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## ORIGINAL ARTICLES

### THE CURABILITY OF LEPROSY

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#### INTRODUCTION

It has always been a heavy and regrettable burden to lepers that their disease has been looked upon as incurable, by laymen and physicians alike. The general idea has been that Dante's words over the entrance to Inferno: "*Lasciate ogni speranza voi ch'entrante*" should be inscribed over the entrance to leprosy hospitals. And it seems that the expression "Once a leper, always a leper" still has its adherents. This view has been unfortunate, not only for the sufferers but also for their hospitals and for the campaign against leprosy in general.

The reason for this belief must be that in most cases in which cure has been effected, permanent and sometimes very disfiguring marks and defects have remained. Many people have doubtless regarded such mutilated persons as dangerous, though actually many of them were cured. Fortunately, experience has of late years brought about a gratifying change in viewpoint.

It is curious, however, that it has taken so long for this to happen. It is almost a century since D. C. Danielssen, the founder of modern leprology, began in 1839 at the St. Jørgens (St. George's) Hospital in Bergen the work which led the Norwegian State to establish the Lungegaards Hospital, primarily for investigating the treatment of leprosy. Danielssen worked there from its opening in 1849

until his death in 1894, and in due course came to the conclusion that leprosy is a curable disease. It is now sixty years since Armauer Hansen discovered the leprosy bacillus, thus permitting a correct understanding of the nature of the disease.

Danielssen's results were published in the *Norsk Magasin for Laegevidenskaben* between 1852 and 1895 (1, 2), in a series of twenty reports, all written by him except the last, which was by the present writer. These results have never been collectively published and are, therefore, more or less unknown internationally, but I believe that a survey of this work will be of interest, not only historically but also with regard to the understanding and evaluation of modern therapeutic results.

#### WORK AT THE LUNGEGAARDS HOSPITAL

Lungegaards Hospital had two sections, one for treatment and the other simply for nursing. In the former section early and moderately advanced cases were admitted if their condition gave hope of arresting or curing the disease. The nursing section was for advanced cases, and patients were transferred to it from the therapeutic section when in spite of treatment their condition had become hopeless. This hospital could not, by a great deal, accommodate all the cases in Norway that needed treatment, but its reputation was such that comparatively early cases from all parts of the country came to it. Most of the advanced cases were admitted to either the St. Jørgens Hospital or the Pleiestiftelsen for Spedalske No. 1 at Bergen, or to the Reknes Pleiestiftelse for Spedalske at Molde, or the Reitgjerdets Pleiestiftelse for Spedalske at Trondheim.

*Gross Statistics.*—The first patient was admitted to Lungegaards Hospital on October 1st, 1849, and the last was discharged on April 20th, 1895, when the hospital was abandoned as a leper institution. During this period a total of 788 cases were treated, 570 in the therapeutic section and 218 in the nursing section.<sup>1</sup> As regards sex, 445 were males and 343 females, a ratio of 1.3 to 1. The diagnoses as regards type were as follows:

<i>Lepra tuberosa</i> ("cutaneous")	.....	310 cases, 39 per cent
<i>Lepra maculo-anaesthetica</i> ("neural")		321 cases, 41 per cent
<i>Lepra mixta</i> ("mixed" cases)	.....	157 cases, 20 per cent

<sup>1</sup> A number of cases were admitted several times, but in the accompanying statistics they are only recorded once, as of the first admission.

Further details, and an analysis of the relations of sex and of form of the disease to the results of their sojourn at the hospital are shown in Tables 1 and 2.<sup>2</sup>

The first of these tables shows that 21.7 per cent of the total number of cases admitted to the hospital were discharged improved, and many of them cured. Taking into consideration only the patients of the therapeutic section the corresponding figure is 29.7 per cent, nearly one-third of the total. Danielssen used the term "improved" when improvement was so marked that complete cure was probable sooner or later. The reason for discharge of these cases was usually that the patient felt quite well and was tired of the prolonged monotony of the hospital. In view of the opinion then prevalent, that leprosy was incurable, the results obtained are quite striking. Even if one considers only the cases that were discharged as cured (11.8 per cent of all patients, and 16 per cent of those in the therapeutic section) the figures are still quite high. They are, in fact, so high that they ought not to be accepted without further discussion.

*Diagnosis.*—The first question to arise is that of diagnosis. It is an undeniable fact that leprosy has often been confused with other diseases. Among these syphilis is foremost, and this error may be made today if we are not aware that leprosy may cause a positive Wassermann reaction. Late in the 18th and early in the 19th centuries tertiary syphilis (*radesyke*) was so prevalent in Norway that special hospitals were established for it, and for a long time it was believed to be the same as leprosy. However, they were known to be distinct when Danielssen commenced his studies, and prior to the opening of the Lungegaards Hospital he had for ten years been in a position to acquire experience in their diagnosis and treatment. Furthermore, *radesyke* occurred chiefly as an ulcerative condition, and Danielssen looked upon the ulcerative forms of leprosy as not suitable for special efforts at cure and, consequently, they were not admitted to the therapeutic section of the hospital.

Of other diseases that I have personally seen confused with leprosy I will only mention the idiopathic pigmented sarcoma of Kaposi, various tuberculous conditions, and erythema nodosum and

<sup>2</sup> These tables show somewhat more maculo-anesthetic and fewer nodular cases than do Danielssen's figures, because all cases called *maculae elephantoides* by him have been transferred to the former group.

Boeck's sarcoid. Among these only erythema nodosum was well known in Danielssen's time, as it had been described by Willan in 1798, but only the acute phase of this affection can have caused wrong diagnoses, and that only exceptionally. Kaposi's sarcoma was not described until 1872, but as it is comparatively rare, it also could not have caused many wrong diagnoses. With regard to the tuberculous conditions—the tuberculoides and sarcoides—these were not generally known at that time, and one cannot arrive at a definite opinion as to whether or not they played any part in the diagnosis of leprosy. However, taking all facts into consideration,

TABLE 1.—Results of treatment at Lungegaards Hospital, 1849 to 1894, all admissions.

