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THE DYNAMIC CLASSIFICATION OF THE FORMS OF LEPROSY

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INTRODUCTION

The prevailing classification of the forms of leprosy is based on the morphological principle. Dependent upon whether the skin or the nerves are affected by the process almost exclusively, leprosy has been divided into nodular (skin), maculo-anesthetic (nerve), and mixed forms, the last being intermediate between the others. This division, however, has long ceased to satisfy leprologists, and changes of one kind and another have been and are being introduced. In 1931 the Leonard Wood Memorial Conference on Leprosy, held in Manila, adopted a classification by which leprosy is divided into "cutaneous" and "neural" types, and each is subdivided into three groups, slight, intermediate and severe, according to the degree of the affection.

This new classification is more suitable for clinical purposes than the older one, but it is based on the principle of the degree of advancement of the leprosy process and is therefore one-sided. A clinician is interested principally in the dynamic process, and in the possibility of finding in each case features which characterize a given phase of the illness. Such features are manifested not only by the spatial spread of the process, but by the general condition of the patient's organism and especially by its immuno-biological condition. The intensity of the infection (i.e., the number and virulence of leprosy bacilli in the organism) plays a very important

role, but the leading role belongs to the organism itself, to its ability to antagonize the bacilli through the processes of immunity.

Almost fifty years ago Mechnikov wrote that leprosy, a chronic disease closely resembling tuberculosis, should be regarded as a prolonged struggle of mesodermic phagocytes against the invasion of the causative bacilli, and that these cells produce a granuloma and function as phagocytes, destroying bacilli which they contain. Mechnikov was a founder of the doctrine of the reticulo-endothelial system, elaborated by Ashoff, Riyono and Landau. The role of this system in the processes of infectious diseases is generally recognized. From the histopathological viewpoint we have, in the majority of cases of leprosy, a chronic hyperplasia of the reticulo-endothelial system, and in studying questions of immunity and response to medical treatment we cannot ignore the functional condition of that system.

Many leprologists agree that adults are immune to leprosy and that infection generally takes place in infancy. At that age the mesenchymal tissues undergo changes which are not favorable for the struggle against micro-organisms and particularly against the leprosy bacillus. The reaction of the active mesenchyme (the reticulo-endothelial system) in infants at the beginning of infection tends much less to the establishment of immunity than in the direction of anaphylaxis. This is expressed by a weak fermentative activity of the system, which does not lead to the complete digestion of antigens in spite of pronounced phagocytosis. This phagocytic activity leads to the micro-organisms being easily retained, thereby explaining the susceptibility to infection, particularly by leprosy, in early childhood. The first signs of the disease in the patient's skin are not to be looked upon as the beginning of leprosy; that must be traced back to the immunity reaction.

Considering the fundamental features discussed, I divide the course of leprosy into four periods. Before describing them I shall review briefly the methods applied in the examination of patients in our clinic. These patients include not only those of our own clinic, but also those of all leprosaria of the North Caucasus.

Besides a general clinical examination, we investigate: (1) The oxidation processes, the acid-alkali equilibrium in the urine, the functional condition of the thyroid gland (determination of the basal exchange and other tests), and the functional condition of the sex glands.

(2) The functional condition of the reticulo-endothelial

system, determining its absorptive capacity by the congo red index. Formerly we used the Adler and Reimon methods but more recently the more accurate and simple one of Nicolaev has been employed. An increase or decrease in the index (normal 0.4 to 0.5) denotes a corresponding change of the absorption function. Patients with kidney disease are not suitable for the test. The leukocyte formula is ascertained, with special attention to the number of monocytes and leukocytes.

FIRST PERIOD, LEPRO I

The first, or latent period of leprosy varies on the average from 2 to 5 up to 10 years. Rogers believes that the length of this period depends upon the mode of infection. It is generally agreed that the presence of pathogenic organisms in the body promotes, in certain cases, a condition of immunization, and that as the immune element of a population increases there is a decrease not only of the obvious and abortive forms of an infectious disease, but also of the latent infections. In leprosy as in other infectious diseases the germs may be harbored under acute and chronic conditions (Malinin). Their acute or temporary presence is an accidental phenomenon and is not of special interest. On the other hand chronic harboring of bacilli is very interesting. In leprosy, in the absence of visible clinical manifestations, that condition must be considered as a latent form of the disease in which the carrier may develop immunity against it or from which clinical leprosy may develop.

