood of the sweat-gland masses there are large nerve bundles composed of fifteen to twenty nerve filaments which are laid extraordinarily compactly, have many curvatures, and also frequently show apparent compressions of small diameter, this giving the fibers a somewhat unevenly cracked or fissured appearance. The connective tissue covering which surrounds the nerve bundles is thickened.

Here and there the whole epidermis, up to the horny layer, appears black because of the mass of half-degenerated, star-shaped argentophil cells. As in the foregoing case there is almost no trace of argentophil granulation in the papillary and subpapillary layers.

Case 3.—Lepra mixta. Patient X., 34 years of age; duration of the disease 6 years. Specimen of an atrophied skin area previously the site of a leprous granuloma. General histology: Unimportant hyperkeratosis which, however, appears to be marked since the thickness of the horny layer is almost double that of the epidermis, which is atrophied and has at most only from two to four cell layers. Interpapillary outgrowths and papillae are entirely absent, the border between the epidermis and dermis being quite even and straight. The accessory structures—hair, sebaceous glands and sweat glands—are markedly atrophied. In the subpapillary layer, and especially in the reticular layer, are more or less conspicuous leprous infiltrations.

Nerve structures.—On the whole the impression gained is of extremely poor innervation. Only twice could penetration of nerve fibers into the epidermis be seen in about 50 preparations examined. Occasionally slightly crooked pieces of large, thickened, intensely black-colored fibers are found in the subpapillary layer. Frequently there are small bundles of two or three of such fibers, which however are straight and are surrounded by thickened connective-tissue sheaths.

In the infiltrations are found nerve bundles that are composed of small numbers of filaments, which frequently do not show any abnormality. Judging from the size of the thickened connective tissue mantles, there must have been present originally in these bundles a much larger number of filaments, most of which in all probability have disintegrated. The small fibers have irregular tumors, but often at the same time the bundle comprises ordinary fibers of black color, while one-third to one-half of them are much broadened and yellowish-brown in color because of pronounced attenuation. Similarly are found thickened, dark brown, fragmented nerve filaments, broken up into shapeless granules. More seldom are there bundles in which a thick fiber forms a loop that turns back upon itself. In the atrophied sweat and sebaceous follicles are sparse remnants of nerve bundles in the form of fragmented pieces of various sizes. The unfragmented fibers are crooked, with uneven, cracked contours.

Penetration of thickened, very crooked black fibers into the walls of veins at the border of the subcutis is noticed. These vessels are abnormal, their walls thickened, the adventitia fibrillated and infiltrated with plasma cells, lymphocytes, polyblasts and fibroblasts, the intima thickened and almost entirely occluding the lumen of the vessel. The nerve fibers almost reach the intima, but it is not possible to determine their ends because they disappear on the surface of the section.

In the subpapillary layer very occasional small, shapeless lumps of argentophil substance are found.

Case 4.—Lepra mixta. Patient X., 34 years of age; duration of the disease, 6 years. Specimen of finger pulp from the index finger, clinically of normal appearance. General histology: Relative hyperkeratosis, the horny layer being 2½ times as thick as the rest of the epidermis. Some condensation and fibrillation of the connective tissue of the subpapillary and reticular layers. The blood vessels are widened and their walls thickened, mainly on account of proliferation of the endothelium; the adventitia is often infiltrated. Here and there, especially around the vessels, there is in-

significant lymphocytic infiltration with an admixture of epithelioid cells and fibroblasts.

Nerve structures.—The number of the nerve elements is not decreased. They are of very varied kinds, but almost all are quite markedly changed.

The nerve fibers penetrate throughout the epidermis, and very often can be followed for considerable distances without difficulty. They are mostly thick, coarse, slightly crooked, often ramified. A part of the ramifications end free, gradually becoming thin; several disappear at the surface of the section. Others approach the Merkel cells, where they show distinctly large discs of neuro-fibrillary structure. The size of these discs and the presence of one to three small, rounded black nuclei suggests that they are abnormal. Much more often there are seen isolated, thickened black fibers near the epidermis, where they frequently course horizontally, proceeding almost to the border of the apex of the outgrowths.