Case group	No. of cases	Sex		Form of disease			Cases showing improvement					
							Complete <sup>a</sup>		Incomplete <sup>b</sup>		Total	
		Male	Female	Nod.	Mix.	M.-A.	No.	Per cent	No.	Per cent	No.	Per cent
Total admissions	788	445	343	310	157	321	93	11.8	78	9.9	171	21.7
Males, total ....	445	445	—	172	105	168	36	8.9	41	9.2	77	18.1
Females, total ..	343	—	343	138	52	153	57	16.6	37	10.8	94	27.4
Males, nodular ..	172	172	—	172	—	—	6	3.5	7	4.1	13	7.6
Males, mixed ..	105	105	—	—	105	—	9	8.6	10	9.5	19	18.1
Males, mac.-an.	168	168	—	—	—	168	21	12.5	24	14.3	45	26.8
Females, nodular	138	—	138	138	—	—	8	5.8	12	8.7	20	14.5
Females, mixed	52	—	52	—	52	—	4	7.7	3	5.8	7	13.5
Females, mac.-an	153	—	153	—	—	153	45	29.4	22	14.4	67	43.8
Nodular cases ..	310	172	138	310	—	—	14	4.5	19	6.1	33	10.6
Mixed cases ....	157	105	52	—	157	—	13	8.3	13	8.3	26	16.6
Maculo-anesthetic	321	168	153	—	—	321	66	20.6	46	14.3	112	34.9

<sup>a</sup> Improvement amounting to cure.

<sup>b</sup> Improvement so marked that ultimate cure expected.

including the fact that it was not until 1873 that the leprosy bacillus was discovered and still later before it became of importance in diagnosis, I am of the opinion that Danielssen's diagnosis of leprosy was probably correct in by far the greater number of cases, and that such erroneous diagnoses as there may have been could not have had any great influence upon the percentage of cures.

*Criteria of cure.*—The next question is whether the cases that were discharged as cured really were cured. By cure is here meant clinical cure, the disappearance of clinical symptoms; the question of absolute cure (i.e., complete absence of bacilli) must be quite ignored in this connection since thorough bacteriological examinations could not have had any important part in the decision except at the



very end of the period in question. In the records one almost always finds a remark to the effect that the patient "is now quite well," or "now presents no signs of illness," or that "all symptoms have now disappeared." Only in a very few cases is it mentioned that there were present "only slight traces of spots," or "now only slight diminution of feeling," or even "still some muscular debility." One can, therefore, take it for granted that in by far the greater number of cases the symptoms had disappeared, with regard to both the skin and the nerves—in other words that clinical cure was a fact.

TABLE 2.—*Results of treatment of the patients in the therapeutic section of Lungegaards Hospital, 1849 to 1894.*

Case group	No. of cases	Sex		Form of disease			Cases showing improvement					
		Male	Female	Nod.	Mix.	M.-A.	Complete <sup>a</sup>		Incomplete <sup>b</sup>		Total	
							No.	Per cent	No.	Per cent	No.	Per cent
Total admissions	570	322	248	209	105	256	92	16.0	78	13.7	170	29.7
Males, total ....	322	322	—	120	74	128	36	11.2	41	12.7	77	23.9
Females, total ..	248	—	248	89	31	128	56	22.6	37	15.0	93	37.6
Males, nodular .	120	120	—	120	—	—	6	5.0	7	5.8	13	10.8
Males, mixed ...	74	74	—	—	74	—	9	12.2	10	13.5	19	25.6
Males, mac.-an.	128	128	—	—	—	128	21	16.4	24	18.8	45	35.2
Females nodular	89	—	89	89	—	—	8	8.9	12	13.5	20	22.4
Females, mixed .	31	—	31	—	31	—	4	12.9	3	9.7	7	22.6
Females, mac.-an.	128	—	128	—	—	128	44	34.4	22	17.2	66	51.6
Nodular cases ..	209	120	89	209	—	—	13	6.2	19	9.1	32	15.3
Mixed cases ....	105	74	31	—	105	—	13	12.4	13	12.4	26	24.8
Mac.-anesthetic .	256	128	128	—	—	256	65	25.4	46	18.0	111	43.4

<sup>a</sup> Improvement amounting to cure.

<sup>b</sup> Improvement so marked that ultimate cure expected.

In this connection I may mention that it was realized that leprosy is usually accompanied by swelling of the lymph glands. The records made on admission very often note the presence of "swelling in armpits and groins," and in the discharge record one usually finds: "glandular swelling disappeared." This strongly supports the assumption of a veritable cure. It was Hansen who first demonstrated the characteristic appearance of leprosy lymph-glands, with their typical yellow color. In Danielssen and Boeck's great treatise (<sup>4</sup>) leprosy and tuberculous glands are confused, as they have been sometimes in later years. In my experience one must, in leprosy as in syphilis, pay attention to the lymph-gland swelling. On several occasions I have found bacilli in the glands long after they and the clinical symptoms had disappeared from the skin. In all probab-

ity the lymph glands form a source of organisms for new outbreaks, or relapses.

*Relapse.*—The surest proof of a real cure is, of course, the absence of relapse, and in this respect Danielssen's material is of considerable interest. Of the 93 patients discharged as cured 14 returned with relapse. As the first hospital sojourn had given such favorable results it is probable that other patients with relapse would similarly have returned had there been any, and it is therefore reasonable to assume that the number of relapses was not much greater than about 15 per cent.

Out of these 14 who returned there were 2 males with nodular, 2 males and 1 female with mixed, and 2 males and 7 females with maculo-anesthetic leprosy. Out of these, 1 patient of the first group, 1 of the second, and 2 of the third were again discharged as cured. The patient of the first group so discharged later returned with another severe relapse, but in due course was for the third time discharged as cured. Many years later he was admitted to the other hospital for lepers as an anesthetic case, with some muscular atrophy and diminution of feeling but no nodules. He was much troubled with ulcerations on legs and arms, and there were also many varicose veins. Bacilli could not be found in the ulcerations. He died of uremia in 1919, aged 56; he had first been admitted to Lungegaards Hospital in 1876, at 13 years. Unfortunately no post-mortem examination was made. I have described this patient so fully as his leprosy took a course that is not at all rare.

