# PLANTAR HYPERALGESIA AND THE PROGNOSIS AND TREATMENT OF LEPROSY

By Gordon A. Ryrie
*Medical Superintendent, Sungei Buloh Settlement*
*Kuala Lumpur, Selangor, F. M. S.*

I

It has been observed for some time past in Sungei Buloh that in a large number of lepromatous cases there appears to be a definite relationship between activity of the disease and plantar hyperalgesia, elicited by firm stroking or pressure along the sole of the foot. The degree of pain so elicited seems in many cases to be in direct ratio to the degree of activation, and it can frequently be detected before other signs of activity are readily discernable. It has thus been found that plantar hyperalgesia gives information of value in the prognosis and treatment of individual cases, and that it may constitute a useful index of intensity of the disease.

Before describing the indications for and practical use of this test it may clarify matters if a description is given of how it came to be evolved. The first indication of its use was discovered here some years ago during the study of lepra reaction.[1] In dark skinned races reaction spots are difficult to see, and in certain cases they may not appear until a considerable time after fever has been established. I therefore endeavored to find confirmatory signs of the reaction condition other than the presence of spots. Only three observations need concern us here. The figures refer to severe, hospitalized cases only.

1. In about 15 to 20 percent of cases of lepra reaction in Sungei Buloh the cerebrospinal fluid is under pressure. The incidence of this phenomenon may possibly vary in different countries. Three years ago, through the courtesy of the physicians at Culion, in the Philippines, I was able to tap the cerebrospinal fluid of 22 reaction cases and in 16 of them it was found to be under pressure. There appear to be no abnormal constituents in the fluid, and the usual routine tests are negative. Removal

[1]The term "lepra reaction" as used in this report applies only to that condition in lepromatous cases.

of the fluid sometimes gives temporary relief from the myalgia which is frequently associated with severe reaction. Pressure seems to occur during the acute rising stage and not during the subsiding or chronic phases.

2. In about 15 percent of cases here, knee clonus can be elicited during reaction. The knee clonus may be unilateral or bilateral. On recovery the sign disappears.

3. In about 25 percent of our cases the knee jerks are exaggerated. This again may be unilateral or bilateral, and again on recovery the reflex returns to normal.

These observations, though they are of definite interest, do not provide a "constant" in lepra reaction. Further investigations, however, revealed that in practically all reaction cases in Sungei Buloh the test for Babinski's sign caused sharp pain. Babinski's sign is not positive—i.e., there is no deviation from the normal toe response—but the heavy stroking along the sole of the foot causes considerable localized pain. This hyperalgesia is modified in cases where there is anesthesia of the soles, a condition I will deal with later.

Two important points were noted with regard to the hyperalgesia in the reaction condition. One was that except where modified by anesthesia it appeared to be a practically constant sign. The second was that, unlike the other changes mentioned, it did not disappear for a varying time after the reaction died down.

II

At this stage of the investigation, then, it appeared that plantar hyperalgesia would be of some theoretical interest, while its practical value would be that of a useful minor confirmatory sign in the diagnosis of lepra reaction. Further work, however, revealed the fact that a considerable percentage of leprosy cases had plantar hyperalgesia although there were no signs of reaction. It was found in varying degrees in 477 out of 1,117 lepromatous cases, as is shown in Table 1.

Further analysis of these cases indicated that they formed at least four separate groups.

1. Cases with plantar analgesia and anesthesia of varying degrees; these are classified as PA−. This group was found to be a heterogenous one, which can be put aside for the time being.

2. Patients with normal plantar sensation, on testing first with cotton wool and then by heavy stroking; these are classified as PA ±.

3. A group in which varying degrees of definite hyperalgesia were elicited by heavy plantar stroking; these are classified as PA+ and PA++, according to the degree of pain.