In the papillae, and especially in the subpapillary layer, there are many thickened black fibers. Some of them are slightly crooked while others are straight. These fibers are surrounded by compact connective-tissue sheaths the thickness of which often exceeds by ten times the diameter of the fiber itself. Branching of such fibers is also observed, the branches proceeding to the papillae. In several instances these fibers are of uneven contour or angular; their color is yellowish-brown.

In both the subpapillary and reticular layers there are nerve bundles of different sizes which run in different directions and therefore are sectioned variously. They are surrounded by more or less thickened connective-tissue layers. The number of the filaments in the bundles varies markedly, but on the whole is not large. The thin, intensely black fibers are considerably fewer than the thick, dark- and light-brown ones, which often are semi-transparent, jelly-like. They are always well contoured, though their outlines are frequently uneven. Also to be found are very crooked thin fibers which here and there form small loops or twisted or spiral figures, afterward continuing in their course. Considerably more seldom are fragmented fibers, though sometimes all of the fibers that form a bundle are in this condition. At certain places in the bundle the fibers begin to divide, producing secondary dividing branches at compact, triangular points and forming entangled nodules the general picture of which becomes still more complicated because of numerous thickenings

and condensations. At the places of the curvatures and divisions, the sectioned nerve filaments sometimes resemble Ruffini's end corpuscles, and their character can be determined with certainty only by comparison of serial sections. Such bundles are even observed in the sweat gland areas.

In the papillary layer the following more or less complicated pictures are encountered: (*a*) Typical Meissner's corpuscles, their connective-tissue capsules colored darker than the surrounding corium. A characteristic peculiarity of these bodies in this case is the complete absence of the Timofejew's apparatus.[1] Possibly the discrete, very small, black granules which are present in the capsule in small numbers are a product of its decomposition. Of the main mass of the fibers that form the central apparatus, two-thirds are thickened, yellowish-brown, semitransparent, often jelly-like in appearance and not infrequently presenting large spindle-shaped thickenings, besides which they are often of uneven, rough contour. Preterminal thinning of the elementary fiber can often be seen clearly. (*b*) More seldom there are found complicated Meissner's corpuscles which differ from the normal through the absence of the fine fibers of the Timofejew's apparatus. (*c*) Equally seldom are observed Dogel's corpuscles with complicated ramifications in the epidermis composed of thick, quite coarse filaments, the ends of which unfortunately cannot be followed. The Timofejew apparatus is also lacking in these corpuscles. (*d*) Simple and complicated clumps of different sizes and stages of development, all formed of much thickened fibers which are not black but dark brown, often with spindle-shaped enlargements and here and there with small globular outgrowths. (*e*) Most infrequently are found Dogel's corpuscles with leaf-like ends, composed only of thickened nerve fibers. (*f*) The Vater-Pacinian corpuscles lie beside the thickened nerve bundles, which occur in groups of three to six bundles. The number of the lamellar sheaths may be as high as 45 to 50; they are quite well developed and the interstices between them are clearly seen; the epithelial nuclei lie between them. The lamellae themselves are shrunken, and between individual groups of them there are quite large empty interstices. The shrinking of the lamellae is often more marked and the interstices occur regularly after every 5 to 10 lamellae. Usually one can neither see the afferent nerve fibers nor find

[1]Timofejewschen Faden-Apparat: fine fibers, possibly sympathetic nerve fibers, in the Vater-Pacinian bodies.

any trace of fibers in the inner capsule. In cross sections, however, when the inner capsule is seen in tangential section, three or four transversely cut, black, thick nerve fibers can be found lying side by side.

In the lower portion of the epidermis there are, here and there, slight accumulations of very fine argentophil granules, laid down in the form of a line or in ramified arrangement. Only occasionally are to be seen more or less well-preserved polygonal argentophil cells, without nuclei, with one to three short branches.

