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TUBERCULOID CHANGES IN LEPROSY

IV. CLASSIFICATION OF TUBERCULOID LEPROSY

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INTRODUCTION

There unquestionably has been a marked improvement of late with respect to classifying cases of leprosy, because of the fairly general adoption of the classification recommended by the Memorial Conference. However, a serious impediment to reasonably uniform practice in this matter still remains in the problem of placing those cases whose principal skin lesions are infiltrated, active leprides of the tuberculoid variety. The matter is of such practical importance as to require examination in some detail.

In practice, classification of tuberculoid cases¹ depends upon whether attention is centered upon the more obvious characteristics of the lesions, or upon the general, ultimate features of the cases as a whole. On encountering these infiltrated, progressive skin changes, obviously caused by an active process in the skin itself and by no stretch of the imagination ascribable to neurotrophic influences, it is

¹ This applies to cases with only tuberculoid leprides, or both those and simple leprides, but not, of course, those with lepromatous as well as tuberculoid lesions, these being obviously of the cutaneous type. The position of cases with flat leprides that though apparently simple are nevertheless histologically tuberculoid cannot be discussed here.

but natural to think of them as "cutaneous" and to classify the cases as of that type. The writer himself once argued for this view, largely because of certain technicalities to be mentioned. To make clear the error of this it is necessary first to arrive at an understanding concerning (1) the meaning of "cutaneous," and (2) the fundamental basis of distinction between the two types into which unmixed cases of leprosy can be divided.

THE WORD "CUTANEOUS"

The ordinary definition: "Of or pertaining to the skin; existing on, or affecting, the skin" is simple and general. Naturally, in leprosy work the word has been much used in this general sense, in which the leprides as well as the lepromata are cutaneous. But it has also long been used in a special, limited sense as the name of one of the types of leprosy, and it was so adopted and defined by the Memorial Conference (13). It would doubtless be advantageous if in leprosy literature the term were to be avoided except in this sense. Unfortunately, there still persists a tendency to classify as of the cutaneous type cases with any infiltrated skin lesions, especially if they appear to be active.

DISTINCTION OF TYPES

About the middle of the last century Danielssen and Boeck (3) began to bring order out of chaos by showing that leprosy appears in only two main clinical forms, which they called *tuberosa* and *anaesthetosa*. Leloir (11) emphasized the fact that the macular, bullous, lazarine, mutilating, etc., forms are not *types* but *varieties* or phases of the disease; and he insisted, as one still must today, that this distinction should be made. Hansen and Looft (5) were dissatisfied with the names mentioned, for, though they characterize the most common and prominent symptoms, they refer to different organs; also, the nerves are affected in both types. They would have favored *tuberosa* and *maculosa*, both referring to the skin, except that macules often disappear and leave only anesthesia; consequently, in place of the latter they adopted the awkward compromise *maculo-anesthetica*.

In the years that have elapsed the basic distinction of these types has long been generally recognized. One represents a limited infection with relatively few bacilli in the body; it shows symptoms and sequelae of nerve lesions, with or without skin lesions (i.e., the

leprides), which when present are typically negative for bacilli by the standard examination and are not composed of lepra cells; the disease is often self-limited, dying out, but usually not without deformity, often leaving the patient "no longer suffering from leprosy, but only from its results." The other is a more or less unlimited, systemic infection with characteristic, usually predominant bacillus-rich skin lesions composed mainly of lepra cells (i.e., the lepromata) and similar lesions of visceral organs; nerve changes are often late in becoming prominent; death usually ensues in a few years after the definite outbreak of the disease.

Though Hansen and Looft were emphatic that the types are clearly distinguishable, they also pointed out that they must be regarded as of the same disease, their skin lesions due to the same agent. However, they had not made up their minds about the reason for the differences. At one moment they seemed inclined to ascribe them to the parasite instead of the host, but they then said:

Does this difference between the two forms depend on a difference in the virulence of the bacilli? If so, this virulence is capable of very rapid changes. We have seen a case of maculo-anaesthetic leprosy, which probably arose by inoculation from a very severe case of nodular leprosy . . . the virulence of the bacilli must have been at once diminished on their inoculation on another organism. And since it also happens that a maculo-anaesthetic case may on a fresh eruption become nodular, the bacilli must be able by cultivation in the organism to re-acquire their power. Both are possible, but the virulence of the bacilli seems to depend, not so much on any constant character of their own, as on the soil in which they live It is also possible that the bacilli always possess the same virulence, and that it is solely dependent on the soil in which they live, whether they multiply freely or no.