The frequency and continuance of latent leprosy may be ascertained by systematic and prolonged study of persons who have been in contact with lepers. Among 235 clinically healthy members of families of lepers in the Cuban District, Malinin discovered 21 who carried the bacilli, almost ten percent. Malinin and Strookov made skin tests with Kulesha's leprin in 16 apparently normal contacts and found leprosy bacilli in the noses of four, together with positive leprin reactions.

Thus the initial period of leprosy is a quiescent phase. Persistent visible skin signs of the disease are not seen, but Hansen bacilli are often found in the nose and glands; the latter may contain the bacilli for a rather long period without any manifestation of the disease. Evidently in some cases this period terminates with the acquisition of immunity. Usually, however, the bacilli increase and give rise to a number of signs which indicate a tendency to the development of the disease. These prodromal

signs may present nothing characteristic, and they may be absent. The occurrence and persistence of these signs is not uniform, but taking into consideration the sources of infection and the nature of the prodromal signs it is possible, in some cases, to diagnose leprosy.

These symptoms are: (a) Dry rhinitis, with scars and cracks of the mucosa, also with bleeding, which tends to appear in dry hot weather. (b) Swelling of certain lymphatic glands. (c) A number of abnormal sensations along the ulnar, superficial peroneal and posterior auricular nerves—burning, itching and tingling sensations in the limbs, with partial loss of sensitiveness and a feeling of numbness in the hands and feet at night. These phenomena increase after physical work. Sometimes they have a neuralgic character, relieved by pressure upon the nerve or by stretching the limbs. (d) Swelling of the face or lower extremities. (e) Headaches, high temperature and general weakness. (f) Pemphigus (rare). (g) Disturbance of the sweat and fat functions.

In the search for persons with leprosy it is important, besides looking for bacilli, to elicit and evaluate the symptoms mentioned. The struggle against leprosy will be successful on condition that we discover cases in the initial period of the disease, which is possible by the investigation of family sources. The methods which in venereal diseases have given gratifying results may, if applied in leprosy, greatly diminish and even in time eradicate this disease altogether.

Leprosy does not develop in every case that exhibits prodromal manifestations; in some cases immunity is acquired and the disease ends. If, however, immunity is not acquired and the disease shows progress the patient enters the second period.

SECOND PERIOD, LEPRO II

The course of the second, or florescent, stage of leprosy (termed *lepra florens*, denoting the tendency of the disease to progress), may be represented in the form of a parabola as it is subdivided into the initial period, the acme of the process, and the end of the florescence. From another viewpoint this stage may be divided into benign and malignant forms. To *lepra benigna* belong neural leprosy and some mixed forms; *lepra maligna* is the ordinary cutaneous type. The designation *lepra tuberosa* denotes only the presence of certain morphological elements of cutaneous leprosy.

At the earliest stage of the second period (*lepra incipiens*) there

appear spots that are of exceedingly diverse appearance and are often puzzling to the physician, especially as the bacteriological examination sometimes gives negative results. It is very difficult at this stage to predict the further course of the disease, whether it will develop into the benign or the malignant form; this will chiefly depend upon the functional condition of the reticulo-endothelial system and the mode of living of the patient.

LEPRA II BENIGNA

If the condition of the organism is unfavorable for the bacilli, the course of the disease may be benign (neural leprosy). The absence of a tendency to exacerbations of the disease (dependent upon leprous bacillemia), is an outstanding feature of the benign form. Abortive cases are encountered which, over long periods, show no other disturbances than one or several anesthetic spots or atrophy of muscles. The benign forms are encountered most often in old endemic foci of leprosy. The average duration of life is longer than in the malignant form. The bacilli, being localized in nerves, cause trophic changes which persist even when the bacilli disappear. It is not necessary to assume the existence of a special neurotrophic strain of the Hansen bacillus to explain this form of the disease, because there are cases in which it develops into the malignant one.

With regard to the functional condition of the reticulo-endothelial system in the initial stage of the second period, and in the benign form of the same period, no marked reaction is found histologically. The absorption, proliferation and fermento-oxidation functions are normal or sometimes slightly increased. All this may be considered as a manifestation of some degree of immunity.

