

PRIMARY AND SECONDARY TUBERCULOID LEPROSY

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Tuberculoid leprosy was first reported as such by Jadassohn in 1898 (3), and then by Klingmüller in 1900 (4). In Japan, this condition was first observed by Dohi in the skin lesion of a case, and mentioned in a report presented at the Berlin conference in 1897 (1). Later, in 1909, Shiota (6) reported the observation of tuberculoid changes in a biopsy specimen of a thickened nerve. Furthermore, photographs published and moulages made before 1900 include examples of what we now call tuberculoid leprosy among the cases that used to be known as "macular" leprosy. There were undoubtedly many such cases in that form of the disease.

The term "tuberculoid leprosy" originated from histopathological nomenclature. The histological picture of the affected skin and thickened nerve is in accord with the so-called tuberculoid picture, consisting of Langhans' giant cells, lymphoid cells, and epithelioid cells. Very few leprosy bacilli are to be found, when any at all, in the Langhans' giant cells. This contrasts strikingly with what is found in lepromatous leprosy, although the two conditions are due to the same bacillus, for it propagates freely in the leproma cells. Why should there be this great difference?

This question, I believe, has been settled by means of the Mitsuda antigen, now called lepromin, which was first made in 1919 from boiled and triturated leproma. Intradermal injections of 0.1 cc. of this antigen were made in the upper forearm.

In lepromatous cases no reaction occurs, even after some weeks. In neural and tuberculoid cases, on the contrary, there appear at the site of the injection erythema, edema, and induration; and the induration persists for several weeks, sometimes for half a year. Ulceration occurs in especially strong positive reactions. The reaction is usually measured after two weeks, but further observation is also necessary. This is what is called the delayed Mitsuda reaction.

The distinction between lepromatous cases and those of neural and tuberculoid leprosy, thus established by the lepromin test, is due to the fact that persons with the latter forms of the disease possess the power of resistance to the leprosy bacillus. In biopsy specimens of the positive reaction nodules one commonly finds Langhans' giant cells as well as lymphoid cells and histiocytes. Although there are great numbers of bacilli in the antigen that is injected, very few can be found remaining in the tissue of the reaction nodule. This fact is entirely in accord with the findings in the lesions of tuberculoid leprosy itself.

If the antigen is injected into the skin of a healthy person, there

follows almost the same degree of erythema and induration as in neural or tuberculoid cases. An example of such a person who showed the strongest positive reaction is a leprosarium nurse who had taken care of the most serious cases, having had close connection with them, and who reacted to the test with a nodule that persisted for several months. This result can be ascribed to enhancement of her power of resistance, resulting from an induced immunity due to the entry of living bacilli into the body of the healthy person when in contact with the patients.

It is possible, I believe, that even dead bacilli such as those in the lepromin antigen can, if injected, endow an individual with the power of resistance to the infection. Just as BCG vaccination and the induction of tuberculin positivity is of value for protection against tuberculosis, so the injection of the lepromin antigen for the purpose of increasing the power of resistance should be practiced among the staff of the leprosarium, if with nobody else.

In the natural, primary, developmental tuberculoid leprosy there is high resistance of the body to the leprosy bacillus. Without ignoring this fact, we should nevertheless always apply chemotherapy to tuberculoid cases, in order to prevent later transformation to lepromatous leprosy.

Among the forms of leprosy, the most serious is the lepromatous one, in which the bacilli are able to propagate within the histiocytes of the skin and mucous membranes, leading ultimately to leontiasis, alopecia, blindness, and multiple peripheral paralyses and deformities. We have gradually succeeded in preventing the propagation of the bacilli, because of the benefits of chaulmoogra oil in former times and of promin and other sulfone drugs nowadays.

According to a report by Saikawa (5) he had, in the period when there was no other remedy than chaulmoogra oil, 51 well-absorbed lepromatous cases in which the condition had become entirely quiescent; and all of them gave positive lepromin reactions.

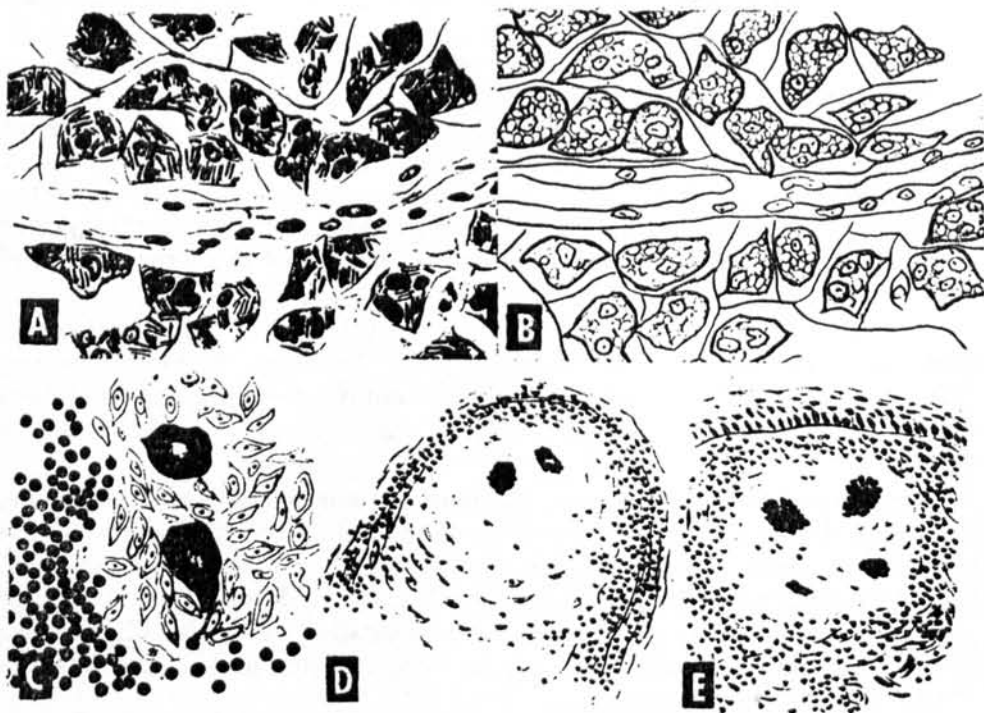
On comparison of the lepromin reactions before and after treatment of 184 lepromatous cases at Aisei-en in the collaborative study set up by Doull (2), it was found that 27 persons, or 14.7 per cent of the treatment group, had changed from negative to positive after 32 weeks of treatment. Doull also reported that in the Westfort leprosarium at Pretoria, South Africa, 38 of 229 cases (16.6%) changed to positive after 48 weeks of treatment. The tests in that instance were made with the Dharmendra antigen.