4. Lepra reaction cases with severe pain on heavy stroking; these are marked cases, PA+++.

TABLE 1. *Deep plantar sensitiveness in 1,117 lepromatous cases in Sungei Buloh.*

| Type | Cases with no response or normal sensation | Cases with plantar hyperalgesia | Total |
|---|---|---|---|
| L1..... | 117 | 128 (52%) | 245 |
| L2..... | 239 | 187 (43%) | 426 |
| L3..... | 284 | 162 (36%) | 446 |
| TOTAL..... | 640 | 477 (43%) | 1,117 |

The two important groups for further study appeared to be (*a*) the normals on the one hand (PA ±), and (*b*) the nonreaction painful group (PA+ and PA++) on the other.

A general examination of the histories of the cases in these groups and of their progress under treatment revealed some suggestive indications. In both groups there were patients improving under treatment, but improvement was more common in the normal group while record of phases of ulceration, rapid spread of leprosy, and reactions seemed to be much more frequent among the hyperalgesic cases. The suggestion began to formulate itself that these PA groupings might represent clinical phases of the disease.

Before further investigations could be undertaken it was deemed necessary to obtain information on the incidence of plantar hyperalgesia in nonlepers.

In the General Hospital in Kuala Lumpur, 422 nonleper patients were tested for plantar hyperalgesia. These cases were as follows: malaria, 32 cases; beriberi, 9; pulmonary tuberculosis, 42; chronic dysentery, 14; tertiary syphilis, 16; general fevers, 97; other general diseases, 212. Of the 9 cases of beriberi, 2 had moderate hyperalgesia. Of the 16 cases of tertiary syphilis, 4 also had hyperalgesia; in these four Rhomberg's sign was positive and the Argyll-Robertson pupil could be demonstrated. Under general diseases, 5 cases with hyperalgesia were found; 3 of these had inflammation of the ankle joints, a fourth had acute neuritis and the fifth was suffering from hysteria. Thus out of these 422 cases 11, or 2.6 per-

cent, had plantar hyperalgesia. In every instance the underlying cause was either obvious or readily demonstrable.

During the examination of these cases close watch was kept for any possible variation between febrile and nonfebrile patients, and also between those who normally wore shoes and the habitually barefooted. There seemed to be little or no difference between febrile and nonfebrile cases. Those who wore shoes or sandals were on the whole more sensitive or ticklish than the others, but no significant difference was observed.

To recapitulate thus far: Plantar hyperalgesia was found in most cases of lepra reaction and in a considerable number of lepromatous cases generally, the impression being that these on the whole were the cases who were not doing well. On the other hand no significant hyperalgesia was found among nonleper patients.

III

Further investigation now became necessary to determine more precisely the significance, if any, of this plantar hyperalgesia, and to ascertain if the groupings under it might represent clinical phases of the disease. Three further experiments were therefore undertaken.

*Experiment 1.*—It was determined to ascertain the relationship, if any, between the existence of hyperalgesia and the sedimentation rate of the blood. Accordingly 61 lepromatous patients, a mixed group of Malay, Chinese and Indian adult males, were selected at random. Normal plantar response to heavy stroking (PA ±) were obtained in 36 of them, while the remaining 25 were hyperalgesic in varying degree; none had plantar anesthesia. None of either group showed signs of reaction or other systemic illness. The sedimentation rate of each individual was determined, and the test was repeated during the next week as a check on error.

The differences between the first and second readings were negligible. In the 36 PA ± cases only one had a sedimentation rate over 40, and six were under 10; the average was 19. Of the 25 PA+ cases there were 4 with rates over 60, a further 9 rating between 40 and 60, and 5 under 10; the average rate was just over 30.

It is obvious that there are objections to drawing any definite conclusions from these figures. The sedimentation rate is not a specific test, and some nonleprotic debilitating factor might

theoretically both raise the sedimentation rate and the pain sensitivity. So far as it goes, however, it provides a certain amount of evidence that the patients with plantar hyperalgesia are less resistant than the normal or PA ± group.