CONCLUSIONS

In the most varied manifestations of leprosy there is a similar picture of degenerative changes on the part of the nerve elements, and there is justification for the following conclusions:

1. The nerve fibers penetrate into the epidermis, but they cannot be followed therein because of the large amount of argentophil granulation in the lower portion of the epithelium.

2. In the subpapillary layer there are few nerve fibers, more at the border of that zone and the reticular layer. Almost all of these fibers are markedly impregnated with silver, show thickening, have uneven contours (tumors, atrophies or shrinkings), are often broken along their length or are fragmented either to cylindrical segments, or occasional loops, or to argentophil lumps and dust; many tumors occur, often very large and uneven. The connective tissue sheaths of the nerves are markedly thickened, and infiltrated.

3. In the affected sweat and sebaceous follicles, and in nerve bundles beside the small remnants of the sweat glands, nerve fibers may show tumors or thickenings or they may be fragmented. Many of them are considerably thicker than normal, coarse and of reddish-brown color.

4. In the lower layers of the epidermis may be found a mass of large, round sac-like bodies without projections or nuclei. The deeper-lying ones appear diffuse black. Only in the deepest portions of the epithelial sheaths of occasional follicles are present distinct, more or less well-developed, star-like argentophil cells, without nuclei. In the papillary and subpapillary layers, however, there is often no trace of argentophil granules.

5. The described changes are best developed in the leprous granuloma, considerably less marked in the infiltrated macule.

6. After the disappearance of the leprous granuloma there

is a decrease of the number of nerve elements in the atrophied skin. In such tissue the penetration of nerve fibers into the epidermis is a rare occurrence. Black clumps of argentophil substance are very infrequently seen in the subpapillary layer.

7. In the clinically healthy finger tips there are changes of the nerve elements which are analogous, though less marked in quantity and quality. The complicated nerve structure of the Meissner's, Dogel's, etc., corpuscles lack completely the very thin fibers of the Timofejew's apparatus. The lamellae of the Vater-Pacinian corpuscles are shrunken, and there are big gaps between groups of five to ten of them. Some of the Vater-Pacinian corpuscles are entirely lacking in nerve fibers; in the others they are observed in cross section, but their condition cannot be judged. Here and there in the epidermis are seen small agglomerations of very fine argentophil granulations.

PLATE 35

FIG. 1. Leproma of the upper arm. Oblique section of the deep part of a hair follicle. Distinct branching Langhans cells, almost diffusely black and without characteristic change. 380X.

FIG. 2. Leproma of the upper arm. Fragmented axis cylinders in the reticular layer of the dermis, between masses of cellular infiltration. 900X.

FIG. 3. Leproma of the upper arm. Branching of a nerve bundle in the depth of the reticular layer. Quite straight-running, thin and thick fibers are seen. 380X.

FIG. 4. Atrophy due to a leproma. Marked thickening of the connective tissue sheath of a branching nerve bundle. 380X.