Deducting the relapses mentioned, the number of actual cures proves to be about 10 per cent of all patients, and 14 per cent of those in the therapeutic section. It is my opinion that at least 10 per cent of those who were brought under treatment at an early stage of the disease were cured. In addition, many of the 78 discharged as improved must also have been cured.

*Relation of type to cure.*—The statistics show that the results differ considerably in the various case groups. Thus (Table 1) for males with nodules the cures were 3.5 per cent while for maculo-anesthetic females they were 29.4 per cent, and other figures show similar differences. The patients with the nodular form gave the poorest results and those with the maculo-anesthetic form gave the best, the mixed cases being intermediate. It is shown strikingly that there is a considerable difference between the nodular and maculo-anesthetic forms with regard to prognosis.

*Differentiation of forms.*—As it is not improbable that leprosy may appear in different forms in different parts of the world, it

is necessary to say a few words about those seen in Norway. Contrary to earlier practice, with its many names and forms, Danielssen and Boeck (<sup>3, 4</sup>) recognized only two forms of leprosy (*elephantiasis graecorum*), namely, the nodular and the anesthetic. Later the combination of these became known as the mixed form. At first Danielssen classified as anesthetic leprosy only cases that presented what one now looks upon as a fairly advanced stage, with paralysis, atrophy and mutilations. The primary stage was not yet distinguished; it was confounded with the first skin symptoms of the nodular form. Both forms commenced, according to Danielssen's description, with spots (maculae), and in cases where infiltration was very distinct these were looked upon as of the nodular form. In cases where the infiltration was slight or absent the lesions were designated as maculae elephantoides. It was not until his treatise on the anesthetic form of leprosy, written in 1862 (<sup>4b</sup>), that he thoroughly described the macules which form the beginning of anesthetic leprosy. It is in view of this that, after a thorough study of Danielssen's records at the Lungegaards Hospital, I have transferred in the statistics here given some of the cases with "maculae elephantoides" from nodular to the anesthetic group, but the number of such cases is not so great that it can alter the findings materially.

In the course of time the term "*elephantiasis anaesthetosa*" that Danielssen employed has been changed to *lepra maculo-anaesthetica*, for the reason that in the first stages one usually finds macules either preceding or together with more or less pronounced anesthesia. One might possibly object to the term maculo-anesthetica on the grounds that macules are not always to be found and that consequently there should be recognized both maculo-anesthetic and anesthetic forms, but experience here in Norway, based on careful examinations, is that very few cases have not presented macules. In determining this point no weight can be attached to the patients' statements, as they are often not observant enough; further, the spots may have been very small, or transient, or so situated as to escape observation. Further, one cannot exclude the occurrence of macules because they do not happen to be seen at a single examination, for one often finds traces of them only after repeated examinations. But quite aside from all that, there is no essential difference between anesthetic and maculo-anesthetic cases as regards course or prognosis.

The diagnosis of "lepra mixta" has been recorded more and more seldom in the official Norwegian statistics, as this form is not a distinct clinical entity. Where typical nodules appear in a pure maculo-anesthetic case this points to an aggravation of the disease and to a poorer prognosis, for its course will be practically the same as that of a nodular case. Such a mixed case ought, therefore, to be recorded as nodular. If, on the other hand, typical macules appear in a nodular case this as a rule points to an improvement of the prognosis. In Norway one usually designates such a case as secondary anesthetic leprosy.

#### METHODS OF TREATMENT USED

The remedies made use of by Danielssen are mentioned in his last work on leprosy (<sup>6</sup>), but they should be discussed more fully on the basis of statements that are to be found in the records of Lungegaards Hospital.

*General measures.*—In the first place, great stress was laid on the patients' general health. If this was poor—which was often the case, as the patients often came from poor homes where hygienic conditions were bad—efforts were made to improve it by good hygiene and strengthening treatment. On admission many were found suffering particularly from scabies; this was promptly treated, and as the treatment was somewhat radical the appearance of nodular leprosy was changed in no slight degree after the disappearance of the scabies. Even from the very first baths of various sorts were used, such as steam baths, hot water baths and—during the summer—sea-water baths, but exhaustion of the patient was avoided. Care was taken that the food should be plentiful and nourishing. This consisted, even very early in the existence of the hospital, of a large amount of good vegetables, such as, cabbage, lettuce, roots, etc. The quantity that was supplied was almost equal to that which is prescribed at the present time, though the fare was not strictly vegetarian. The general conditions were, of course, totally different from those in the homes of the patients in most cases, and the change undoubtedly was beneficial. This was especially the case in the first few years of the Lungegaards Hospital's activity.

*Blood-letting and counter-irritants.*—One of the first and most important forms of treatment was regular and frequent letting of blood by cupping, venesection, or leeches, and by scarification. It



is to be recalled that Danielssen was a keen advocate of the theory that leprosy was due to a dyscrasia (<sup>4</sup>), an abnormal accumulation of albumen in the blood. Also connected with this theoretical assumption there was his extensive use of counter-irritants, such as an ointment of antimony tartrate, one of potassium chromate, and vesicants such as Spanish fly, (*Ol. cantharidatum*), and oil of turpentine. Considerable local suppurations were produced. Continual application of tincture of iodine was also employed as an irritant.

*Drugs administered internally.*—Besides the strengthening fare, cod liver oil, arsenic, iron and phosphorus were also used. The last mentioned remedy was specially used in maculo-anesthetic cases as a nerve tonic, and iron was also much employed in this form as these patients were often pale and anemic. A gold preparation of Danielssen's was used, but I have not been able to find further particulars on this point. As an antifebrile remedy in high fever and strong reaction he employed potassium nitrate and, as it also appears, bismuth as *magisterium bismuthi*. Of other internal remedies, iodine and antimony were much used in the earlier years, the former generally as potassium iodide or ferrum-iodine, the latter as tartarus stibiatus ( $C_2H_3O_2K.SbO$ ). This drug was often used in large doses and for so long that symptoms of poisoning might appear, but many patients are said to have felt benefited. Potassium iodide was particularly used in the nodular form, ferrum-iodine (as the liquor or syrup, or as pills) chiefly in the maculo-anesthetic form.

