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VIRCHOW'S LEPROSY FROM DIE KRANKHAFTEN GESCHWULSTE

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(Berlin, 1863)

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(PART II. CONCLUSION)

The nodules (*tubers* or *tubercula*) appear chiefly in the skin, but in part in the subcutaneous tissue. Similar nodules may appear in the mucous membranes or tissues of internal organs. The first precise investigations, those of Danielssen and Boeck, have perhaps gone too far in putting into the same group a whole series of tuberous diseases of lungs, liver and abdominal cavity, since it is readily possible that a certain number of these are in actuality due to tuberculosis. More recent investigations of Carter in Bombay have yielded nothing specific in these organs. Such nodules do occur in some deeper internal parts, however, especially in peripheral nerves, where these growths infiltrate as a sort of neuromatous swelling which often extends over long stretches. In other cases multiple areas are involved, giving swollen nerves the appearance of a rosary. Likewise, these changes are found in the larynx, lymph nodes and testes. I have had no independent experiences with other internal organs, nor have I had opportunity to investigate suitable preparations. The great collection of Danielssen was lost in the fire at Lungegaard Hospital in Bergen. thus there is nowhere in Norway a supply of material. This is a matter for the future.

The lesions of the skin are outstanding, since they are present in every type of leprosy, whether nodular or flat in type, and so far as is known these are always the first manifestations to indicate establishment of the disease. Following a protracted prodromal stage there appear at first hyperemic spots, relatively dark in color, at first bluish, later becoming brown. The epidermis is little changed or not at all. The skin itself shows palpable thickening or swelling. Many of these spots regress and disappear, others progress, and it may be years before further development takes place. Size and form of the spots are most variable. They are often small and lenticular, or at other times quite large and irregular in form, especially when they coalesce. Involvement of the cutaneous nerves commonly develops at an early stage, leading to partial loss of sensation. This

is the form which in the Middle Ages was called *lepra rubra*, and in many ways confused with *gutta rosacea* (acne). Lately it has been widely known as *mal rouge de Cayenne*. Among the Negroes of the west coast of Africa and of the West Indies, Guyon identifies it with the disease known as *cocobe*. Fonseca pictures it in Brazil as *lepra rubra* and Carter as "leprous eruption."

As nodular leprosy develops the spots, which first occur on exposed surfaces, remain stationary but become more and more swollen, more tender, and red or blue-red when exposed to cold. They become elevated above the surface, and form rounded tumors of hazelnut to walnut size, which have a broad base and a smooth, often shiny surface, forming fairly compact yet freely movable masses. In course of time many become more and more elevated, almost polypoid; I have seen them on the upper eyelids so marked that the eye was obscured by the overhanging nodules. Others are more deeply seated, extending into the subcutaneous tissue, with only slight outward convexities on the surface. After a certain degree of development redness disappears, the surface becomes pale red or a dirty yellow or brown, the consistency is flaccid and wrinkled, sometimes fluctuant, somewhat translucent in appearance. In hairy areas, such as the eyebrow or on the chin or lips, the surface becomes astonishingly hairless, and it is readily seen that since ancient times this alopecia has had a special diagnostic significance. Leprous alopecia differs from the syphilitic kind in that it appears only in the immediately involved areas. Other hairy parts of the body, which almost always remain free of leprosy, show no alopecia. In the immediate neighborhood of flat hairless nodules the hairs are often quite coarse and their sheaths unusually large.

Nodules occasionally are isolated, but more often they are multiple and grouped together in such manner that whole clusters grow out, sometimes closely pressed together, or separated from each other by narrow clefts. This occurs most frequently on the face. Although for the most part such lesions are in areas where the skin is loose, as in the eyebrows and eyelids, they are found next in frequency on the *alae nasi*, lips and earlobes. The physiognomy of the patient thus acquires a strange character, not infrequently animalian in quality, as indicated by the ancient names *satyriasis* and *leontiasis*, which suggest comparison with the features of the monkey and the lion.