LEPRA II MALIGNA

In cases in which the condition of the organism is such as to favor the development of the bacilli, the process spreads and new, permanent lesions are formed in the skin and the mucosa of the nose, mouth and larynx. The bacilli are found easily and in great numbers in the infiltrations and nodes that develop in the skin and also in the nasal excretions and in gland-puncture material. This is the malignant form of the secondary period, or nodular leprosy according to the morphological classification, and it includes a majority of the mixed forms.

This form often begins with fever and a papular or roseolate rash. Some of the spots disappear but others begin to infiltrate, giving rise to nodules and infiltrations. Lepers are in general sub-

ject to fever, but the malignant form of leprosy is characterized by exacerbations or reactions of special nature. Lepra reaction is a leprous septicemia, and in the majority of cases it is possible to find bacilli in the peripheral blood. During the reaction there is hyperleukocytosis. Sometimes new lesions appear, with increase of the inflammatory phenomena in old ones; the reaction itself is evidence of dissemination of the bacilli. After such a reaction there is extension of the leprous process, numerous new granulomas of one kind or another appearing in the skin and mucous membranes. Skin lesions also extend by continuity because of the spread of the bacilli along the lymphatic vessels and tissue spaces. With the development of the process described the number of leukocytes is at the highest limit of normal. In consequence of all this the course of lepra reaction is in some cases very acute, in others subacute, and in still others weak.

Patients with the malignant form of leprosy are subject to lowering of the oxidation processes and, at times, a change of metabolism toward acidosis. My colleague, Peshkovsky, has observed that this tendency coincides with clinical deterioration. Therefore it is important to avoid all factors which weaken and exhaust the organism and promote acidosis, such as pregnancy, chills, psychical trauma, bad nutrition, serious surgical interference and incorrect therapy.

As for the functional condition of the reticulo-endothelial system, which Peshkovsky has studied extensively: (a) In the less advanced cases (in which the process has affected only the face and the peripheral parts of the extremities) the absorptive function is normal or increased. Monocytosis reaches on the average 16 percent, with a decrease of the polymorphonuclear leukocytes and lymphocytes. (b) With the spread of the process, when it is at its height monocytes still average 14 to 16 percent but absorption is lowered; the leukocytes show a shift to the left and they and the lymphocytes are fewer than normal. Since with increase of the reticulo-endothelial cells there should be increase of absorption, there is a seeming contradiction here, but this disappears when we consider that the abundance of the products of cell decomposition and the enormous quantities of bacilli must cause a blockage of the reticulo-endothelial system. (c) When the malignancy of the process is very marked, leading to almost universal involvement of the skin, the functional condition of the reticulo-endothelial system is further lowered, affecting both its absorptive and proliferative functions, monocytes being

at the lower limit of normal. Leukocytes show a marked shift to the left. The more developed the process is, and the more marked the blockage of the reticulo-endothelial system, the greater will be the tendency to acidosis and to lowering of the oxidation processes.

However, the course of the disease does not always go in this direction. Decrease of the process and even retrogression of some lesions occurs from time to time, with temporary approach of the functional condition of the reticulo-endothelial system to normal and increase of the oxidation processes. But this improvement is not constant and later the condition becomes worse than before. This wavelike course of the malignant form of leprosy leads some physicians to believe this spontaneous improvement to result from treatment, while others become pessimistic and think that nothing helps. It is important to try to prolong these spontaneous improvements by means of an adequate regime and careful therapeutic measures. It is necessary to avoid augmenting the blockage of the reticulo-endothelial system, which aggravates the process. Leprous infiltrations occur in the larynx and obstruct breathing; this increases the tendency to acidosis and to aggravation of the process, and makes it desirable to perform tracheotomy promptly.

Besides the kind of lepra reaction that has been discussed, our clinic distinguishes another kind, which causes no aggravation of the disease and which we call benign lepra reaction, or inflammatory exacerbation. Commonly the Hansen bacilli are taken up by monocytes, but various workers have found them in neutrophils; this has been studied in detail by Peshkovsky. In cases of the benign form of reaction there is fever and reddening of the lesions, as in the other form, but the inflammatory condition goes on to suppuration. The purulent exudate does not give rise to any growth on culture media. Microscopically one finds great numbers of neutrophils which have taken up masses of leprosy bacilli that are in different stages of degeneration. There may be leukocytosis, with increase of the neutrophils. With regard to the reticulo-endothelial system, there is increase of the absorptive function, while the proliferative function does not exceed normal. At the end of this acute condition the ulcerated lepromata heal by scarring. Blood lymphocytes are increased while the leukocytes have decreased to normal. This benign reaction must be distinguished from the general lepra reaction accompanied by bacillemia and monocytosis, with the appearance of new lesions. It

denotes increase of the fermento-oxidative processes in the reticulo-endothelial system (i.e., the immuno-biological processes), and after it is over the patient is improved.