At the outset Danielssen had great faith in iodine preparations, but later he abandoned them more and more because they frequently produced symptoms of poisoning and serious reaction phenomena. However, he continued to make use of the reaction-producing property of potassium iodide, as this was considered a control test for cases that seemed to be cured, and it is still used in this way here in Norway. Long experience seems to have proved that if prolonged use of fairly large doses of this remedy produces no reaction phenomena one is justified in looking upon the case as cured. There has been an inclination to blame potassium iodide for dissemination of the disease in the body and the production of new lesions, but in my opinion this danger is considerably exaggerated. I think that what one has looked upon as being new efflorescences have—at any rate to a great extent—been caused by collections of

bacilli that were without tissue reaction and therefore not discoverable by ordinary methods of examination, but which the potassium iodide reaction has made evident, not by increasing the number of bacilli but by producing a reaction on the part of the tissue. It is a fact that in the skin of lepers many bacilli and collections of bacilli are only to be demonstrated microscopically, particularly in the more advanced cases of nodular leprosy.

In this connection it may be added that Danielssen administered rather large doses of Koch's tuberculin, which produced high fever and a local reaction. But the fever became so severe that he considered it injurious and even dangerous, and so he stopped using this material.

Danielssen also tried various remedies that originated from tropical plants, but without result. Most of these are now, presumably, merely of historical interest with the exception of chaulmoogra oil. This, in the form of *Ol. gynocardiae odoratae*, seemed to have no healing qualities; in fact Danielssen found it detrimental. It must be stated, however, that it was given internally almost exclusively, per os. It may also be mentioned that he tried the so-called *mudar* or *madar* of the roots of the Indian plant *Asclepias gigantea*. It is an old remedy, and the Norwegian physician, B. Ebbell, who has worked on leprosy for many years in Madagascar, has informed me that in Egyptological studies he has found that a preparation from this plant was used in a prescription for leprosy in ancient Egypt, about 1250 B. C.

*Antibacterial remedies.*—When it became evident that leprosy must be attributed to bacteria Danielssen used other appropriate remedies such as mercury, carbolic acid, creosote, potassium chlorate, and sodium salicylate. He had great confidence in the last-mentioned and concluded his attempts at treating leprosy by recommending its continuous use. Unna's methods of treatment with pyrogallol, chrysarobin and ichthyol were also tried but no favorable results were obtained with them.

The remedies enumerated here are by no means all that Danielssen tried; they are simply those which were the least indifferent. It seems to me that most, if not all, who have treated leprosy over a number of years and who have attempted to judge critically the curative value of methods employed will agree that it would be difficult to explain Danielssen's favorable results solely on the basis

of the remedies that he used. The fact that after so many years' experience he considered sodium salicylate the best remedy is in my opinion an indirect admission that those used were really of slight curative value. The patients themselves arrived at that conclusion, and in consequence it has been impossible of late years to make any serious attempt at prolonged treatment; the patients have lost faith and do not wish to undergo therapeutic experimentation.

#### WORK AT THE PLEIESTIFTTELSEN NO. 1

As yet I have only discussed the results obtained at Lungegaards Hospital. As stated, practically no treatment experiments were undertaken in the other four institutions. However, Pleiestiftelsen for Spedalske No. 1, in Bergen, has been an exception since Lungegaards Hospital was discontinued as a leper hospital, though conditions there have not been favorable for therapeutic experiments. It would be interesting could one submit statistics corresponding to those from Lungegaards Hospital, but it is unfortunately impossible. On the other hand one has essayed to study, as thoroughly as possible, the course of leprosy by pathological-anatomical and postmortem examinations.

*Cases found cured at autopsy.*—This work has proved that in many cases the leprosy bacilli have wholly disappeared from the organs—i.e., that not only clinical cure but actual cure has taken place—and that without treatment. On looking through the records of the 130 postmortem examinations made in the last generation it seems very possible that of the 56 cases of the maculo-anesthetic variety examined, 30 (53 per cent) had been cured. In only seven of them were bacilli found in active processes which had not run their course. A number of cases presented only slight traces of the disease in the nervous system (i.e., a very few bacilli could be found in the nerves), and in a few cases a few bacilli were found in the lymphatic glands. All active processes, and all bacilli, had long since disappeared from the skin. On the other hand, out of the 74 nodular cases examined postmortem only 6 (i.e., 8 per cent) seemed to have been cured, all nodules and infiltrations having disappeared leaving only scars, and only secondary, non-leprous processes being present in the nerves.

As will be noted, I have expressed myself with great reserve with regard to the absolute value of these figures. This is because each case must be examined very carefully, the examinations de-

manding much time and great patience. However, I have previously discussed in detail twenty cases thoroughly examined post-mortem (8). Ten of these were typical nodular cases with masses of bacilli in various organs. Two others had had nodules at the outset of the disease but these had disappeared, and the examination revealed only changes in the nervous system, and some few bacilli. Eight cases had been purely maculo-anesthetic, and in four of these it was impossible to find bacilli in any organ, so one is strongly inclined to believe that they were completely cured, even though the disease had left great defects in various organs. The cases are too few to be used statistically, but they point in the same direction as do the statistics from Lungegaards Hospital.

It is important to realize that these cured cases had for the most part received only palliative and symptomatic treatment. From this one is led unavoidably to conclude that there must be a spontaneous or natural cure in many cases of leprosy. One of the interesting facts observed in this connection is the great difference as regards curability between the nodular and maculo-anesthetic cases. Another is the exceedingly long time that the bacilli can persist in nodular cases even when there is clinical cure. In the two cases mentioned in which the disease had commenced with nodules but later resembled more the anesthetic form, bacilli were found in spite of the fact that they had been leprous for 50 and 40 years, respectively. The four maculo-anesthetic patients in whom bacilli were found had not been leprous so long, viz., 35, 16, 13, and 3 years, respectively. As for the question where the bacilli remain during such long periods, they disappear relatively soon from the skin in many of the maculo-anesthetic cases, remain much longer in the lymphatic glands, and persist by far the longest in the nervous system, especially the central nervous system—mostly in the cells of the spinal ganglia, less in those in the spinal cord.