I have carefully examined such nodules repeatedly. In the Reknas hospital in Molde patients presented themselves formally to me to be rid of the largest and most disfiguring of these nodules by extirpation. Healing of the wounds took place readily and quickly. Our collection also contains skin of the face, hand and forearm of an Egyptian leper on whom Bilharz had operated; H. Meckel had brought him from Egypt. Investigation gave constant results in all cases, showing a cell-rich granulomatous tissue forming the nodules without infiltration of adjoining tissues.

In the smaller tumors, in which the hairs were not destroyed [Fig. 1]

vertical sections showed that the granulomas always extended close to the unchanged epidermis, as with lupus, and also deeply into the subcutaneous fat. Usually they did not form a homogeneous mass, but consisted of large infiltrating columns of tissue which interlaced among each other extensively, showing their greatest development in the neighborhood of the roots of the hair follicles, as though having their points of origin there. As with naevi, these infiltrates extend from the skin without interruption into the subcutaneous tissues. They are recognizable with the naked eye by their pale, shiny, more transparent grayish-white or yellowish appearance, wherefore in this respect, too, they are quite similar to the infiltrates of naevi. Normal areas lying between them are distinguished by a whitish or yellowish appearance. Enlargement of the papilla was never present; on the contrary, the epidermis took on a more regular form. Vessels extended into the mass from its base, being present only in moderate numbers.

With greater magnification, the young masses are predominantly composed of cells which, dependent on their developmental condition, exhibit varied sizes and shapes. I have rarely seen the development of simple spindle and stellate connective tissue cells through the stages of nuclear and cell division as well as demonstrated as here [Fig. 2,A]. The immediate products of cell division are shown in the clearest manner. The more cell division takes place, the more small round cells arise [Fig. 2,B], between which the old intercellular substance becomes so diminished in amount that it is only possible to recognize quite small narrow bands between the infiltrating groups of cells. Within these connective tissue strands little more than nuclei are seen, and in preparing the specimen for examination many cells are destroyed, so that "free" nuclei (cytoblasts) appear in numbers. The epidermis atrophies more and more with advance of the process. Sweat glands and sebaceous glands are lost; hairs degenerate and show rosary-like swellings in their deeper parts, together with small bulbous masses of epidermal cells, as I have described in lupus. The hair breaks off at the skin surface, producing the *lepra alopecia* of the Arabians.

For the most part, those observations are in agreement with those of Danielssen and Boeck, with the understanding that their descriptions are not clear because of the limitations of the histologic technique then available. Danielssen's recent contributions are in closer agreement with mine. Kobner has obtained similar results independently, and Carter, although he speaks largely of nuclei which he derives from an exudate, has none the less obviously viewed the same pictures I have described. The delineations of G. Simon are similar, and from having investigated the same cases as he, I can verify his findings. Ordonez, who described fibrotic and elastic tissue changes, seems not to have had fresh material for examination.

With regard to the cells, when fully developed they are round, pale, slightly granular, easily injured structures, with single nuclei that for the

DESCRIPTION OF PLATE

PLATE (15)⁴

FIG. 1. Section across a nodule from the face. The epidermis, quite thin and smooth, is penetrated by three hairs which are little changed and only slightly thinned. The follicles are more or less exposed by the cut. The dark mass which is seen in elongated streaks and thick layers is the leprous proliferation, which shows its greatest development about the hair follicles on the left. In the middle, at the top is seen the elastic tissue of the skin intact, and at the bottom the subcutaneous adipose tissue. From a preparation I made in Bergen, August 24, 1859, taken by Dr. Holmboe from a tumor of the skin of a man at Lungegaards Hospital who had nodular leprosy.

FIG. 2. Microscopic structures of the leprous tumor. A. Isolated elements. The progressive development is represented left to right. On the left are connective tissue cells, very large; the majority are stellate, with one nucleus and one nucleolus. Next, division of nuclei (cells with two nuclei) and of the cells. Toward the right, some granular cells, more or less round, with one or more nuclei. B. A part of the tumor intact to show the arrangements in layers or clusters of granular cells.

⁴These translations of the legends of the pictures were supplied by Dr. Chapman H. Binford. The pictures were copied photographically from the original source by the Armed Forces Institute of Pathology, Washington 25, D.C.