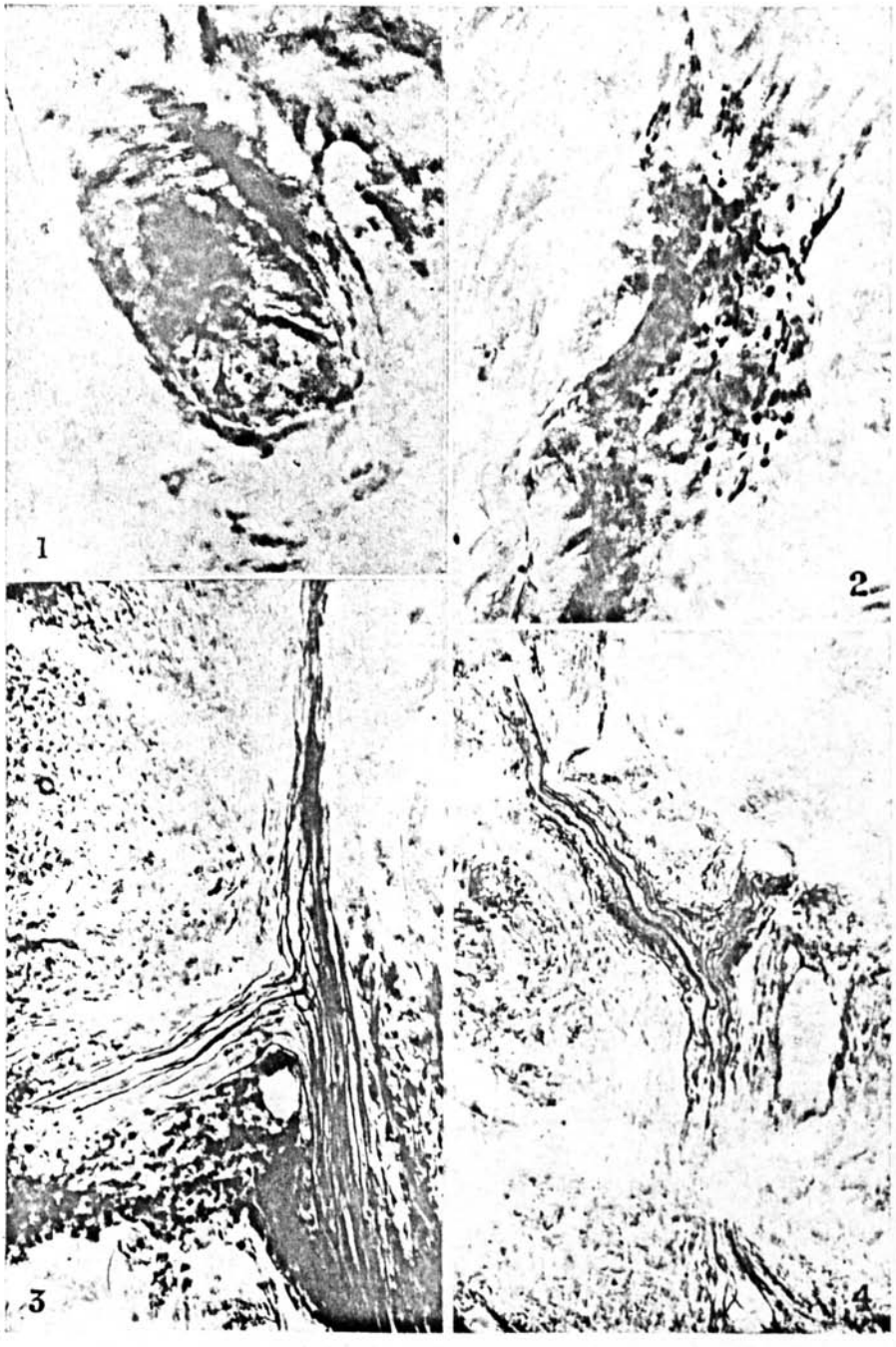

PLATE 35

PLATE 36

FIG. 5. Atrophy due to a leproma. A nerve bundle composed of thick and thin nerve fibers, with localized thickening of the background of lepra cell infiltration: 350X.

FIG. 6. Atrophy due to a leproma. Slight hyperkeratosis, marked thinning of the epidermis, the lower border of which is practically a straight line. Almost the entire epidermis is very black because of marked accumulation of argentophil substance. Nerve bundle in the reticular layer. 250X.

FIG. 7. Clinically normal finger of a leprous patient. Of the Timofejewsky apparatus only a fine, argentophil granulation remains. The branches of the ground-fiber are hazy of outline. 850X.

FIG. 8. Clinically normal finger of a leprous patient. A Vater-Pacinian corpuscle with shrunken capsule, between the layers of which are groups of large clefts. In the center is a cross-sectioned thick nerve fiber. 350X.