*Experiment 2.*—A second experiment was made by estimating the incidence of positive bacterial findings in thick blood films. From 85 fresh patients chosen under the same conditions as in the previous experiment, blood was taken from the clinically normal finger tips by needle prick, after thorough cleansing of the part with alcohol. It is not proposed to discuss here whether positive findings by this method indicate bacillemia or otherwise; for the purpose of this investigation the point does not arise. Of the 48 cases of this group that had plantar hyperalgesia, 28, or 60 percent, had bacteriologically positive thick blood films. Of the 37 PA ± cases, 15, or 40 percent, were positive.

It is impossible to draw any definite conclusion from this experiment—almost any inference could be regarded as a *non sequitur*. So far as it goes, however, it tends to support the general impression gained in the investigation so far, namely, that plantar hyperalgesia appears to be connected with the more active phases of the disease.

*Experiment 3.*—In search of more definite information it was decided, if volunteers could be had, to take a further group of cases and give them gradually increasing doses of potassium iodide with the object of producing reaction in order to observe the plantar sensation daily during the stages between quiescence and reaction. It is perhaps to be regretted that the sedimentation rate was not taken daily as well, but there are limits to what a patient will stand and remain cooperative. Indeed, I was in considerable anxiety about the advisability of this experiment and about its possible clinical results. After full explanation twelve patients volunteered for it, on agreement that at the very first sign of reaction the potassium iodide should be stopped and vigorous antireaction treatment initiated.

Each patient was given one-quarter grain of potassium iodide each day for two days, then one-half grain daily for two days, then one grain a day for the next two days. Thereafter one grain was added to the dose every second day. Each day the plantar sensation was tested and any symptoms were noted. The results are so interesting that the cases are described individually.

CASE 1.—Chinese, L2, aged 27, PA ±. Became PA+ on the 7th day of the experiment (when receiving 1 grain). On the 14th day (when

receiving 5-grain doses) he complained of dryness of the mouth. On the 16th day there was flushing of the skin and the lesions appeared erythematous and more prominent. KI was stopped and an intravenous injection of 10 cc. of a saturated solution of fluorescein was given. This was repeated four days later (i.e., on the 20th day), when the lesions were observed to be subsiding. He remained PA+ until the 24th day, when he reverted to PA± and has continued so since.

CASE 2.—Chinese, L2, aged 33, PA±. Became PA+ on the 6th day (after the first 1-grain dose). On the 13th day complaint of loss of appetite. On the 15th and 16th days pain in the bones and knee joints. On the 17th day reaction spots appeared. KI was stopped and fluorescein treatment instituted as in the previous case. On the 24th day he became PA− and has remained so.

CASE 3.—Chinese, L3, aged 45, PA+. Became PA++ on the 15th day (after reaching the 5-grain dose), and complained of dryness of the mouth and chilliness. On the 18th day he felt feverish and reaction spots appeared. Antireaction treatment was given and the reaction subsided in a few days. On the 25th day he reverted to his original PA+ condition and has remained so.

CASE 4.—Chinese, L2, aged 21, PA±. On the 7th day (when on 1-grain doses) he became PA+. On the 11th day he became PA++ and on the 14th day reaction spots appeared. Antireaction treatment was started and by the 29th day the reaction spots had disappeared, but the patient has remained PA++.

CASE 5.—Chinese, L1, aged 42, PA+. On the 8th day he became PA++. On the 10th day he complained of weakness of hands and legs. One reaction spot was seen on the 14th day, and on the next day there were reaction spots on both legs. Antireaction treatment was given and on the 24th day the reaction had completely cleared up. The patient became PA± again and has remained so.

CASE 6.—Chinese, L2, aged 46, PA±. Complained of abdominal pain on the 4th day and became PA+ on the 6th day. On the 22nd day complained of chilliness and oral pain, and became PA++. Continued for 41 days without reaction, but remaining PA++ and complaining of general malaise. The experiment was then terminated.