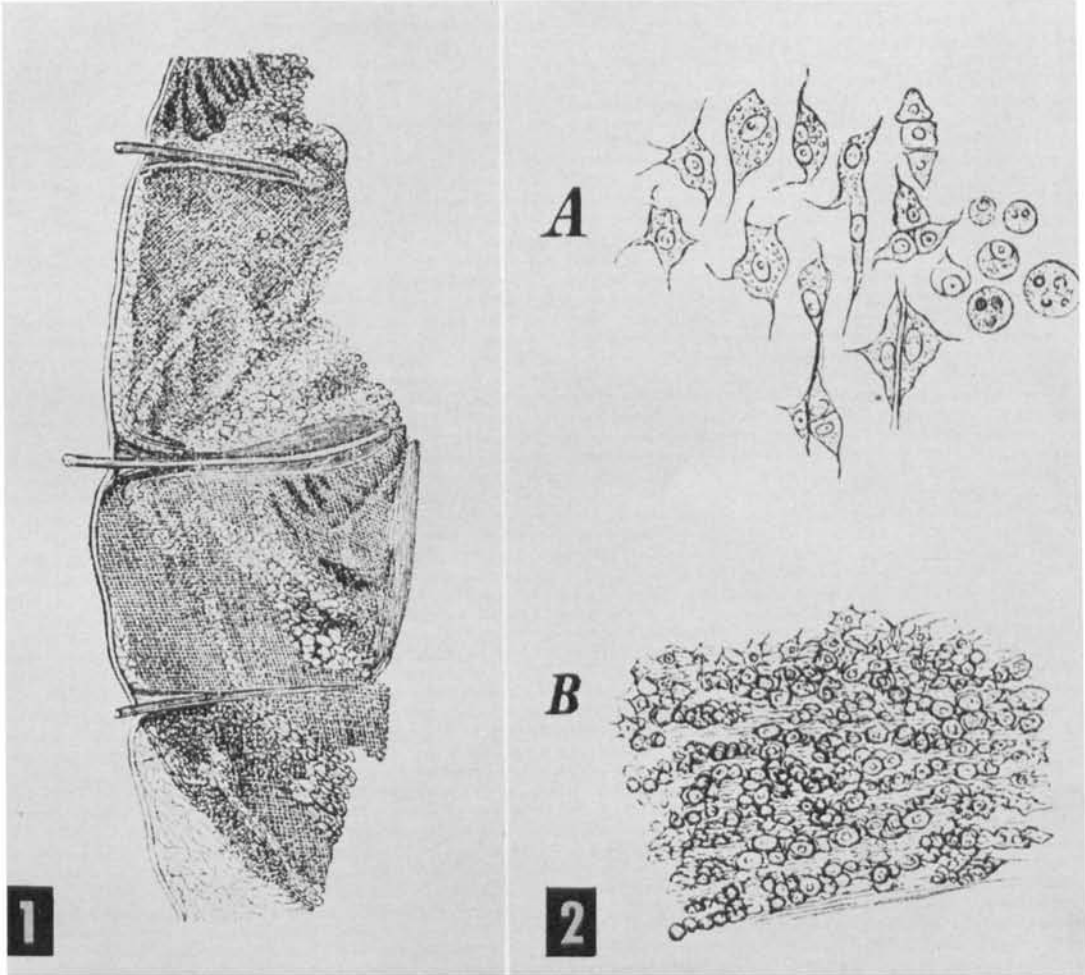


PLATE 15.

most part are of moderate size, also granular, containing nucleoli. In the fresh state they have one characteristic that is especially noteworthy, i.e., their tendency to form a sort of vacuole, apparently from taking up water, so that under the circumstances they acquire a wholly physaliferous appearance. Their size varies extremely. Many are no larger than red blood corpuscles, most are of the size of ordinary lymphocytes, many others reach the size of the largest mucosal epithelial cells.

Between the infiltrations and masses of growing tissue there remain, as already said, other parts of the tissue which are either wholly unchanged or are undergoing simple enlargement. The latter I have seen in striking manner in the arrector pilorum muscles.