There is a difference of opinion as to the desirability of the occurrence of lepra reaction during treatment. The Philippine leprologists, Lara and Rodriguez, consider it undesirable, whereas Rogers looks upon it as beneficial. To my mind the question does not have a single answer. In patients in whom the defensive functions are lowered, reaction results in aggravation of the disease. In the benign reaction the defensive power is augmented, and as a result there is steady clinical improvement. Such a reaction is therefore desirable. If the majority of our patients would respond to the invasion of the bacillus in such a manner, leprosy would not be as serious a disease as it is. Unfortunately, this form of reaction rarely occurs.

THIRD PERIOD, LEPRA III

The second period gradually develops into the third, the period of relative stability, in which there has been acquired a considerable degree of immunity, because of which the tendency to exacerbation of the disease has almost disappeared. According to the morphological classification this period corresponds to the so-called "closed" forms of nodular or mixed leprosy, with the regression of the lesions, and those forms of nerve leprosy which have passed into a stable condition. The patient may hope to be relatively cured except in so far as there has been permanent injury which may disable him. Bacilli are not found on examination of the mucous membranes and skin. By administering potassium iodide by mouth one may get evidence as to whether there are any fresh foci of the disease or any predisposition to exacerbation. Potassium iodide tends to cause increased hydremia of the tissues and increased proliferation of monocytes. The latter change, without elevation of the fermento-oxidation function, promotes the development of lepromas; this, with hydremia of the tissues, stimulates dissemination of the infection through the body. If the potassium iodide test causes no disturbance in a patient who for several months has not been given antileprosy treatment and has shown no evidence of relapse, the patient may be looked upon as apparently symptom-free and noninfectious.

The ultimate prognosis depends upon the conduct of the patient. In releasing him from the leprosarium as relatively cured, account should be taken of the circumstances under which he will

live; under unfavorable conditions relapse is likely to occur. The experience of the Philippine leprologists has shown that relative clinical cure may be assumed if in the course of four years no relapse occurs and the skin and mucous membranes remain negative for bacilli. It appears that the liver and spleen become free from bacilli in a relatively short time whereas the nerves, lymphatic glands and testicles retain them for a long period.

Sometimes it is difficult to decide whether a patient is still in the second period of leprosy, toward its end, or has entered the third period. Clinical observations and a number of investigations will help to solve this question. At this period the oxidation processes are normal and the functional condition of the reticulo-endothelial system shows no marked abnormality.

FOURTH PERIOD, LEPRA IV

Some patients, having passed the first three periods of leprosy, emerge into the fourth one—the healed period, beyond danger of relapse. This as a rule is a rare occurrence. By this time patients have extensive anesthetics, have acquired deformities through muscular atrophy and the loss of bone or cartilage, and often have lost vision and voice. The body has overcome the infection but is in a deformed condition. These patients are invalids, needing appropriate care which is best given them in special institutions and not in the regular leprosaria, where their outward appearance will affect unfavorably the new patients.

CLASSIFICATION AND TREATMENT

Every classification is to a greater or less extent conditional, as it is impossible to reflect in any one all of the manifold clinical manifestations of the disease. The classification offered by me has justified itself in connection with therapeutic treatment, which is the main basis of any classification. Medical treatment of leprosy is full of contradictions, and it is almost impossible to form a clear idea of why certain remedies have given gratifying results in some cases and have failed to be beneficial in others. This has been shown conspicuously by recent reports on dye therapy. There is no single specific remedy for leprosy analogous to mercury and salvarsan for syphilis or quinine for malaria; Paldrock's method with carbon dioxide snow and salganol cannot be considered of that nature. In the treatment of leprosy by new remedies there exists empirism and infatuation. Treatment of such a chronic disease must be based on the dynamics of the process and the immuno-

logical condition of the organism, and not alone on the spatial spread of the disease process.