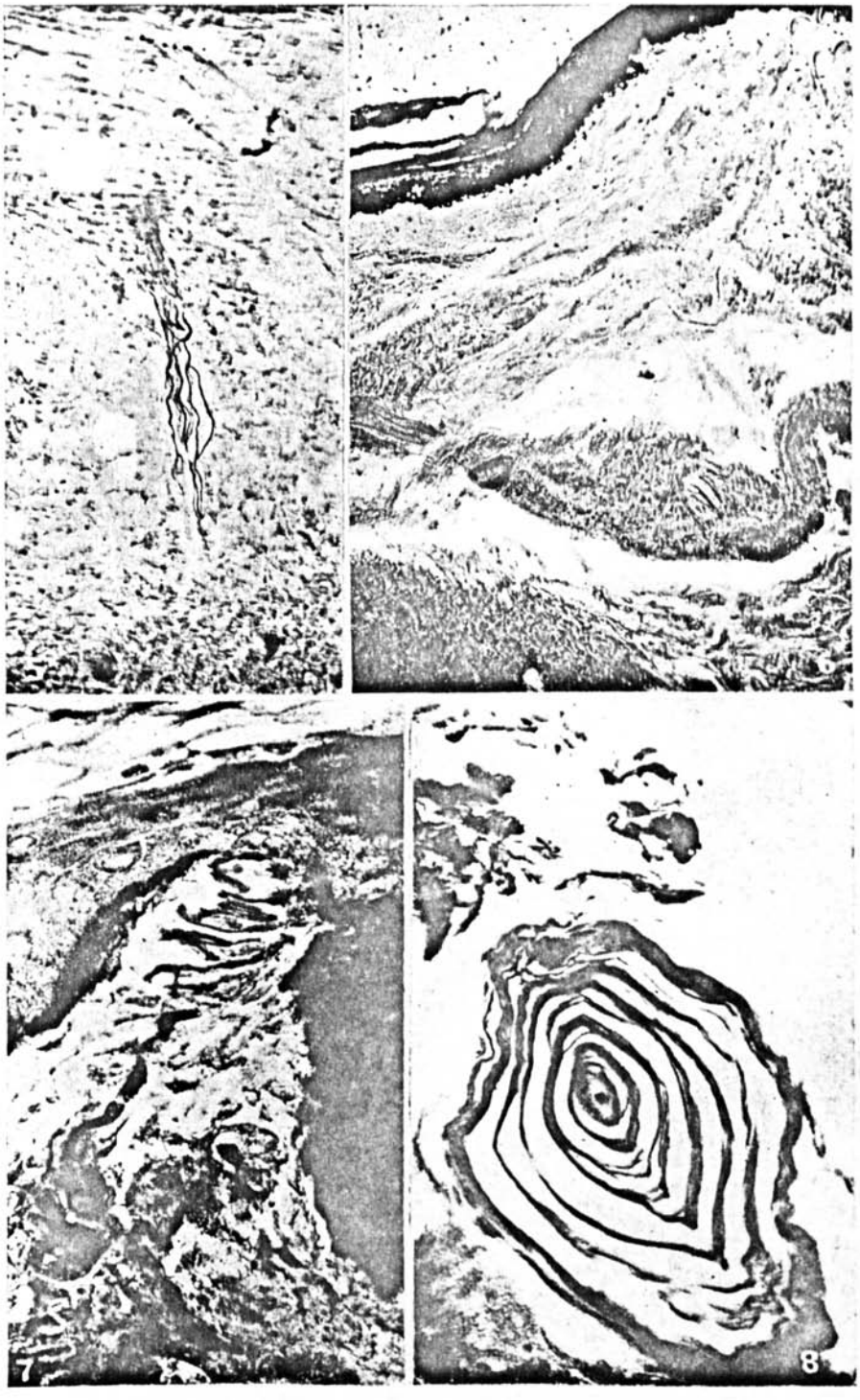

PLATE 36