It is obvious that this picture bears a strong resemblance to that of lupus. In respect to site, long duration, and slow development, it is much more like lupus than syphilis. In both [of these conditions] nodules may in time soften and ulcerate. The leprosy ulcer on its surface ordinarily has brown or dirty crusts, under which lies a thin ichorous secretion, and, in the beginning at least, a softened fluctuant mass of tissue. Yet leprosy has no special tendency to ulceration. As a rule, unfavorable external effects are required to produce this change. Patients who are much exposed to the disturbing influence of weather, storm, rain and snow, as a rule acquire ulcers. But under favorable conditions, as in hospitals, there is often no tendency to ulcer formation.

In these cases the nodules may remain for many years in a condition that, if not precisely unchanged, is almost stationary. Among the several types of granulation-tissue growths, they are almost the most durable of all, approaching in this respect the naevi, differing obviously from syphilitic gummas and nodular lupus. A certain change does manifest itself, however, in that the nodules become more flaccid and wrinkled, and as a rule take on a dirtier brownish color. Partial metamorphosis of fat and regressive changes enter into this picture, as with gummas. The fat metamorphosis is never as extensive, and the resolution never as rapid, as in the latter condition, and when the nodules reach a moderate size, metamorphosis of fat and resolution are only partly in evidence, and complete regression is not found. On the contrary, the old eruptions are almost always followed by new ones, so that although the process partly becomes quiescent, on the whole it has an ever-progressive, unending character.

In those cases in which new lesions are quite limited, complete regression may occur. This is true especially of the previously-mentioned macular form, in which characteristic nodule formation is not present. The studies of Danielssen and of Carter showed that the skin in these cases also is filled with granulation tissue. Regression of such lesions is a long-known phenomenon, and is reminiscent of the old morphea (*miselsucht, mesellerie*) of which two main forms, white and black, were described.

Morphoea nigra is not to be considered as being really black. It shows a grayish, brownish, or black-brown appearance, as it would have to have in order to fall in line with the old supposition of an atrabiliary (melancholic) nature of the dyscrasia. A genuine hyperpigmentation is present, which has its site chiefly in the malpighian layer of the epidermis. As this develops, hyperemia disappears, swelling recedes and skin lesions become more compact than previously. Similar changes are recognized in nodular skin syphilis.

Morphoea alba is evaluated as the worst form, and a chief (principal symptom) manifestation of leprosy. It was once the fashion to needle the area; and if this was painless, and if clear fluid (serum) exuded instead of blood, the case was considered incurable and leprosy. Both these signs demonstrate that related nerve changes are always present, wherefore most authors regarded this type of morphoea simply as lepra (elephantiasis) anaesthetos, while at the same time scarring conditions appears in the skin lesions. These scars or callosities extend outward from a central point which grows deeper, while the skin at the same time becomes thinner or more compact. At times, the overlying epidermis separates, forming peculiar small white scales; the hair in the involved areas is often white, as was portrayed in the well-known descriptions in the Mosaic Testament. Yet nothing was constant with regard to these phenomena, whence rise the numerous controversies over the explanations of the ancients, and the many misunderstandings about lepra graecorum (the scaling exanthem). The important thing is the condition of the skin, and the regressions that take place. Danielssen recently indicated that these regressions may lead to a true healing. However, as a rule the healing is only local, and, as with the serpiginous form of syphilis and the similar type of lupus, the disease progresses further in adjoining areas, quite possibly advancing in the course of time to become outspoken anesthetic leprosy.

Naturally, these forms differ somewhat among colored races and southern peoples, as compared with white races and northern peoples. Among the former, morphoea alba is more striking; here it is morphoea nigra. Opinion on this dissolves readily in the fact that in the neighborhood of white, scarred or scar-like areas the skin becomes darkly pigmented, so that both types are closely related in the single case. This was most strikingly shown in the Egyptian material in our collection.

These milder morphoeic types, which also appear sporadically here and there, are predominantly common in the clothed parts of the body, the buttocks, and upper segments of the limbs, although not absent from exposed areas such as the face. Again the exposed parts are for the most part involved in nodular types, so that the influence of air and temperature, humidity, etc., certainly cannot be dismissed as unimportant factors in the production of this type. Likewise, morphoea progresses to anesthetic leprosy most frequently in the face, hands, and feet.

