

# Prognosis in Leprosy.

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## INTRODUCTION.

THE more a disease is dreaded the more important is a reliable prognosis. Leprosy is not a fatal disease. In northern India the majority of clinically diagnosed cases never progress to the more serious forms of leprosy, and cause little or no physical inconvenience. But fear of the severer forms and of the well-known deformities may cause mental depression and distress which may in itself predispose to the increase of the disease. On the other hand a hopeful prognosis, when founded on reliable data, is often a most valuable asset in helping towards recovery.

## DETERMINING FACTORS.

The important determining factors in making a prognosis in leprosy may be summarised as follows :—

The degree of natural resistance, which may possibly vary in individuals, though definite proof of this is lacking.

The age factor. The resistance to leprous infection is low during the first few years of life.

The general health. The more chronic and non-toxic an infectious disease is the more relative importance does this factor assume.

Depressed immunity due to hyperinfection.

Acquired immunity as the result of small (subliminal) infections.

1. *Natural resistance* to leprosy is strong in healthy adults. Human leprosy has never been transmitted to experimental animals as a progressive disease, and their high resistance is apparently shared by healthy human adults. As

in most other infectious diseases the degree of natural resistance to leprosy is probably greater in some subjects than in others, apart altogether from the state of their general health. It has been stated by some writers that this natural resistance not only applies to the individual, but also that in areas where leprosy has for a long time been endemic the more susceptible races are gradually eliminated and that thus a race immunity is evolved. While this may possibly be argued from the analogy of certain other diseases, there is but little actual direct evidence in its support.

2. Natural immunity is most markedly influenced by the *age factor*. In early childhood the natural resistance to leprosy is very low. Our recent surveys in Calcutta and in the Bankura District of Bengal show that children who have lived in close contact from their earliest days with infectious relatives or servants, in households where special precautions were not taken, seldom escape the disease; and the majority develop the severe infectious cutaneous type of the disease. Older children and adults exposed apparently to the same infection commonly either escape the disease or develop mild non-infectious lesions of the neural type.

Children infected in the first few years of life often show the 'juvenile' type of the disease. Slight depigmented macules with roughening and keratosis of the surface of the skin appear on different parts of the body from time to time, but bacteriological examination of these lesions is generally negative. About the age of puberty these macules may disappear permanently with recovery of the patient, or they may develop and show the cutaneous and infectious type of the disease; much depends upon the general health as the determining factor.

3. The majority of those infected after the susceptible age period—say after the tenth year—escape the severe and infectious type of the disease. If however the general health is severely depressed, or is even slightly depressed for a long period, the cutaneous (severe) type of the disease may develop. Such depression of health may be caused by a variety of causes: complicating diseases, dietary errors, pregnancy, etc.

4. *Hyperinfection*.—Another cause of weakened resistance to leprosy is of a more specific nature, viz. the increase of the infection in the body beyond a certain degree. Thus a vicious circle is produced, the bacillary concentration facilitating the further increase of bacilli and paralysing the mechanism which would arrest that increase.

5. *Acquired specific immunity*.—In contrast to the above, is the effect of small infections, which generally tend to increase or supplement the natural resistance. Thus, in patients who have passed the age of increased susceptibility and are in fairly good health, contact even with highly infectious cases may, with or without the appearance of mild leprous lesions of the neural type, develop an acquired immunity, as shown by the leprolin test (described below). Even in healthy young children this specific immunity may be formed, provided that contact be not too frequent and the degree of infection be not too great.

While large infections diminish resistance, small infections increase resistance. Among healthy adults, there therefore tends to be a considerable hiatus between what we term 'resistant' and 'non-resistant' cases. In the former the disease frequently dies out or remains stationary for long periods of years without showing any tendency to increase; in the latter it tends to progress.

The hiatus between the resistant and non-resistant case may however be broken down by anything which impairs the general health. The infection often spreads in the peripheral nerves with or without any clinical signs. As however the number of bacilli increases, the hyperinfection factor comes into play and still further reduces resistance, so that the skin (which is naturally more resistant to the infection than the nerves) becomes infected, and the cutaneous type of leprosy develops.