Leprologists in general agree that the differences in type must be ascribed to the host rather than the bacillus—to differences in suitability for its multiplication and in reaction to its presence rather than in its own virulence. The matter is summed up in the word "resistance" or, rather better, "relative resistance," as was perhaps first pointed out by Arning. The following quotation from one of his articles is pertinent:

Für die Lepra habe ich schon ausgesprochen [*Deutsche Med. Wochenschr.*, 1909], dass die Differenzierung in sogenannte anästhetische Form (Lepra nervorum) und Knotenform (Lepra tuberosa) sich in diesem Stadium vollzieht, je nach der Menge und der Anpassungsfähigkeit des Giftes einerseits und der Abwehrkraft des Organismus andererseits. Die relativen Werte dieses reziproken Verhältnisses erklären die so ausserordentlich differenten klinischen und

anatomischen Bilder der Lepraerkrankung. [Lepra und Syphilis, eine Parallele. *Deutsche Zeitschr. f. Nervenhe.* 68/69 (1931) 277.]

The relatively refractory condition that determines the neural type is, of course, due to an "immunity" of some sort, whether natural or acquired, general or specific. Concerning its nature, the discussions by Muir in 1925 (19) and Wade in 1927 (26) indicate the paucity of positive knowledge at the time. Not a great deal has been established since then, though of late considerable attention has been given the leprolin skin test (1, 6, 16). However, there is evidently a high natural immunity among non-contacts—at least adults—as evidenced by the small number who acquire the disease when exposed. There is also indication that that resistance may become heightened where the disease is endemic³, whether by the acquisition of some degree of specific immunity, or by the process of natural selection as is maintained by Molesworth (15); and immunity in some phase is undoubtedly responsible in large degree for the cure of the disease when that happens.

Whatever precisely may be the nature of the influences at work, there are several possible eventualities when a person is exposed to infection and nothing is done to interfere with the course of the process.

1. *Complete resistance.*—The organism fails completely to gain a foothold and is eliminated. This is evidently the outcome in the vast majority of instances.

2. *Latent infection.*—The organism gains a foothold, but is held so effectively in check that it does not cause symptoms. How frequently this happens is quite uncertain. Whether such an infection will (a) ultimately give rise to symptoms, or (b) persist but remain latent, or (c) in time be eliminated, depends evidently upon the state of resistance.

3. *Clinical infection, abortive.*—The infection, whether with or without a latent phase, advances sufficiently to produce pathological changes that are

³When leprosy was introduced into the Loyalty Islands the infection rate was high and the disease relatively acute, but later the rate lowered and more neural cases appeared. An anomalous report that in Nauru the "cutaneous" case became more predominant some years after the outbreak of the epidemic suggests the possibility that tuberculoid changes may have been mistaken for lepromatous. The same possibility is brought to mind by the statement that "a large percentage of early cutaneous cases remain stationary . . ." in a recent report by Atkey on leprosy in the Sudan. [See the special article, this JOURNAL, 3 (1935) 73.]

apparent clinically, perhaps as nothing but a numb spot though commonly as one or more small, hypopigmented, usually more or less anesthetic areas, but the patient's resistance interrupts the process and, as recently emphasized by Cochrane (2), the change noted may remain without evidence of activity for a long time or may disappear spontaneously.

4. *Clinical infection, benign: neural leprosy.*—The process, often starting as described above, progresses and causes more marked signs and symptoms, but the patient's resistance continues sufficiently high to limit the spread of the infection in the body and the number of bacilli in the lesions. Both skin and nerves are typically involved, but the neural changes usually predominate sooner or later. Prognosis is relatively favorable as regards overcoming the infection, but permanent mutilations often occur.

5. *Clinical infection, malignant: cutaneous leprosy.*—The infection is relatively unchecked (or the resistance in a benign case breaks down), the bacilli multiplying in great numbers and giving rise to typical lepromatous lesions in the skin and deeper organs. Symptoms of nerve involvement usually arise sooner or later. Prognosis is unfavorable except in the event of effective interference, but occasional cases recover, usually with (secondary) neural residua or sequelae.*

As stated, the limitation of the neural case can only be ascribed to a partial or relative immunity which tends toward complete resistance rather than toward full susceptibility. This resistance may break down with the result that lepromatous lesions develop, while on the other hand such a resistance is evidently built up in a cutaneous-type case when its lepromatous lesions are overcome and the secondary neural condition remains. This conclusion is supported by findings with the leprolin test. That there is a specific element in the immunity is entirely probable; that there is a qualitative difference in this respect between the two types of the disease, and not merely a quantitative one, seems possible.