#### COMPARISON OF TYPES

How may one explain the great difference in curability of the two clinical forms of leprosy? With our present knowledge we can only connect it with differences in capacity of the organism to resist the bacillus, the power to react against it. Not having succeeded in cultivating it yet, we have been unable to test its virulence and we have thus only the leprous tissue and its histological changes

to work on. One does not wish to be understood as saying that leprosy presents only the two main types, for there are, of course, transition forms. However, the distinction between the types is clear. It not only is made clinically and histologically, but also can be supported experimentally by allergic skin reactions which, one is almost tempted to say, indicate a qualitative difference between the typical forms.

*Skin reactions.*—Histological sections show how exceedingly strong is the tissue reaction against the usually very small number of bacilli in the maculo-anesthetic form as compared with the very slight reaction against the enormous masses of bacilli in the nodular form. Anyone who has compared a typical macule with a typical nodule must have observed this. In the latter one sees a slight proliferation of the tissue, and nearly all cells bursting full of bacilli, and may even find bacillus-containing cells in the act of multiplication with no evidence of pathological changes (7). On the other hand the typical macule presents a considerable cell infiltration around the small vessels and the fine nerves and nerve branches, while among these cells one frequently can find no bacilli, or if they are found—often after a very long search—they are very few. A nodule begins as a rule slowly and insidiously, without subjective symptoms, and if it disappears it also does so slowly. A macule, on the other hand, often appears suddenly and is accompanied by the flush of an inflammatory phenomenon and some swelling, together with burning and painful sensations, at times very severe. When such a macule disappears it may do so very quickly, after an existence of only a few days, though it often does so slowly.

Mitsuda's allergic skin reaction (9) gives positive results in 97 per cent of maculo-anesthetic cases but only 8 per cent of nodular patients (10); at the same time it gives positive results in non-leprous cases. Montañes (11) arrived at quite similar results with a similar method, obtaining 100 per cent positive reactions in non-leprous persons, 80 per cent positive in leprosy cases in which no bacilli were to be found (mostly nerve cases), and 100 per cent negative in undoubtedly positive leprous cases. It seems hard to escape the conclusion that these reactions are of allergic nature; and this seems clearly demonstrated by the reaction changing from positive to negative when a maculo-anesthetic case changes to the nodular form, and vice versa from negative to positive when a nodular case



changes to the nerve form (Hayashi). That the transition from nodular to nervous is an expression of a pronounced tendency towards recovery has long been acknowledged by clinicians. The few cases in which the reaction does not agree with what one might expect may be ascribed simply to the transition forms. All phenomena thus seem to indicate that the bacilli find much less favorable conditions in the skin of the maculo-anesthetic case than in that of the nodular case.

✓ *Nerve changes.*—A similar difference is seen in the nervous system, though not to so pronounced a degree. In both forms of leprosy there are, as a rule, many bacilli in the peripheral nerves, but the maculo-anesthetic patient reacts the more strongly against them and soon complains of pain—often exceedingly much—while the nodular patient may go for many years without any pain worth mentioning. The same is the case with anesthesia; nodules are but slightly anesthetic when at all, while this symptom is the most pronounced characteristic of the macules, even at a very early stage. Histologically, round-cell inflammatory infiltration is much more severe in the peripheral nerves in maculo-anesthetic than in nodular leprosy, both in the cutaneous branches and in the large trunks. At the points of predilection, as the elbows, the infiltration may be so great that abscess-like round-cell accumulations may form, and in these there may be considerable lime deposits (8), a thing that I have not found in any pure nodular case. In the maculo-anesthetic patients the bacilli often totally disappear from the nerves, while in the nodular cases they are almost invariably found there on postmortem examination. Bacilli also remain for a very long time in the central nervous system, particularly in the nodular cases. One has succeeded in finding them in the nerve cells of spinal ganglia and in those of the anterior horn of the spinal cord as long as 40 to 50 years after the onset of the disease, and after all nodules had disappeared and the picture—clinically—had gone over to the secondary anesthetic form. On the other hand, bacilli have been absent in many corresponding cases of maculo-anesthetic leprosy. I am firmly of the conviction, though it would be difficult to prove, that the bacilli remain latent in the central nervous system long after the clinical symptoms have disappeared because the ganglion cells do not react against them. This is an important factor in connection with a decision as to cure, especially in nodular cases, in which it seems as if the bacilli can

remain latent an exceedingly long time and may possibly cause late relapses.

*Visceral changes.*—With regard to the viscera, it is well known that one has scarcely ever been able to find bacilli in the liver, spleen, or other internal organs in maculo-anesthetic leprosy, while great numbers are always present in the nodular form. It is, therefore, logical to assume that in the visceral organs, as in other tissues, the power of resistance against the bacillus is greatest in the maculo-anesthetic form.

*Blood reactions.*—The various blood reactions also show marked differences in the two forms of leprosy. The Bordet-Wassermann, Sachs-Georgi and Kahn reactions are positive in most nodular cases, but negative in by far the greater number of the maculo-anesthetic ones. Different workers have obtained different results in this matter, presumably because of differences in the material examined as regards transition forms and secondary anesthetic cases. Similarly with the red-cell sedimentation test; the rate is only slightly increased if at all in pure maculo-anesthetic cases, but always increased—and at times very greatly—in nodular cases. However, one must bear in mind that large neurotrophic ulcers or other accidental conditions may cause considerable increases of the sedimentation rate.

Regarding the nature and genesis of these reactions, our knowledge is so slight that one dares not draw any definite conclusion from them regarding the reactive power of the patients against the bacillus. However, it does not seem improbable that positive reactions are an expression of an accumulation of pathological products in the patient, and one may therefore assume that these reactions indicate that maculo-anesthetic cases do not present such good soil for the bacilli as do the nodular cases.