#### ESTIMATION OF RESISTANCE

In determining the resistance of the patient we chiefly rely upon the clinical and bacteriological examination. In addition however the *leprolin test* is of considerable value in distinguishing between specifically resistant and non-resistant cases, and the *erythrocyte sedimentation test* in estimating the general resistance.

*The Leprolin Test*.— This test, first used by Mitsuda and more generally adapted by Hayashi, is of immense value in testing the degree of natural and acquired immunity and the degree of depressed immunity due to hyperinfection. There is not room here to go into the details of the test, so a short description must suffice.

In the modified form of the test used in Calcutta two leprolins are used: (a) a suspension of ground up human lepromatous material (Hansen leprolin), and (b) as a control a similar suspension of omentum, spleen, and liver of rats

suffering from advanced rat leprosy (Stefansky leprolin). These two suspensions contain respectively *M. leprae* and *M. leprae muris*, mixed with tissue debris. They are sterilised by heat and standardised so that they give equal reactions when 0.2 c.c. of each is injected intradermally in human subjects who have not been infected with leprosy. These leprolins when injected into the skin produce within a week or two at the sites of inoculation small nodules having the consistence of a pea, and varying in size with the degree of resistance; the greater the resistance the larger is the nodule formed.

In young children and in those with bad general health the reaction to both leprolins is weak or negative. In those who have acquired resistance due to small infections with leprosy, the reaction to Hansen leprolin is increased and appears stronger than that to Stefansky. Where however hyperinfection has taken place, and the bacilli have increased in the body, the reaction to Hansen leprolin is weak or negative, though in adults whose general health is otherwise good the reaction to Stefansky leprolin may be as strong as in non-lepers.

*The Erythrocyte Sedimentation Test.*—This test has been found of great value in estimating the general resistance of leprous patients. As a rule steady improvement takes place in patients whose sedimentation index is consistently low; i.e., whose erythrocytes when tested at regular intervals always sediment slowly. Almost all pathological and physiological conditions which cause increased rapidity of sedimentation also lower the resistance of the body to leprosy.

*Physical development.*—As in tuberculosis so in leprosy physical training is of great importance. In the former disease this has to be carried out slowly by carefully graduated exercises. In leprosy physical training can be carried out more rapidly as vital organs are seldom involved. As the muscles become firm the erythrocyte sedimentation index is in many cases gradually found to diminish (i.e. the cells fall more slowly), and progress towards recovery becomes more rapid. In lazy patients or in those who will not take sufficient exercise, improvement seldom takes place whatever treatment be used.

*The mental equipment of the patient.*—In a disease like leprosy which requires a painful form of treatment often extending over several years the mental condition and character of the patient are of vital importance, especially as the main part of the treatment (that of keeping himself

physically fit) depends upon the intelligent persistence of the patient.

#### MAKING THE PROGNOSIS.

Prognosis in connection with leprosy may be conveniently divided under three main heads:—

In infectious contacts (contacts with infectious cases) without signs of the disease, what is the likelihood of leprosy developing?

In those in whom leprosy has developed, and definite signs are present, what are the chances of recovery, how long will it take, what are the chances of relapse, will recovery take place with or without deformities and disablement?

How long should treatment be continued after active signs have disappeared, and how long should the patient be kept under observation?

1. *Infectious contacts*.—We use this term to indicate those who have been in contact with infectious cases of leprosy, but who have not so far shown any signs of leprosy.

In making a prognosis the most important point to be ascertained is the age when contact first took place. If this was within the first few years of life, and especially if there was prolonged and close contact with a highly infectious case, then, even though several years may have passed since then and no signs of the disease have been noticed, it is possible that a generalised infection may have taken place which will show itself sooner or later. In such cases the leprolin test is of great value. If the reaction to Hansen leprolin is stronger than that to Stefansky then the prognosis is good, as it indicates enhanced resistance to *M. leprae*. In such cases if there had been any considerable leprosy foci in the skin or peripheral nerves they would have induced cellular reaction and shown themselves clinically, and no slight bacillary foci are likely to survive long in such resistant cases, as they would be phagocytosed.