THE MEMORIAL CONFERENCE CLASSIFICATION

For many years leprologists have used the distinction of types indicated above as the basis of classification. However, this was done in a more or less general way and with so much variation in application and terminology that the matter was sadly confused. The matter was perhaps the most important one dealt with by the Leonard Wood Memorial Conference, in 1931. After considering especially the systems then in use in Cullion and Calcutta it adopted

*The foregoing tabulation of potentialities is very similar to that appearing in an article by Spindler, in the next number of the JOURNAL, though it was arrived at quite independently.

a modification of the former. This, it may be recalled, is based primarily on clinical considerations; it recognizes two types, "neural" and "cutaneous," the so-called "mixed" cases being looked upon as essentially cutaneous because of the relative importance of that element; and it makes a distinction between primary and secondary neural cases.

A second, separate classification was also adopted, by which cases are considered "open" or "closed" according to the bacteriological findings, but this is "administrative," not clinical. To the "open" group belong all cases found positive, whether they are of the ordinary cutaneous type, or simple neural cases with positive nasal lesions, or tuberculoid cases that have become positive either as a result of lepra reaction or from some other cause.

The definitions of the two clinical types are quoted here. Since the existence or absence of "leprotic" lesions is the main distinction between them, the definitions adopted for that term and also for "leproma" are quoted as well:

Neural (N).—All cases that show evidence of actual or previous nerve involvement; i.e., alterations of sensation with or without changes in pigmentation and circulation, trophic disturbances or paralyses and their consequent results: atrophies, contractures, ulcerations. These are not accompanied by leprotic changes in the skin.

Cutaneous (C).—All cases showing leprotic lesions in the skin. Such cases may or may not show, at any given time, clinical manifestations of nerve involvement.

Leprotic.—... those changes which present clinical or microscopic evidence of inflammatory processes, typically of granulomatous nature, which are apparently caused by *Mycobacterium leprae* in them. In such lesions the organism can usually be demonstrated by the ordinary methods of examination.

Leproma.—The term "leproma" is applied in a general sense to any lesion of a leprotic nature, as defined herein.

THE TUBERCULOID CASE IN CLASSIFICATION

The question of the position of the tuberculoid case in classification was not brought up at the Memorial Conference, but during a tour that the writer made shortly thereafter it was met repeatedly, especially in Japan, South Africa and India. Ignoring the indications afforded by isolated cases reported in the past (except to recall that the first case to which the term "tuberculoid" was ever applied, that reported by Jadassohn in 1898, was specified as in "nicht tuberöser Lepra"), the practice in these countries will be considered.

Japan.—In Japan, where the official classification recognizes three "types" of cases, nodular, neural and macular, the Conference classification met with criticism because it does not provide separately for the last-named group. Examples seen had lesions that clinically and histologically were tuberculoid, and Mitsuda (14) agrees that these lesions are of that nature, while Hayashi (7) refers to them as "macula tuberculoid." However, it appears that these cases are not actually considered a real type, but rather a sub-division of the neural one, for Hayashi (6) speaks of the "neuro-macular" type and says that cases are designated neural or macular according to whether nerve changes or macules predominate.

South Africa.—Here, also, was met the question of the classification of cases of a variety which has been shown to be tuberculoid (21, 22). Le Roux (12) describes the principal lesions of the maculo-anesthetic type as (a) trophic changes, "primary neural macules," and (b) infections, "primary cutaneous macules." Both are hypopigmented areas that spread radially and recover centrally, but the former does not have raised borders while the latter, spoken of as "bacillary active skin lesions, sometimes the site of primary infection,"* have raised, indurated, hypopigmented borders and are evidently the tuberculoid lesions. This confirms personal observations that in South Africa, as in Japan, these cases are looked upon as neural.