In addition to the cutaneous eruptions of leprosy, there is a similar series of involvements of the mucous membranes. Exact knowledge of these is limited to the changes in the eye, nose, mouth and larynx; it is doubtful if other mucosal surfaces can suffer in similar manner. Loose diarrheas appear fairly often toward the end of life, but many of these are definitely of other nature, dysentery for example, and it has yet to be determined if there is a genuine gastrointestinal leprosy. Arateus mentions nodules of the tongue under the characteristic name of chalazion-like processes, and throughout the Middle Ages the *vox rauca* ranked as an infallible diagnostic sign. Carl Wolff and Moura-Bourouillon recently confirmed this, using the laryngoscope for investigation of the condition. All these disease processes begin with nodular granulations which for a time bear close resemblance to syphilitic mucosal papules (condylomas) or follicular bubos, and differ principally through their greater solidity and vascularity. They often assume the character of a diffuse infiltrative process. In the conjunctiva red flat granulations appear to best advantage. They lie at times above the white of the eye, pushing over the corneal rim and infiltrating into the cornea proper: *pannus leprosus*.

All these mucosal nodules have a definite tendency to ulceration, being much more destructive here than in the skin. In the eyes, corneal perforations, synechia, prolapse of the iris, staphyloma, and atrophy of various structures are in general common, although as we shall see many of these forms belong to anesthetic leprosy. In the nose, the ulcers extend down to the cartilage, rarely attacking the bone; the true perforation of the septum with collapse of the parts as in syphilis is customarily absent. Ulcerations of the tongue are common, but are usually transformed into deep scars which, with their thick callosities, extend into the tongue muscles. In one case I found the callosity itself in turn infiltrated by yellow cords, which under the microscope were made up of growing cells in columns quite like lymphatic vessels. Likewise, I have seen ulcerations of the larynx and the trachea in which firm, sinewy scars extended deeply through the submucosa and elastic tissues, even involving the fat tissues with leprous growths. Most severe stenosis results from the cicatrization. Danielssen and Boeck have presented numerous examples of this type of ulceration, and from their illustrations it appears reasonable to suppose that the process may extend even more deeply into the bronchi. How similar changes of this kind are to that of lupus, I don't need to discuss.

As for *lepra anæsthetica* in the narrow sense of the word, careful investigation shows that the process which involves the nerves is identical with that which we have recognized as "tuberculous" of the skin and mucous membranes. Anesthetic leprosy is also tuberculous, merely having its particular site in the nerves—in brief, *lepra nervorum*. The growths in the nerves are generally not so marked that tumors, strictly speaking, arise. The process is often a moderate involvement of long stretches of nerve, so that one is more inclined to call it a chronic inflammatory

process (perineuritis chronica leprosa). It is usually regarded as somewhere between a genuine tumor and a diffuse inflammatory swelling. The thickenings are more or less spindle-shaped, rounded or flattened. During life many of the thickened nerves are readily palpable, such as the ulnar nerve at the elbow. These nerve swellings are also present in individuals with nodular skin lesions, so that there is no sharp dividing line between skin and nerve leprosy.

This type, too, has a chronic course as a rule, drawn out through many years. It generally begins with hyperesthesia, becoming anesthetic so gradually at first that in many areas of the body severe pains arise while complete anesthesia appears in others. There is much diversity; nerve endings are involved in one instance, whole nerve trunks in another. According to the unconfirmed experience of Danielssen and Boeck, there appears at times a diffuse inflammation of the meninges of the spinal cord and brain, especially along the nerve roots, in the most severe cases.

I obtained nerves of this sort from Danielssen himself when I was in Bergen, and in the very first preparations found a growth, similar to that of the cutaneous nodules, which obviously extends along the perineurium, the interstitial tissue of the nerve, and frequently is associated with a marked change in the neurilemma (nerve sheath). Danielssen portrayed two such preparations. Later, I obtained further material, partly from an autopsy I performed in Bergen, partly through the kindness of Hoffmann in Molde. The recent observations of Carter agree so completely with those of Danielssen and myself in main points that there can be no doubt of the general validity of the evidence.