Of 700 lepromatous cases at Aisei-en who have recently been treated by promin injections by Saikawa, no less than 190 (27%) have given positive lepromin reactions. This rate of positivity is almost twice as high as that reported by Doull.

These findings contribute to the evidence that DDS derivatives are

effective against lepromatous leprosy. Such positive conversions are expected to increase more and more in the future.

Yokota (7) has studied the histopathology of the positive lepromin-reaction nodules of these cases converted from negative. In every instance he found the tuberculoid granulation tissue.



TEXT-FIG. 1. A. Lepromatous leprosy; lepromin reaction negative. B. Foamy-cell leproma; lepromin reaction negative. C. Primary tuberculoid leprosy; lepromin reaction positive (3+). D. Secondary tuberculoid neuritis, in a case of secondary tuberculoid leprosy with supraorbital neuralgia; lepromin reaction positive (3+). E. Tuberculoid picture in the late nodule of the lepromin reaction, of the same patient.

Thus, the positive conversion of the lepromin reaction in lepromatous leprosy demonstrates that the individual has acquired the power of resistance to the leprosy bacillus. In that event, I conclude, the immunological characteristics of the individual are similar to those responsible for the production of *primary* tuberculoid leprosy in a newly infected case. Hitherto such recovered lepromatous cases have been called "secondary neural leprosy." We can, however, sometimes find among these cases new foci showing the tuberculoid granulation in skin and nerves. So I advocate applying to them the special term, *secondary tuberculoid leprosy*.

SUMMARY

1. Primary tuberculoid leprosy is a manifestation of power of resistance against the leprosy bacillus on the part of the infected individual.

At this stage of the disease, suitable treatment will prevent its transforming to lepromatous leprosy.

2. The infiltrations and nodules of lepromatous leprosy, under treatment, are gradually absorbed, and the bacilli in the lepra cells are changed to lipid granules. When that happens, there is evidence of the individual's recovery of the power of resistance in the change of lepromin reactivity from negative to positive.

3. The histopathology of the positive leproma-reaction nodule in the "secondary neural" case corresponds to that of the tissue granuloma of tuberculoid leprosy. For this reason I advocate calling such cases "secondary tuberculoid."

4. The positive lepromin reaction should be determined by the delayed reaction, the lesion of which shows the tuberculoid histology.

RESUMEN

1. La lepra tuberculoidea primaria es una manifestación de la facultad de resistencia al bacilo leproso de parte del individuo infectado. En este período de la enfermedad, el tratamiento adecuado impedirá su transformación en lepra lepromatosa.

2. Las infiltraciones y los nódulos de la lepra lepromatosa, bajo tratamiento, se absorben gradualmente y los bacilos de las células leprosas se transforman en gránulos lipóideos. Cuando así sucede, hay signos de la recuperación por el individuo de su facultad de resistencia en el viraje de la reactividad a la lepromina de negativa a positiva.

3. La histopatología del nódulo positivo en la reacción a la lepromina en el caso "neural secundario" corresponde a la del tejido granulomatoso de la lepra tuberculoidea, por cuya razón se recomienda la designación de esos casos como "tuberculoideos secundarios."

4. En la reacción a la lepromina, la positividad debe determinarse por la reacción tardía, cuya lesión muestra la histología tuberculoidea.

Editor's note.—In the letter which accompanied the manuscript of this article, Dr. Mitsuda stated his views in somewhat different terms, essentially as follows: When under treatment with a drug like promin, which has been used to good effect in Japan for about ten years, the bacilli in the lepromatous lesions undergo disintegration and diminution, the lepromas are absorbed, and the reaction to lepromin changes from negative to positive. If the lepromin—reaction nodule is biopsied, the tuberculoid condition is found; the histological picture is very similar to that of the ordinary tuberculoid lesion, and very few of the injected bacilli of the antigen remain. In such cases thickening of nerves may be found, especially sensory nerves of the face, perhaps accompanied by neuralgia; and biopsy of such a nerve will reveal the tuberculoid picture. Such cases should be called "secondary tuberculoid."

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