India.—Information as to the situation in India is fragmentary, but the matter is important. That the tuberculoid condition is common there is evident from the literature, notably certain of Henderson's articles (8, 9), and one by Muir and Chatterji (18) which describes lesions supposedly located in the nerves of the skin. Hayashi found this condition more common there than in Japan or the Philippines, and Muir (17) writes that cases with such lesions constitute 50 per cent or more of those seen in his clinic. However, the workers in India generally avoid the term tuberculoid, and Henderson (10) even protested its use because he understood it to imply some relation to tuberculosis. Under a description published in

*The significance of this is not understood. Practically all cases of this kind which the writer examined in South Africa, except those in lepra reaction, were bacteriologically negative. However, it is not questioned that these lesions are due to the presence of the infecting agent in the lesion—as is probably also the case with the simple leprides, though some look upon them as trophic.

1925 (19) Muir would have called such changes "nerve lesions" of the skin, provided they were anesthetic to light touch, in contradistinction to "skin lesions," described as positive for bacilli and not anesthetic to light touch. He has stated (4) that cases with tuberculoid lesions would be designated A1 under his old scheme of classification⁵, which would usually be quite as it should be, though exceptional cases like those of prolonged reaction described by me (23), that while still tuberculoid had become bacteriologically positive, would fall into the "B" class. It is said (7) that at present tuberculoid cases are being classified in India as neural, and Muir (16) speaks of "indurated, raised, erythematous lesions of the nerve type, i.e., the tuberculoid lesions," and also of "cases of nerve leprosy especially the macular type" (sic). However, Santra (20) says that in the absence of facilities for microscopic examinations it was the practice of the India Leprosy Survey party (which discovered some 16,000 cases of leprosy in 60 different parts of the country) to classify cases with tuberculoid lesions as either neural or cutaneous according to whether anesthesia could be detected or not. It would seem that, in some places at least, tuberculoid lesions are frequently not definitely anesthetic, especially if early or slight, and if that is the case in India this method of establishing the type of cases would lead to considerable errors.

Disposal as cutaneous.—In spite of the practice in the countries referred to of placing these cases in the neural group, there are many places where they are regularly classed as cutaneous. This is not to say that they are so classified deliberately, after recognition; it is done, rather, because they are not recognized. This practice has been observed in clinics visited personally; it is strongly suspected of other institutions from reports published by them, and it has

⁵ According to this system a case was given the symbol A or B according to whether it was found bacteriologically negative or positive. Each case was also given a sub-classifying numeral according to its supposed position on a graph which comprised two main curves rising from a base line. One, the A curve, which kept below a second or B line drawn parallel to the base, represented "nerve (anesthetic) leprosy." This was divided horizontally into A1 and A2 for primary or secondary cases, respectively, or, as stated in one place (4) for circumscribed bacteriologically negative patches and acroteric lesions, respectively. The other curve, after crossing the B line, represented "skin (nodular) leprosy" and had three subdivisions vertically, B1, B2, and B3, cases being sub-classified according to the number of bacilli found in smears.

been admitted by correspondents who have become interested in the matter. It is because of this practice, and the unavoidable confusion that results, that the matter is gone into so fully here.

THE NEURAL NATURE OF TUBERCULOID CASES

Characteristics that determine the classification of this variety of leprosy are to be found in the clinical, bacteriological and pathological fields, and there are also immunological indications.

Clinical.—Outstanding is the fact that its course and prognosis are those of neural rather than cutaneous leprosy; it is relatively benign, indefinitely prolonged, and often self-healing. Typical tuberculoid leprides may develop in an ordinary neural case without a change anything like that which follows the appearance of lepromata in such cases. Without going into details regarding the lesions it may be pointed out that the tuberculoid leprides like the simple ones are more sharply limited, less diffused, than lepromatous infiltrations often are. The question of sensory changes is interesting in that they apparently are often less marked than in simple neural leprides. A tuberculoid lepride without anesthesia is particularly liable to be mistaken for a leproma.

Bacteriological.—It is of the greatest significance that typically the tuberculoid lepride gives negative smears in the standard examination. When an untreated infiltrated lesion proves negative it is open to more than a mere suspicion of being tuberculoid, provided the examination is properly made. For the present at least it seems that a clinician working without the benefit of histological diagnosis is quite justified, if not compelled, to accept this as the principal diagnostic criterion. The relatively few tuberculoid cases which in the writer's experience have proved positive showed very few bacilli in lesions which, had they been lepromata, should have had very many.