Examination of a larger nerve, such as the ulnar, median, or peroneus, as a rule shows swellings repeated at certain intervals, rather than a diffuse enlargement. These swellings lie most frequently where the nerve is most exposed to mechanical or thermal influences, such as where it passes through superficial layers, or lies in close relationship to bones. Thus I found the median nerve most affected where it is covered above the bones of the wrist, beneath the lig. carpi volare, whereas the ulnar regularly showed the greatest swelling at the elbow. Color changes are measurably predominant in the more thickened areas. The nerve becomes gradually more gray than white, somewhat translucent, at times with a touch of brown, at other times darker (smoky gray). The nerve becomes firm and hard, almost solid (sclerotic). On cross section, the inner part is more homogeneous than normal. Microscopy, even under low magnification, shows the main relations clearly. The loose connective tissue (the outer nerve sheath), which holds several nerve bundles together, is little altered, at most showing thickened walls of the vessels contained therein. The nerve sheath proper (perineurium) is usually changed, although varying from one case to the next. At times the change is very slight, but in other cases the perineurium is converted into a hard, thick, sclerotic mass. Yet the most important changes lie deeply within the inner septa

of the nerve bundles, and in the interstitial nerve substance proper (endoneurium). The changes begin close under the perineurium, where sharply delineated masses are found, and continue from there along the larger septa which divide the nerve bundles into a series of smaller bundles.

With higher magnification, the dark masses which fill this area are found to be composed of compact groups of cells (nuclei, according to Carter,) and these cells infiltrate not only along the coarse connective tissue septa but also even between single nerve fibers, surrounding and enveloping them. A neat picture is thus produced; nerve fibers with their central axis-cylinders compose a mesh with the net of leprous cells woven around them.

In cases of longer duration, I found two main alterations. In one case there was marked fatty metamorphosis of the lepra cells leading to the formation of large granular cells, so that under low magnification these cells appeared quite black. This was apparently a regressive phenomenon, and it can hardly be doubted that it can be introduced by resolution and healing, which may possibly become total provided that it starts early enough. But more commonly another change already accompanies the others, namely, complete atrophy of the individual nerve fibers. Like Carter, I have never seen this happen via the route of fatty metamorphosis. In the first case, I observed the myelin sheath broken down into coarse bits of myelin, which became smaller and smaller and finally disappeared. At this state, there was nothing left of the axis cylinder to be distinguished.

It is understandable that suspension of function of the involved nerve fibers runs parallel to the advancing destruction thereof. The skin sensitivity is so predominantly affected as to be selected as a basis for naming the type of leprosy. Motor paralysis also may be present, predominantly so in certain cases. The particular examples of lagophthalmos and a peculiar crookedness of the hand may be mentioned in this regard. The latter at times presents a great similarity to the recognized position of the hand in lead paralysis (Duchenne). The feet may be similarly affected, and associated with this, as was known in olden times, is severe emaciation of the flesh, even more strikingly than in progressive muscular atrophy. However, compared to the sensory disturbances, the motor changes lie in the background. My conceptions are derived from the more superficial site of the sensory nerves, which are more closely related to the cutaneous lesions and more affected by external conditions.

The fact must not be overlooked that not every case of leprous involvement of nerves leads to loss of function. In many cases of nodular leprosy I have found the ulnar nerve at the elbow enlarged and painful, yet with neither anesthesia nor paralysis present. The nerve is much as I have also frequently observed in nonleprous individuals. Where functional disturbance is present, as a rule not all of the individual fibers in a bundle are

involved, but only a certain number, small or large as the case may be. This explains why, in regions of distribution of a single nerve, some areas are anesthetic while others have normal sensation, and also why one muscle atrophies while a closely related muscle preserves its normal status.