CASE 7.—Chinese, L1-N1, aged 68, PA±. Became PA+ on the 4th day. Developed slight fever and a single reaction spot on the 15th day. Antireaction treatment given, with rapid disappearance of symptoms. Reverted to PA± on the 28th day.

CASE 8.—Chinese, L2, aged 32, PA±. Became PA+ on the 4th day but varied between ± and + until the 12th day, after which he remained PA+. On the 15th day the lesions became inflamed and antireaction treatment was given. On the 22nd day he reverted to PA±, but complained of numbness of the feet. On the 29th day he became PA− with slight edema of the legs. Admitted into hospital for concomitant disease.

CASE 9.—Chinese, L1, aged 48, PA±. Became PA+ on the 8th day and PA++ on the 13th day. On the 22nd day complained of pain in the legs and showed three reaction spots. The usual treatment was given

and the spots disappeared on the 24th day. On the 25th day he became PA+, and on the 27th he reverted to PA±.

CASE 10.—Chinese, L3, aged 56, PA±. Complained of fever, numbness of the feet and slight ulceration on the 15th day, but was still PA±. The experiment was stopped and restarted after three weeks. On the 2nd day after the restart (when the dose was still only ¼ grain) one reaction spot was seen; patient found to be PA++. Treatment was given and the reaction rapidly subsided. On the 11th day the patient became PA+; on the 15th day PA±.

CASE 11.—Indian, L2, aged 20, PA±. Became PA+ on 11th day and PA++ on 12th. Had fever on the 15th day and reaction spots on the 16th. Under treatment this condition cleared up rapidly. On the 22nd day he became PA+ and on the 30th PA±.

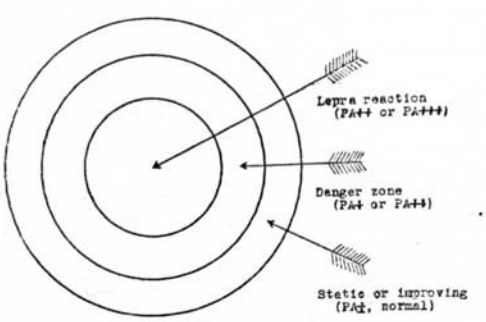
CASE 12.—Indian, L2, aged 20, PA±. Became PA+ on the 6th day and PA++ on the 9th. Had reaction spots on the 13th day, which cleared up under treatment. On the 21st day he became PA+, on the 23rd PA±.

These cases are extremely interesting and may be considered further. Twelve nonreaction lepromatous cases were given graduated doses of a drug that is known to induce lepra reaction. After varying amounts had been administered, 11 of the 12 developed reaction spots. It will be seen that in each of these cases the first observable sign in their induced progress towards reaction was the stimulation, or exaggeration, of the sensory response to pressure applied to the deeper structures of the foot. It cannot reasonably be assumed that potassium iodide itself (sometimes in doses of only a single grain) has the property of causing plantar hyperalgesia. It seems, therefore, a legitimate conclusion that in these cases the appearance of the plantar hyperalgesia was the first observable sign of activation of the disease.

We may again review the evidence so far gathered. Plantar hyperalgesia does not appear to be a significant feature of general, nonleprotic disease. It is, on the other hand, a usual feature of lepra reaction except where the disease itself has caused impairment of sensation. It occurs in a large number of nonreaction lepromatous cases, in general among those whose histories show that they are not doing well. In twelve cases where reaction was carefully induced with potassium iodide, it proved to be the earliest objective evidence of activity. The evidence that plantar hyperesthesia is associated with a higher sedimentation rate and increased incidence of bacteriologically positive thick-blood films cannot be held to be of any great significance in itself; it can only be considered as affording possible indications pointing in the same direction. These facts, together with consid-

erable general experience here, lead to the conclusion that for patients in Sungei Buloh we have an early objective danger signal of leprosy activation.