Histological.—The principal evidence which the histopathology affords in the present connection is negative, namely, that the condition is not lepromatous. But it does give an indication of the degree of reaction to the infecting organism, much greater than in typical lepromata, and it may prove to be more directly indicative of the case type if it turns out that the tuberculoid change, in slight degree, is common in simple, flat leprides. It is significant that the tuberculoid change is rarely if ever seen in the nerves of unmixed cutaneous leprosy, but is the rule in at least the skin nerves in the tuberculoid variety, and in India, peculiarly, often goes on to necrosis and liquefaction (24).

Immunological.—Hayashi (7) states that the leprolin test will differentiate between tuberculoid and cutaneous-type infiltrations, and Muir (16) says that cases with tuberculoid lesions give even stronger reactions than ordinary neural cases. Certainly the frank, florid tuberculoid case suggests that there has been some change which has greatly exaggerated, and perhaps even basically modified, the reaction to the infecting agent that is shown in the ordinary neural case. This increased sensitivity presumably involves some change of resistance to that agent, but whether it is an increase or decrease has not been shown. The familiar ques-

tion of sensitization (allergy) versus true immunity is involved here, for it is not seen to what factor other than allergy the tuberculoid tissue-reaction can be ascribed. However, if there is a decrease of resistance it clearly does not approach the breakdown that is seen when lepromata develop in a neural case.

From the foregoing it appears that those who place tuberculoid leprosy in the neural type are well advised in doing so. This the writer was not prepared to do when in Japan early in 1931, because of lack of familiarity with the condition and over-emphasis on one technicality of the Memorial conference definition of "leprotic," but by the end of the year I had come to agree with this view ⁽²¹⁾ and further consideration has only served to strengthen that conclusion. However, these cases should be recognized as a group apart. This can be done by simply recognizing them as a variety or sub-type of the neural (N) type, which can be designated by the symbol Nt.

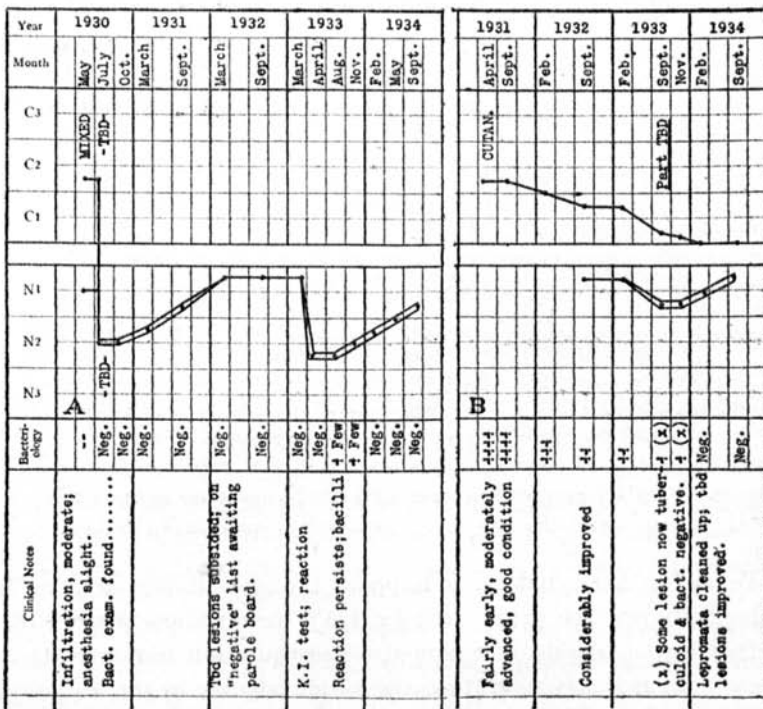
The only possible alternative to this disposal would be to create a separate, third type for these cases, which seems far from justified. It is true that they may be looked upon as an intermediate *variety* in certain respects—the gross infiltration of the lesions and their granulomatous nature, and the fact that in some cases they come to contain enough bacilli to be demonstrable in smears—but as shown the alliance is clearly with the neural rather than the cutaneous type. Some writers look upon this condition as an intermediate *stage*, one of progression from the ordinary neural macule to the leproma, but as has been pointed out elsewhere ⁽²¹⁾ this has yet to be established. This can be done only by continuous observation of numbers of proven cases, and not by assumption from single observations in groups of cases.