In nerve leprosy, there is a further extensive and quite important series of symptoms, which are not directly connected but arise from simple complications. Of prime importance are certain bullous eruptions, particularly the example of pemphigus leprosus. The older writers allied these diseases to the impetigos. Schilling first called attention to the similarity of this condition to blisters resulting from burns and to their acute development, often in the course of a single night. He called it *lepra sub adustionis specie latens*. Danielssen and Boeck contributed information concerning the location of the process, and were the first to determine its course with accuracy. There are blisters of most variable size, some quite small, but ranging up to the size of a hen's egg. They are filled with a cloudy fluid which accumulates rapidly and often unnoticed. They quickly burst, leaving either a simple desquamating or superficially ulcerating surface. They are often solitary, occur chiefly in the extremities or around the joints, and recur at various intervals.

The skin itself, which previously was disfigured either by morphea or occasionally by nodules, now becomes the site of a diffuse inflammation as a result of which it becomes thickened and retracted. As fat, muscles, and even bones atrophy, the hard tense skin shrinks and contracts about them. The glandular structures of the skin atrophy, the sweat glands and sebaceous glands gradually disappear, and the surface has a singular dry quality, very thin, flat and glistening, or cracked and rough. Ulcerating lesions of pemphigus often last a long time, healing with hard wrinkled scars, intense white in color.

As far as I can judge, this is the condition which was known in the Middle Ages as *malum mortuum*, later *malmorto*. The Four Masters (the Quatuor Magistri of the School of Salerno) associated *malum mortuum* with pustulation of the lower leg. Matthioli used the expressions *vari* and *morbilli melancholici* as synonyms, and Hans von Gersdorff allied the condition with *impetigo*. The poor prognostic significance of these conditions is emphasized by the usually bad end results.

Later on, still other changes are provoked in this abnormal skin. Areas of inflammation form with marked livid reddening, which soften and often take on a gangrenous character. These are apt to begin in the skin, but extend rapidly to deeper tissues. At other times they begin in deeper areas, especially near the periosteum. Bone necrosis and amputation follow quickly. One phalanx after another may be lost, until nothing remains but the disfigured stumps of hands and feet. It is even possible for whole members to fall away, and although it sounds scarcely credible, the entire

nose may separate all at once, and even the head be broken off,³ whence it is certain that the entire foot or hand can be lost.

In the Surinam colony Boasie-grond (on the Coppenam River) Hasselaar found two unfortunates whose arms had fallen off at the elbows, and one whose legs had fallen off at the knee joints.

Most strangely, all of these ulcerations may heal completely. Naturally, there is no restoration of lost parts, but scar formation progresses so favorably that recovery regularly follows without difficulty even the most severe mutilation. As a rule, severe general disturbances are present; yet these are often lacking and the patients endure the whole series of destructive and scarring processes with a certain mental indifference, yet with a good disposition and good appetite. When it is remembered that the troubles are not confined to extremities, but occur also in the face, and that the eyes are endangered in most cases, it is possible to understand the fear to which this disease has given rise in all ages.

The whole series of changes which comprises *lepra mutilans* in the narrow sense of the word has, in my opinion, nothing to do with the specific process which provokes leprous nodules. Ulceration does not arise from nodules, but from malignant inflammation, which develops as a result of anesthesia and parallels a type seen frequently in the eyes, the well recognized neuroparalytic inflammation, which may serve as standard for this type. It is not possible to be firmly convinced that the lack of innervation of itself provokes no inflammation, but for the most part passive changes, especially atrophy, take place, even though these are not constant. In Molde I saw a man with mixed (tuberoanesthetic) leprosy whose hands, although totally anesthetic, showed no other alteration. As a rule, atrophic changes are present. But these lead to inflammatory changes only as a result of definite causes which are usually of external origin—traumatic, chemical, rheumatic, etc. The more certainly will the individual retain his members, in spite of nerve deficiencies, when external causes are prevented.