We can now visualize, as in Text-fig. 1, three leprotic zones which gradually merge into each other, but which can be differentiated by this test. So long as the patient is PA ± (i.e., with a normal response to heavy stroking of the foot) we may assume that the disease is not progressive, that either improvement is taking place or there is a more or less established symbiosis between tissue and bacillus. As I shall show later, this statement applies more particularly to L1 and L2 cases; findings in advanced lepromatous cases are somewhat complicated. When the patient becomes PA+ or PA++ however, it means that he is, so to speak, within bombing range of reaction, that his resistance is lowered and that the disease is activated.




TEXT-FIG. 1. Graphic representation of three zones in lepromatous leprosy, differentiated by the test for plantar hyperalgesia.

The possible value of this test in prognosis and treatment is at once apparent. One of the greatest difficulties in the therapeusis of leprosy is the elimination of "mass treatment." Mass treatment of groups of lepromatous cases means—unless the dosage is kept so low as to lessen effectiveness in many cases —that some proportion of them are definitely receiving unsuitable doses, and it will be agreed that unsuitable dosage can and does activate the disease. The fundamental difficulty has been that no readily available method for determining the optimum individual dose has hitherto existed. The sedimentation rate may be used as a guide, but in practice it is cumbersome if large numbers of patients are being treated, it is not very practicable in outpatient work, and many patients dislike it. Otherwise

dosage is a matter of empyricism—skilled or otherwise. An intelligent estimate of the proper individual dose needs considerable clinical experience, together with careful and repeated observations of the patient and periodical examination of bacteriological smears. In a great many cases it is largely a matter of trial and error.

What may be termed the P.A. method of determining individual dosage in lepromatous cases is now being tentatively employed in Sungei Buloh. When deep plantar sensation is normal, the dose is pushed up to what is considered to be a satisfactory maximum, and it is lowered when there is the slightest indication of hyperalgesia. When plantar hyperalgesia is elicited, patients are examined for concomitant ailments—pyorrhoea, helminthiasis, anemia, septic foci, etc., and prophylactic antireaction treatment is given. In addition, resistance is reinforced as far as possible by diatetic means. The aim is to get the patient back to a state of normal plantar sensation. The assumption is made that every patient with PA+ or PA++ is to be regarded as in danger until by general and specific methods his hyperalgesia is lowered.

*Technique of the test.*—The method used to elicit the plantar response is as follows: With a coarse wisp of cotton wool, brush lightly and without pressure over the plantar surface to determine if tactile sensation is intact. Hyperkeratosis if present has to be allowed for. Then with the wooden end of a pen or some similar instrument stroke firmly and evenly along the plantar surface from heel to toes. It helps if an assistant talks to the patient while this is being done. The normal sensory response is a feeling of pressure and ticklishness.

There are certain minor difficulties connected with the test. In some languages and with some patients "pain," "ticklishness," and "normal sensation" are not easily differentiated. This is especially the case where interpreters are employed, because of the almost universal tendency of interpreters in the East to avoid giving an exact translation of what has been said. It also arises when doctor and patient are using a *lingua franca* foreign to both. Nervous withdrawal of the foot sometimes occurs, more frequently with Indians than with Malays or Chinese, and this can be a real obstacle with some patients. The nervous effect may be marked—rarely there may be uncontrollable laughter, and in two instances I have seen the test cause spontaneous micturition.

Nervous withdrawal of the foot occurs immediately on the first touch or pressure; pain on the other hand occurs during the actual stroking. Response to pain varies considerably in different races and individuals, and this has to be allowed for. A Chinese patient, for instance, may state quite truthfully that the test has caused considerable pain although there has not been the slightest flicker of muscular response to indicate it. A Malay or Indian, on the other hand, may display a marked motor response to a lesser degree of pain. Another minor difficulty in practice is that patients in a queue tend to imitate the person previously examined, in their anxiety to do what is apparently expected of them.