TUBERCULOID LEPROSY AND THE CONFERENCE CLASSIFICATION

If one believes, as the writer does, that the Memorial Conference classification has proved of real value in the way of bringing some degree of understanding and uniformity of practice among leprosy workers, and that its usefulness should not be interfered with, it becomes a matter of some concern whether the conclusions indicated can be reconciled with its specifications.* Examining first the

*It has been said ⁽⁷⁾ that the writer wishes to modify the Memorial Conference classification, which is overstating the case. The Conference itself realized fully that its recommendations would probably require amending as new knowledge is gained, but at the present stage of things one would interpret rather than change its classification.

definitions that have been quoted, it is evident that "leprotic" is used there in a special sense, actually synonymously with "lepromatous," which of course refers to the condition universally accepted as characteristic of the cutaneous type of the disease. Recognizing that this lesion (defined by the Conference, with the greatest conservatism, as a granulomatous change in which bacilli can "usually" be demonstrated by ordinary methods), is the bacillus-rich lesion composed chiefly of the lepra cells of Virchow, it would be a misconception to



TEXT-FIG. 1.—Illustrating the charting of: A, a tuberculoid case originally called cutaneous, and B, a cutaneous case that developed tuberculoid lesions.

confuse or include with it the tuberculoid granuloma, which is typically negative for bacilli and essentially epithelioid in nature. As stated, the latter condition was not discussed by the Conference; its frequency and importance were not recognized at the time. Therefore, "leprotic" as used by it is to be realized to mean "lepromatous," and with that understood no difficulty is seen, even under the Conference classification, in putting the tuberculoid case in the neural type, where it so clearly belongs.

CHARTING TUBERCULOID CASES

A question arises about recording tuberculoid cases on the case-progress chart described by Wade and le Roux (25). Should they be distinguished from ordinary neural cases, and if so, how can it be done? They should be distinguished, the writer believes, and this can be done very simply by (a) using a doubled line (or one drawn in color) instead of the usual single (or black) line, and (b) writing in conspicuously the word TUBERCULOID or the abbreviation TBD (Text-fig. 1).¹ Various changes can be indicated readily:

(1) If a case, at first believed to be cutaneous and so charted, were later found to be tuberculoid it would only be necessary to transfer the curve from the upper part of the chart to the lower and write in the distinguishing word, as in Text-fig. 1,A.

(2) If a real cutaneous case, as a result of increased resistance, should develop tuberculoid lesions (as other neural manifestations often appear), the fact would be indicated as in Text-fig. 1,B.

(3) Should a tuberculoid case later develop actual lepromatous lesions the fact would be indicated by a single line in the upper part of the chart.

Illustration.—In Text-fig. 1, Part A represents a hypothetical case that was recorded originally as cutaneous (no bacteriological examination having been made) but later recognized. This case did well under treatment, the skin lesions becoming apparently healed, but a test dose of potassium iodide precipitated a lepra reaction and the leprides became more numerous and more active in appearance than ever. A year after the reaction began a few bacilli were found in smears. Part B represents a case of actual cutaneous leprosy that, while improving under treatment, developed (secondary) tuberculoid lesions.

When, as may sometimes happen, the skin lesions become bacteriologically positive (as in Text-fig. 1,A), the question arises whether the classification should be changed. This question is related to that met when an ordinary neural case is found positive in the nose, which is emphatically to be answered in the negative. However, it with others cannot be answered conclusively until more knowledge of this variety of leprosy has been established.

SUMMARY AND CONCLUSIONS

Preliminary to a discussion of the classification of tuberculoid leprosy there are considered: first, the use of the word "cutaneous" in its general sense, which should be avoided, and in its special sense

¹ Thanks are due Dr. N. D. Fraser, of Swatow, for certain suggestions on which the method of charting here proposed is based.

as the name of a type of leprosy; and second, the basic differences of the two types, neural and cutaneous, which undoubtedly are due to differences of resistance to the organism and of reaction to its presence. Persons exposed may exhibit: (1) complete resistance, no infection occurring; or (2) latent infection, without clinical symptoms; or (3) abortive clinical infection; or (4) benign clinical infection (neural leprosy), usually ending in self-cure, often with deformity; or (5) malignant clinical infection (cutaneous leprosy), which usually terminates fatally unless effectively treated. Finally, the definitions which form the basis of the classification recommended by the Leonard Wood Memorial Conference are quoted.