On this principle the patients in our clinic are divided, with respect to treatment, into two large groups according to the functional condition of the reticulo-endothelial system and the oxidation processes. The first group (A) comprises the milder forms of the disease. To the second group (B) belong the bulk of our patients, who are in the stage lepra II maligna (lepra cutanea, C2-C3) in active forms.

GROUP A

Subgroup 1.—Patients with lepra incipiens showing unique lesions as regards morphological classification (lepra macan).

Subgroup 2.—Patients with lepra II benigna (lepra nervosa), no account being taken of the extent or degree of the process.

Subgroup 3.—Patients with lepra II maligna (lepra cutanea, C2-C3) in a stage of prolonged remission.

Subgroup 4.—Patients with lepra II maligna (lepra cutanea, C2-C3) with a tendency to benign lepra reaction.

Subgroup 5.—Patients with lepra III (lepra cutanea; C2-C3), without disturbances of the functional condition of the reticulo-endothelial system.

Such patients are subjected to energetic chaulmoogra treatment, aurotherapy, and carbon-dioxide and other irritative treatment. They are suitable for trial of dye therapy.

GROUP B

Subgroup 1.—Patients with lepra II maligna of moderate degree (face and peripheral parts of extremities involved), with increased absorptive and proliferative functions of the reticulo-endothelial system and normal oxidation processes.

Subgroup 2.—Patients with lepra maligna at the acme of its development (the face, extremities and often the body being involved, with affection of the eyes and the upper respiratory tract); they are subject to frequent lepra reactions. The absorptive function of the reticulo-endothelial system is lowered and the proliferative function is still elevated; there is decrease of neutrophils and marked shift to the left; the oxidation processes are lowered and there is a tendency to acidosis.

Subgroup 3.—Patients in which the process is still more marked. The number of monocytes reaches the upper limit of

normal; the shift to the left is more pronounced. Lepra reaction takes place less frequently and is generally mild.

Comparing the last two subgroups, in the second one there is blockage of reticulo-endothelial system but increased proliferation expressed clinically in the extension of the superficial lesions. In the third one there is no further proliferation or extension of the process, the latter having become nearly universal. Lowering of the oxidation processes is more pronounced than in the second subgroup.

Treatment of these subgroups differs. In the first one we recommend the careful use of chaulmoogra preparations, together with gentle cauterization. With regard to the second and third subgroups, considering that the patients are as if clad with leprous tissues, it is necessary primarily to increase the tissue exchange and by this to promote diminution of acidosis and increase of the absorption function of reticulo-endothelial system. Neutral baths are very beneficial. A suitable regime, with regular nutrition and a temporary salt-free diet are required. An attempt should be made to increase the fermento-oxidation processes by any means possible. For this purpose intramuscular injections of urogravidan have so far given the best results; a number of organo-therapeutic preparations have been used with no success. If a remedy can be found that will elevate those processes over a prolonged period, leprosy will be less serious than it is now, when we are practically powerless to render these patients any help.

Antileprosy treatment (chaulmoogra, dyes, aurotherapy, CO₂) of patients in the second subgroup only tends to aggravation of the disease, with in some cases untimely loss of vision. However, when such patients pass into a stage of more or less prolonged remission (cessation of the process, lowering of monocytosis, increase of neutrophiles, and disappearance of acidosis), it is permissible to resort to antileprotic therapy (see Group A, subgroup 3). Such treatment of the third subgroup I consider useless; none of the known remedies can benefit them in any way. These patients need a sanatorium regime and general tonic therapy.

For lepra reaction, at the beginning we generally apply auto-hemotherapy, followed by the intravenous injections of calcium. Antileprosy treatment is given, if at all, only after the reaction has subsided.

In conclusion, it is my belief that the classification of the future will be the dynamic one, and not a modification of the

morphological one. The perfecting of the dynamic classification should occupy our attention, and should be given our joint collective efforts and judgment. This is not to be understood to mean that the morphological classification is to be ignored, but that the dynamic one should take the predominant place. The morphological classification must be secondary, as when I write, for example: *Lepra II benigna: maculae anaestheticae corporis et extremitatum*; or *Lepra II maligna remissiva seu progressive: infiltratio frontis et tubercula faciei et extremitatum*.