*Blood-cell picture.*—One might have hoped to find indications of reaction against the invading bacilli in the blood-picture, but this method has proved unsatisfactory. Leprosy being so very chronic, it is not surprising that little evidence is seen of the activity of the bacilli. Furthermore, other diseases that disturb the blood-picture are often met with. However, what has been found points in the same direction, viz., that maculo-anesthetic cases react otherwise, and more actively, than do the nodular cases. Thus Japanese investigators hold that leucocytosis is found in the former type, but not in the latter. On the other hand W. F. Hartwig, assistant

physician at the leper hospital here, has been unable to confirm this, but he has found leucopenia in severe cases of nodular leprosy with pronounced ulcerations.

*Tuberculoid leprosy.*—So far I have discussed only nodular and maculo-anesthetic leprosy, but not the so-called tuberculoid leprosy. This must be very rare here in Norway, for despite energetic search only one single case has been found, namely, that described by Bruusgaard (12). In that case the symptoms disappeared sooner than I have seen happen in any other leper with such marked infiltrations of the skin. The reaction in the infiltration tissue was very considerable, though I was not able to find any definite bacilli. The impression of great reaction power in this condition has been strengthened by examination of tissues from a few other cases of this form of leprosy from the tropics, in all of which I found bacilli, though in very small numbers.<sup>3</sup> Further examinations of more material in countries where this form of the disease is frequently met with will, it is hoped, clarify this matter.

*Reaction versus virulence.*—The evidence all points to the conclusion that the chances of cure increase with the power of the body organism to react against the invading bacilli. With regard to the virulence of the bacilli, I suppose that we can take it for granted that, as in tuberculosis, it is about the same in all cases. This reactional power, which is the most important factor in deciding the fate of a leprous patient, is by far the greater in the maculo-anesthetic patient. However, nodular patients who appear incapable of overcoming the bacilli may be completely cured when, for whatever reason, they are made to react. Here lies the most important problem regarding the therapy of leprosy, namely, to bring about a reaction at as early a stage as possible.

*Age at onset, and duration.*—It seems indubitable that the liability of contracting leprosy is greater at an early age than later, though this does not exclude the fact that the body's power of resistance can be lessened in time. This is, of course, a point that would be difficult to prove. At present the evidence is principally to be sought by statistical methods. I have, therefore, examined particularly the statistics of Lungegaards Hospital.

<sup>3</sup> These specimens were kindly sent me by Dr. J. J. du Pré le Roux, of Pretoria, Union of South Africa.

Of all those who were cured, 11 per cent were 10 years old or younger when leprosy broke out, while of those not cured only 4.6 per cent were as young at the onset. Similar proportions existed in patients who were from 10 to 20 and 25 years old at the outbreak, 49 per cent and 75 per cent, respectively, for those cured, 30 per cent and 54 per cent for those not cured. The chances of a cure are not great when the disease appears after the age of 25. The oldest patient cured was 47 at the outbreak of the disease.

Similar, if less marked, relations are shown by the statistics for the duration of the disease at the time of admission to hospital, though it must be noted that in many cases the statements regarding the duration of the disease are somewhat doubtful. In 67 per cent of those cured the disease had only lasted one year or less, and in 55 per cent of those not cured. In 83 per cent of the cases cured the disease had lasted two years, and in 76 per cent of those not cured. It is remarkable to see how long the disease may have existed and yet be cured. In several instances the duration had been 6 to 7 years, and in one it was 20 years.

#### APPARENTLY CURED NODULAR CASES

The following are abstracts of the records of certain cured nodular patients from Pleiestiftelsen for Spedalske No. 1.

CASE I, No. 1591.—M. B., male, born 1859, present age 75. Mother leprous. At 5 contracted smallpox; leprosy noticed in 1870, 64 years ago. Admitted August 16, 1873, to Reknes Pleiestiftelse with extensive nodules on face and extremities. These steadily increased until 1878 when he became ill from some unknown cause, being bed-ridden for long periods; after two or three years of this all nodules had disappeared. Transferred in 1885 to Pleiestiftelsen No. 1, in Bergen, with only scars, some slightly pigmented spots without infiltration on the extremities, and a large ulcer under one toe. Skin sensation somewhat reduced over the feet. He is still at the hospital and, considering his age, feels fairly well (Fig. 1). Leprosy has left only hairless eyebrows and scattered scars; no swelling of lymph glands or nerves, no bacilli to be found. The disease must have been quite overcome for more than a generation.

CASE II, No. 1558.—K. H., male, born 1865; died at 63, fifty years after onset of the disease. A half-sister leprous. Admitted to Lungegaards Hospital March 13, 1878, with *lepra tuberosa*. Eyebrows partly gone; numerous pea-sized nodules present, especially on the face; also numerous macules, particularly on the extremities, partly confluent, bluish-violet, much infiltrated and squamous. Swelling of the lymph glands, but no nerve swelling and no anesthesia. The disease had commenced a fortnight before, with a severe general illness. He was kept in bed for six weeks and given a little sodium salicylate; the nodules

gradually decreased and the spots faded. Discharged on May 31, 1879, at his own request.

Some time later he became very ill from some unknown cause and was bed-ridden for five years. Admitted to Pleiestiftelsen No. 1, August 12, 1890, an anesthetic case, thin and meagre, with no nodules or macules but a curious mottling of the skin of the extremities, especially in cold weather. Muscles of hands, feet and legs markedly atrophic; he could not walk, going about on his knees. Most of the fingers and toes were bent, and the outsides of the feet appeared mummified. Skin sensation was somewhat reduced over the feet. He soon improved, increased in weight and became very strong. No trace of leprosy remained except scars of nodules, poor eyesight, slight permanent enlargement and hardness of ulnars, and inability to walk. He felt well for a whole generation, and suddenly fell dead on September 9, 1928, from *ruptura cordis*, on account of fatty heart. Postmortem examination showed scarcely any arteriosclerosis. It was impossible to find bacilli in any of the organs generally infected. The enlarged ulnars showed degeneration of many nerve fibrils with considerable increase of connective tissue, and a number of vacuolated lepra cells were found, but neither here nor in the central system could we find bacilli.