In reference to other local lesions, I have only a little to add. The common involvement of lymph nodes must be given a thought. Gadesden has mentioned swelling of the inguinal nodes in *malum mortuum*. But I have found massive enlargements in every type of leprosy, nodular, macular and neural, and in the various parts of the body. Inguinal and cer-

³ *Translator's note:* This last remark indicates Virchow's overt tongue-in-cheek doubt of these extravagancies, which he fortifies by two references, evidently his only knowledge of such phenomenon. These are: 1. Schopff relates the following "*ridicula historia*" (condensed) of a patient who lost his nose while dancing, the nose having fallen to the ground and been lost, to the general amusement, wherefore this particular dance could never be forgotten. 2. A. van Hasselaar recounts (from the reports of persons whom he considered reliable and worthy of belief), that a leprous mulatto, who previously had been known to him personally, on entering his dwelling struck his forehead against the door and had fallen upside down, at which moment his head fell from his trunk.

vical nodes are involved as well as cubital and submaxillary, according to the principal sites of the peripheral lesions. The swollen nodes are firm and slightly tender.

I have only once had occasion to investigate leprosy bubos in the cadaver. In this case, there was an extensive *malum mortuum* of the lower extremities. The nodes were five to six times normal size, being spherical or egg-shaped, fairly regular in size. The more superficial comprised small groups, moderately solid, pale, translucent, clear, yellowish-gray in color, rather flaccid in consistency. Reddish areas were found only in isolated locations. On the convex walls, opaque yellow-white points and networks could be seen under the magnifying glass to unravel into reticular spots. Greatly enlarged and thickened, gray-white, lumpy lymph vessels entered the nodes here and there. On cross section, the nodes looked in many instances like the adrenal gland, the cortex showing the same cloudy, yellow-white, fatty appearance. It was never dry or caseous, but moist and flaccid in consistency. Under the hand lens, many of these areas were composed of follicular spots which, toward the periphery, intermingled extensively with homogenous areas 0.5 to 1.0 cm. in diameter. The remaining part was greatly enlarged, moist, translucent, grayish-yellow or brownish-yellow in color. The color darkened on exposure to air. Under the hand lens, fine cloudy yellow flecks were seen here, too, against a blue-gray translucent background. The microscope showed, for the most part, hyperplasia. In the yellow spots there was new growth with larger cells showing fatty degeneration in parts. The hilus was large, the medullary substance normal and sharply demarcated.

Since there is no doubt that we are dealing here with leprosy alteration of the lymph nodes, it becomes simply a question of their frequency and extent. Their relation to the local skin lesions may well be the same as that of syphilitic bubos to the cutaneous processes of syphilis, and there is little hesitancy in suggesting transportation of injurious substances from the peripheral areas to the nodes, in which participation of the lymph vessels plays a significant role.

With regard to true visceral leprosy, in a metastatic form, I can at least present one definite observation, namely leprosy of the testis. I found the tunica vaginalis thick and sinewy, the albuginea especially thickened, and the small solid testis contracted from scarring. On cross-section, the substance of the testis was a marked gray-brown. Fibrous strands extending from the scarred contracted mass encased small areas of soft yellow content. This material was composed almost entirely of round cells of quite variable size, generally like those of the cutaneous nodules. Most were mononuclear and granular, many were pale and small like lymphocytes, others were larger and more strongly granular with numerous vacuoles, of the size of mucosal epithelial cells. Single cells reached the size of ova and the form of true giant cells, so that many with their large vacuoles almost gave the impression of infusoria, and reminded

me vividly of the presentation of one of Linnaeus' students, who wanted to trace leprosy back to the entozoa.

Further investigation is necessary to determine whether the field of visceral leprosy extends further, as the work of Danielssen and Boeck indicated was probable. At present all I can say is that, in my extensive experience, the disease as a rule concludes with cachexia and marasmus. I can confirm from my own investigations that chronic nephritis with edema often appears terminally, as well as the diarrhea previously mentioned.

In addition to the previously considered diseases which are characterized by granulomatous growths—syphilis, lupus, and leprosy—there are certain others, both endemic and sporadic, which have at one time or another been related to one of these three. They are the group of nodule-forming (tuberculous) processes, most of which also ulcerate. Some are differentiated as syphiloids, others as leproids, and lupoids may be added to these. However, the general spirit of the day or the individual tendency of authors has been to assign the syphiloids to syphilis and the lupoids to lupus without further ado. The difficulties involved are more readily comprehended if it be remembered that we are dealing with endemic diseases present in separate localities, and the coexistence of syphilis, lupus and leprosy in them has provoked much dissension of opinion.