Patients with anesthesia of the feet are difficult to assess, and each case must be considered individually. Obviously anyone with anesthesia of the soles and analgesia on heavy stroking is beyond the reach of this test; the prognosis, however, at this stage is usually obvious. On the other hand a patient may have anesthesia but be PA ± on heavy stroking. Here the overlying anesthesia may have dulled a response that might have otherwise been acutely painful. This has been observed in cases of actual reaction. The patient's statement that his feet are not anesthetic is no criterion; it is surprising how many patients are unaware of anesthesia of the soles. Such cases may be masked PA+, and would then have to be treated accordingly. A little practice enables one to form a fairly accurate judgment of them.

The results of this test in advanced cases require further elaboration. The prognosis and the response to treatment of L3 cases is unfortunately only too well known, without any test. It is, however, desirable to know if an advanced case is likely to develop a reaction. The results of the test in these cases are somewhat confusing to begin with. For instance, an L3 case may show obvious clinical activity and yet be PA ±. In general the more advanced the case the more feeble does the pain response or intensity index become. A PA+ in the L3 case must usually be interpreted as PA++, and the PA ± must often be regarded as PA+. As stated, the test is mainly of value in the L1 and L2 cases.

Although a PA+ or PA++ reaction indicates a poor prognosis so long as the patient remains in that state, normal plantar sensation should not be interpreted as indicating a hope

of cure. I believe that condition to be an indication that the progress of the disease is slow, or that it is quiescent for the time being, or that there is improvement. Clinically normal plantar sensation indicates that the patient will stand a good deal of therapeutic interference without any special risk of harm. Patients with plantar hyperalgesia may improve, but as long as they remain PA+ they are in the danger zone and improvement cannot mean much. The case with more or less continuous plantar hyperalgesia is on the reaction threshold all the time; he has accelerated the pace and will probably reach the burnt out stage more quickly.

Plantar hyperalgesia may be elicited in the tuberculoid variety of neural leprosy, but this has not been found to be of practical value. In such cases anesthesia and deformities are much more common than in lepromatous cases, which renders the test more difficult. But to the experienced eye tuberculoid activity is at once obvious, without any test. Furthermore, the treatment of that condition in practiced hands is so much more satisfactory than that of the lepromatous type of leprosy that special tests are not of the same value.

In actual application in Sungei Buloh the test has proved extremely satisfactory. With a little practice it gives patient and doctor confidence in the individual dosage. It takes little time, calls for no special equipment, and can be done by any reasonably intelligent and careful patient. Where the staff is limited it is a quick method of selecting those patients who need special attention.

## SUMMARY

1. Hyperalgesia of the deeper structures of the foot, as elicited by heavy stroking of the sole, has been found to be a usual accompaniment of lepra reaction in the lepromatous type of leprosy.

2. Out of 1,117 lepromatous cases examined, 477, or 43 percent, had plantar hyperalgesia of varying degrees. The records of these patients showed that most of them were not doing well.

3. Out of a control series of 422 nonleper patients, only 11, or 2.6 percent, had plantar hyperalgesia. In each of these cases the underlying cause—inflammation of ankle joints, etc. —was readily discernable.

4. In a small series of cases, patients with plantar hyperalgesia showed a tendency towards a higher erythrocyte sedimentation rate than did those with normal plantar sensation.

5. In a similar series, patients with plantar hyperalgesia showed a greater incidence of positive bacteriological findings in thick blood films than did cases with normal plantar sensation.

6. Twelve patients, ten of whom had normal deep plantar sensation and two of whom had slight pain on pressure, were given carefully graded, increasing doses of potassium iodide. In all of these cases the first indication of increased activity of the disease was increase of pain on plantar pressure. Upon recovery, sensation tended to revert to normal.

7. From the above experiments it is suggested that lepromatous leprosy can be divided into three zones (*a*) static or improving, with normal plantar sensation, (*b*) activated, with plantar hyperalgesia, and (*c*) "reacting," associated with considerable pain on plantar pressure.

8. The method by which this test came to be evolved is described and its practical use in prognosis and treatment is outlined.