CASE III, No. 1951. A. M. V., female, born 1865, present age 69 years. Uncle leprous. Affection noticed 47 years ago (1887); admitted to Reknes Pleiestiftelse December 8, 1890. Numerous nodules on face; right cheek seemed erysipelatous; eyebrows almost devoid of hair; on the extremities numerous infiltrations and scars left by sores; no diminution of skin sensation. Early in 1891 she became very ill, with fever and evident outbreak of new nodules practically all over the body; this condition lasted about 2 years, when she gradually improved, the nodules disappearing and the sores healing. Skin sensation and sight somewhat weakened. When transferred from the Reknes Pleiestiftelse in 1895 (it having been closed as a leper hospital), she felt quite well. This condition has remained unchanged (Fig. 2), and the disease must be looked upon as having quite disappeared more than 30 years ago. Apart from a little sodium salicylate—which she says she always vomited—she received no special treatment.

CASE IV, No. 1953.—M. K., female, born 1865, present age 69 years. Brother leprous. Disease first noticed 50 years ago, 1884; admitted to Reknes in 1889, with nodular leprosy. Eyebrows bare; numerous nodules on face and extremities, with ulcerations beginning. The disease progressed slowly, both before and after transfer in 1895 to Reitgjerdets Pleiestiftelse. Sight of right eye almost lost; skin sensation diminished over hands; occasional plantar ulcers, at times compelling her to stay in bed. In 1902 she contracted severe "erysipelas" on the face and left upper arm, during which the nodules on her face disappeared. She improved slowly; the nodules disappeared everywhere, but her hands became a little less sensitive and weak, the fingers somewhat bent. Since 1905 she has felt quite well, with occasional small, rapidly healing plantar ulcers, and impairment of sight of the left eye by corneal ulcers. Bacilli not to be found. The disease must have quite disappeared many years ago (Fig. 3).



CASE V, No. 1900.—M. M., female, born 1866, present age 68 years. Onset in 1879, 55 years ago, when during a general illness she developed large red spots on the extremities; she had several eruptions. In 1882 she was energetically blood-cupped, after which the spots disappeared but nodules broke out on her face and extremities. Admitted to Lungegaards Hospital, 1882, with numerous pea-sized nodules on her face, buttocks, and extremities; the nodules were bigger on the legs and some were ulcerated. Skin sensation somewhat reduced on hands and lower arms, possibly on legs also. Both ulnars swollen, lymph glands not. Treatment symptomatic except for sodium salicylate. In October, 1886, she contracted "erysipelas" of the face, this recurring in May, 1887; she also suffered greatly from eye pains, with iritis. In August "erysipelas" again, with redness and swelling of nodules; also in October and November, these attacks leaving her very weak. In December many of the nodules had disappeared or decreased. She improved gradually and was removed to Reitgjerdet in 1888 as "improved." In 1893 the small nodules had disappeared, but anesthesia had spread to above ankles and wrists. In 1913 admitted to Pleiestiftelsen No. 1, with no nodules, only scars; skin sensation only moderately reduced, having improved greatly; sight of both eyes impaired, but no active process. Since 1920 she has always felt well, with no sign of active leprosy. (Fig. 4.)

CASE VI, No. 1615.—G. M., female, born 1866, present age 68. An aunt leprous. Early in 1893, 41 years ago, she had a nodule on the right hand. When admitted to Pleiestiftelsen No. 1 on December 28, 1894, the face was of a dirty brownish color, with nodules about practically hairless eyebrows. Nodules and infiltrations on the extremities, some swelling of the lymph glands and nerves. In the ensuing years the disease spread slowly, involving mucous membranes and eyes; occasional erysipelas-like attacks occurred. In June, 1897, she became seriously ill with a severe attack, the redness, swelling and soreness involving all nodules and infiltrations; also mucous membranes of nose, mouth, throat, and larynx. Evening temperature for a long time was between 39° and 41° C., with marked daily fluctuations. The condition reached its height in January, 1898, when there were extensive hemorrhages in and around the leprous skin lesions, enlarged and sensitive spleen and liver, considerable albumen in urine. Slow improvement followed; out of bed at the end of March; subsidence of lesions accelerated, few remaining, subcutaneously on thighs. Skin sensation over hands, feet, and legs, much reduced during the attack, gradually returned; fingers bent irregularly, their movements limited. Description in 1903 records eyebrows smooth and hairless; sight of left eye impaired, the result of earlier iritis; ear lobes thin, scarred; nose sunken, due to defect in cartilaginous septum (Figs. 5 and 6); no nodules or infiltrations, only scars; no swelling of lymph glands or nerves; movements of fingers limited; anesthesia now slight, over very limited areas. This condition has remained practically unaltered, patient feeling quite well, with only an occasional complaint of rheumatic pains in arms. In August, 1929, a sprain of right wrist was followed by tuberculous joint affection with fistulas, but this healed leaving scars and some stiffness. It has not been possible to find leprosy bacilli in skin or mucous

membranes since the beginning of the century. Treatment has only been symptomatic.

CASE VII, No. 1974.—J. H., male, born 1873, present age 61. Mother leprous. In 1897, 37 years ago, noticed two small nodules on forehead; a year later another appeared; after a further year one appeared on right eye, others gradually developing on face and hands, the first ones disappearing by ulceration. Patient became very ill, his physician looking upon the condition as acute rheumatic fever since almost all joints were stiff, especially the knees. Bed-ridden, with fever and severe pains, for about four years, during the latter part of which he had attacks of cramps with passing unconsciousness and temporary loss of memory. The nodules disappeared, skin sensation was lost over the extremities, fingers became bent, and sight suffered to the point of blindness (1906). Plantar ulcers began to appear later (1913). Admitted to Pleiestiftelsen No. 1, February 24, 1913; no nodules or infiltrations, only scars; eyebrows quite hairless; completely blind, both eyeballs atrophied; nose somewhat sunken (Fig. 7); fingers and toes bent, with small defects; ulcers on left leg and soles of feet; skin sensation much reduced over the extremities; ulnar nerves a little swollen and sensitive to pressure. No bacilli found in the nasal mucous or the ulcers. In the hospital, where he still is, the condition improved, the ulcers healing; swelling and soreness of the nerves have long since disappeared; no glandular swelling. Treatment has only been symptomatic.