If the reaction to Hansen leprolin is negative, or weaker than that to the control, the prognosis is unfavourable. In such cases careful clinical examination with the aid of a suitable light will often reveal macules which had escaped notice before; or careful and repeated bacteriological examination of the skin or mucous membrane will show acid-fast bacilli.

In addition to these cases we have the 'juvenile' type of leprosy. The age factor, referred to above, lowers the resistance to the disease, and thereafter the hyperinfection

factor steps in and maintains the lowered resistance. The absence or obscurity of clinical signs is due to the state of symbiosis set up in the non-resistant tissues of the body, the cellular and other responses which are responsible for the appearance of lesions being at a minimum. If the general health of the child is poor then the possibility of general infection having taken place is considerably enhanced.

In the case of healthy adults who have been in contact with infectious cases and show no signs, the prognosis is as a rule much more favourable. If a considerable period has passed since contact took place then definite signs of the neural type of leprosy would probably have declared themselves if infection were present in the body. But here too the leprolin test is of great value.

In adults who are or who have been in a poor state of health, the danger of the infection developing is much greater. If there is a history of severe or prolonged disease or of other predisposing conditions during the interval since contact took place, if the sedimentation index is high, and if the reaction to Hansen leprolin is negative or weak as compared to the control, then a very guarded prognosis is necessary; re-examinations of the patient clinically and bacteriologically may reveal positive signs sooner or later.

Contact with leprous cases (whether infectious or not) frequently gives rise to '*leprophobia*'. This is particularly common in doctors who have treated cases of leprosy, but whose experience of the disease is meagre. Some light macule due to leucoderma, seborrhoea, tinea or some other skin disease is mistaken for a leprous lesion; or neuritis, connected with a septic condition elsewhere in the body, is mistaken for a leprous nerve condition. If the patient is in good health and his suspected lesion is clearly not leprous, then a definite negative diagnosis may set his mind at ease. Often a form of neurasthenia centres round this phobia, and the patient takes leave from his work and spends his time brooding over his supposed ailment. In such cases it is important to have the leave cancelled; assuring the patient that there is no danger of leprosy, and the return to absorption in work may be sufficient to clear up the neurasthenia.

2. *Patients with leprous lesions.*—In making a prognosis the important points to ascertain are the degree of infection and the special and general resistance of the patient to the disease. All patients should be divided into resistant and non-resistant groups. In doing this it is important to go carefully into the medical history of the patient especially

with regard to predisposing causes; also the general appearance, bacteriological examination, and the extent of the lesions may give a clear indication. The leprolin and sedimentation tests are of great value.

The following table gives the main distinction between resistant and non-resistant cases as seen in Bengal :—

*Resistant.*

One or only a few macules with anaesthesia to light touch, and with marked erythema; thickening and induration of the skin either through out the lesion or at the margin.

Thickening and tenderness of the sensory or mixed nerves connected with the macules.

Generalised infection of the skin is never present, the disease of the skin being confined to a few macules.

Lesions grow slowly or remain stationary for long periods, often for years.

Bacteriological examination of the skin shows few or no acid-fast bacilli.

There is strong reaction to Hansen's as compared to Stefansky's leprolin.

*Non-resistant.*

More numerous and widespread and flatter lesions without marked erythematous thickening or induration, the margin merging with the surrounding skin. Erythema less marked. Hypopigmentation is more noticeable.

Nerve thickening as a rule not marked.

In advanced cases skin involment may be widespread, covering the whole body, with no appearance of macules. While in some of these cases there is noticeable thickening and nodulation, in others it is difficult to recognise the presence of disease on inspection though bacteriological examination shows widespread infection.