Regarding tuberculoid leprosy, the question of its classification was not considered by the Conference. In Japan such cases constitute (or at least are assigned to) one of the three official "types," the macular; but this is admittedly only a sub-type of the neural. In South Africa cases of this kind have also been classed as neural—maculo-anesthetic with "primary cutaneous macules." In India where the condition is undoubtedly common the situation seems confused, but it appears that in general the cases are put in the neural group. However, in other regions this practice is far from the rule, for many men classify them as cutaneous, with consequent confusion of the whole leprosy situation.

Features that indicate the proper classification of these cases are: *clinical*—benign course and relatively favorable prognosis, development of tuberculoid leprides in ordinary neural cases without essential change of course or prognosis, circumscribed character of the skin lesions; *bacteriological*—typically negative findings on standard examination; *histological*—non-lepromatous character of the lesion, the extraordinary degree of reaction to the infecting organism, and also possible merging with clinically simple leprides; *immunological*—an indication of high resistance to the organism concurrent with increased sensitivity to it, and an apparent differentiation from the cutaneous type and relation to the neural type by the leprolin test.

It is concluded that these cases are properly classified as neural; that the creation of a separate type for them would not be justified; but that they should be considered a special sub-type of the neural. This view can be reconciled with the Memorial Conference classification by recognizing that the intended basic distinction between the

two types is the leproma, which differs fundamentally from the tuberculoid lepride. On that basis the tuberculoid case falls into the neural (N) type; the sub-type may be indicated by the symbol Nt. These cases can be charted readily and satisfactorily on the Wade Roux case-progress chart; this is discussed and illustrated.

This matter, it is submitted, is not merely academic. It is important in connection with administrative measures (closed *vs.* open cases); with epidemiological investigations, in which the predominant type of case is believed to be significant; and in connection with treatment and its evaluation, for as ordinary neural cases differ from cutaneous cases in response to treatment, so these are to be expected to differ from them, if not from the ordinary neural cases as well. It is to be hoped that recognition of these cases as a group apart will rapidly become general, and that careful studies of them will be made wherever they occur in numbers.

ADDENDUM

It has been indicated in the foregoing that the view that the tuberculoid case should be classed as neural is in agreement with practice in Japan. Since this article was put in press (its publication having been delayed), I have had the privilege of seeing an article by Hayashi (which appears in this issue of the JOURNAL), in which he discusses the question of classification. He points out that the Japanese workers have not been in favor of the Memorial Conference classification for the reason that it has been their understanding that it would place cases of the "tuberculoid macular" variety in the cutaneous type, and adds that they would support any accepted classification if the tuberculoid cases were put in the neural type. It would thus appear that, if my interpretation of the Memorial classification is accepted, there is no further barrier to its adoption by the Japanese workers.

Also while this article was awaiting publication there has appeared an interesting article by Muir [*Indian Jour. Med. Res.* 22 (1934) 393], on the relationship of skin and nerve leprosy, in which the matter is approached from the pathological viewpoint. It has seemed to me important to consider it here primarily from the viewpoint of those dealing with patients, wherefore stress has been laid on the features of the general clinical picture that determine the differentiation of types. However, as I have tried to show ⁽²²⁾, the distinction is certainly supported by pathological findings, even

more clearly than would appear from Muir's description of them. It is noteworthy that he does not use the word "tuberculoid"—he does not mention the recent articles on the subject that have appeared in this JOURNAL (22, 23, 24) and elsewhere—but his description of the "neural macule" is entirely that of the tuberculoid condition, both clinically ("raised and indurated") and histologically. It would appear as though in the clinical picture of neural leprosy (except in children of lepers) there were no simple, uninfiltrated, hypopigmented, anesthetic macules histologically characterized by simple round-cell infiltration with no tuberculoid element. This is in striking contrast with the fact (22) that Lie, of Bergen, who in the forty and more years of work with leprosy as seen in Norway has done a great deal of histological work, stated to me when shown my tuberculoid specimens from South Africa that he had never encountered that condition himself. At that time, and later in discussing the paper read by me in London (21), he was not prepared to absolve the condition from tuberculous complication, though it is believed that he would do so now. It would be out of place to discuss here the pathological findings described by Muir and the conclusions drawn from them, but it is to be noted that he concludes that they support the view that the "main factor determining the one type from the other is . . . the degree of resistance."

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