CASE VIII, St. Jørgens Hospital, No. 327.—O. G., female, born 1866, present age 68. A neighbor leprous. Disease commenced in 1884, 50 years ago, with falling of eyebrows, exanthema on upper arms and calves. Admitted to Lungegaards Hospital in June, 1885. Face then somewhat puffed, with bluish-red infiltrations, mostly on the forehead; on the upper arm a squamous eczema-like rash and several nodular infiltrations, particularly externally; on legs small, slightly infiltrated spots; no swelling of lymph glands or nerves. Tar treatment and ichthyol pills administered. In December had an eruption on arms and legs, with severe pains in elbows and arms. She was blood-cupped and became better. Reverted to ichthyol pills, whereafter she had a new outbreak of nodules, and an iritis; after blood-cupping the nodules disappeared. In 1886 had an eruption of spots on extremities and shoulders; the spots disappeared in the course of the year; was given sodium salicylate and ichthyol pills. In July, 1887, there were no infiltrations; patient felt well and medicine was stopped. In October had an outbreak of brownish-red spots on the face, back and extremities, lymph glands a little swollen; shortly after had erysipelas of the face, with swelling of hands and scaling over the extremities, especially externally; abundant albumen in urine. In July, 1888, the nodules had disappeared everywhere, only traces left; no albumen in urine; patient felt well. In 1895 removed to St. Jørgens Hospital, where she still remains; no changes except those due to age. The skin of the face is atrophic, greatly wrinkled; earlobes atrophic; eyebrows quite hairless (Fig. 8); on face and externally on upper arms small scars of previous lesions; both eyes show signs of previous iritis, sight impaired; skin sensation somewhat reduced on hands

and legs; no swelling of lymph glands or nerves. This case must have been cured a long time ago. No treatment since 1888.

#### GENERAL VIEW OF LEPROSY

When we attempt to obtain a general view of the nature of leprosy and its course we find that the causative agent, the leprosy bacillus, may encounter very different conditions in different individuals, and may this have quite different effects. Many observations and theoretical considerations lead to the assumption that many people, perhaps most, possess an absolutely unfavorable soil for this microbe, and that in such persons it loses its pathogenic power. In other words, the number of those infected with the leprosy bacillus is greater than the number who actually suffer from leprosy.

Among those who acquire the actual disease the bacillus in certain cases finds good soil for life and multiplication, meeting with little or no resistance; in such cases the duration of the disease may be short, though acute leprosy with a fatal outcome is rare. The more common occurrence is the well-known chronic form of the disease, for in most cases the human organism resists the invader. Unfortunately, this attempt is often too late and is ineffective, whereupon we see the common picture of nodular leprosy, with its unfortunate outcome after many years. However, even in this form of the disease the human organism may ultimately be the victor, and this more frequently than we have been inclined to believe, though in these cases victory is paid for very dearly.

In other instances the organism resists the bacillus at an early stage and hinders its multiplication to a very considerable degree. In some cases this may result in the disease being completely cured in a relatively short time. Such cases, quite surely, occur more often than we have been inclined to suppose. Many of them never come up for clinical observation, and may not even be noticed by the patients themselves. For this reason proof of this assumption may be difficult to obtain, but in my opinion careful clinical and pathological observations during the course of leprosy make it perfectly justified. However, in most cases where the invading bacillus meets resistance the disease assumes a more or less chronic course, presenting the clinical picture of the maculo-anesthetic type (in which is included pure nerve leprosy), which possesses a distinct tendency to cure.

Leprosy, even in its most severe forms, is by its very nature a curable disease. Medical science, therefore, must never cease striving to arrive at that which nature has shown to be obtainable. It would seem, at this stage of medical science, that the way or at least one of the ways to attain this goal is to arouse and strengthen the reaction-power of the human organism against the intruding entity, the leprosy bacillus.

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## DESCRIPTION OF PLATES

## PLATE 1.

FIG. 1. Patient M. B., Case I, aged 75, leprosy first noticed 64 years ago, presumably cured for more than a generation.

FIG. 2. Patient A. M. V., Case III, aged 69 years, leprosy first noticed 47 years ago, presumably cured more than 30 years ago.

FIG. 3. Patient M. K., Case IV, aged 69 years, leprosy first noticed 50 years ago, presumably cured for many years.

FIG. 4. Patient M. M., Case V, aged 68 years, onset 55 years ago, no signs of activity for at least 20 years.



PLATE 1.



PLATE 2.

FIGS. 5 and 6. Patient G. M., Case VI, aged 68, first record of leprosy 41 years ago, presumable cure more than 30 years ago.

FIG. 7. Patient J. H., Case VII, aged 61, leprosy first noticed 37 years ago, presumably cured for many years.

FIG. 8. Patient O. G., Case VIII, aged 68, onset of leprosy 50 years ago, presumably long cured.

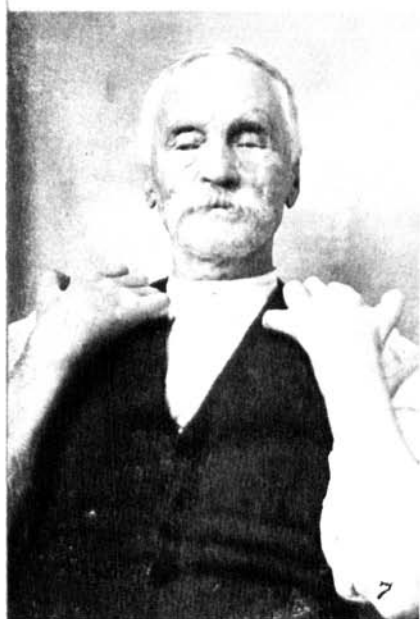


PLATE 2.