New lesions continually appear and macules grow rapidly in size and coalesce, until almost the whole skin is involved.

Bacilli are found in lesions of the skin and nasal mucosa in greater or smaller numbers.

Reaction to Hansen's leprolin is absent or very weak.

In resistant cases the prognosis is excellent provided the patient remains in at least moderately good general health. The lesions should disappear under treatment in a comparatively short time (a few weeks to a few months); and the danger of relapse, once all signs of active disease have disappeared from the skin and the nerves, is very small, provided that the patient's general health is maintained.

In non-resistant cases the prognosis is much more doubtful. If the general health is good, or if under suitable treatment it becomes good, and especially if the sedimentation of erythrocytes is slow, then a favourable though guarded prognosis may be given. The period of treatment necessary will however be much more prolonged. In many cases of low resistance a definite prognosis should be delayed until there has been time to observe the progress made under

general and special treatment. The effective treatment of complicating diseases, along with the carrying out of a strict régime of careful diet, active and suitable exercise and regular habits, is often found to bring about within a few months, or it may be in one or two years, improvement up to a certain point, after which the patient progresses steadily towards recovery, though several years may be necessary to get rid of all active signs.

The question of recovery, with or without permanent lesions and deformity, is an important one for the patient. The earlier treatment is begun and the more carefully it is carried out, the less likelihood is there of the development of trophic lesions of the hands, feet, and face. Carefully planned physical exercise is very important in this connection. Nerve reaction in the ulnar and peroneal nerves, which so commonly results in claw hand and drop foot, seldom occur in patients with firm well-developed muscles. In most cases a certain amount of anæsthesia and, if the larger mixed nerves have been involved, of trophic changes in the small muscles are likely to persist. These should not be mistaken for active signs of disease.

3. The length of treatment and the period of observation necessary after the cessation of treatment are matters of extreme importance. Treatment is frequently stopped far too soon, and relapse follows causing disappointment to the patient and loss of confidence in the treatment of leprosy.

In non-resistant cases clinical appearances are most deceptive. Lesions will often disappear due to the effect of complicating diseases, the resultant depression of cellular reaction to *M. leprae* giving a false appearance of improvement. Bacteriological examination should be carried out thoroughly and repeatedly till the results become negative in smears taken from all parts of the body, before the disease is declared quiescent. The disease should have remained quiescent for at least two years before it is declared arrested. Thereafter the patient should remain under observation for several years until the reaction to Hansen leprolin becomes stronger than that to Stefansky leprolin. The reason for this prolonged observation period after routine bacteriological examination has become negative is that, though bacilli may be absent from the skin and nasal mucosa, they may still remain present in the peripheral nerves.

In resistant cases the necessary period of treatment and after-observation is much shorter. In most of them bacteriological examination is negative from the beginning or only



very few bacilli can be found in the lesions. In resistant cases the criteria of quiescence and arrest must therefore be based chiefly upon clinical appearances; (*a*) lesions are flattened out, so that the finger on passing along the surface from the normal skin to the lesion cannot detect any raised margin, and the skin picked up between finger and thumb feels no thicker than the healthy surrounding skin; (*b*) thickened nerves lose their tenderness on pressure or percussion, and became reduced to their normal size; (*c*) no new lesions appear, and the original lesions no longer increase in size; (*d*) the areas of anæsthesia, though not entirely disappearing, remain stationary in size; neither increasing nor diminishing.

#### SUMMARY

1. A reliable prognosis in leprosy is important because of the dread in which the disease is held, and because mild, easily arrested resistant cases are apt to be confused with and bear the stigma attributable to the more serious incurable and infectious forms of the disease.

2. The degree of general and specific resistance of the patient is all-important in making an accurate prognosis. The methods of determining the resistance by clinical and bacteriological examination, with the aid of the leprolin and erythrocyte sedimentation tests are described.

3. The danger to young children in contact with infectious cases is discussed.

4. We described the methods of determining the length of treatment and how long the patient should remain under observation after the disease is *arrested*.