

At the time of the Leonard Wood Memorial Working Clinical Conference on Leprosy, held in Japan in September 1952, advantage was taken of conversations with Drs. Kensuke Mitsuda and Yoshinobu Hayashi to clarify the history of the origin of the Mitsuda reaction.

This development began about 1917-1918, when Mitsuda was the director of what was then called the Zensei-en prefectural leprosarium, near Tokyo. Hayashi, who was his first assistant at that time, had been trying to grow the leprosy bacillus by incubating thin slices of nodules in Ringer's solution, and he believed that multiplication had occurred. With the suspension of bacilli so obtained he made some skin tests in leprosy cases, and reported his findings in 1918.¹ It appears that he also tried out a more concentrated leproma suspension in skin tests, but little was said of that. The reaction that he sought, he says, was one analogous to the tuberculin reaction, and in that he was disappointed. Because of pressure of other work, he being the executive officer of the leprosarium, he did nothing more in this field.

Mitsuda took up this matter from another point of view. He used three antigens prepared from lepromas, of which one was the supernatant of a suspension of fresh leproma which after separation was heated at 60°C. and phenolized; the second—the prototype of lepromin as it is usually made—was a suspension of a leproma which had been boiled for two hours in saline; and the third—if we understand it correctly—was the fluid in which the leproma had been boiled, containing very few bacilli. He not only observed the reactions during the first few days, but also watched them during the subsequent weeks, and thus he discovered the peculiar delayed reaction which bears his name. He appreciated the marked differences of results in lepromatous (tuberosa) cases on the one hand, and the "neural" (nervosa and maculosa) cases on the other hand, and made a few tests on asymptomatic children of leprosy patients and nonleprosy adults. His report of this work was published

¹ HAYASHI, Y. On a pure culture of leprosy bacilli, and a skin reaction by means of the pure culture suspension. *Saikingaku Zasshi* (*J. Bacteriol.*) No. 272 (1918) 51-53 (in Japanese).

in 1919²—not in 1916, as was erroneously stated in a later report by a then junior assistant, Fumio Hayashi.³

This work was unknown outside of Japan until Mitsuda reported it, very briefly, at the Strasbourg Conference in 1923.⁴ Whether or not that was the stimulus of the work reported by Mariani⁵ in the two following years, and by Bargehr in 1926,⁶ cannot be said because neither made mention of Mitsuda's report. Even in Japan the matter was given little attention until Fumio Hayashi took it up anew about 1930.

Drs. Mitsuda and Hayashi, when the matter was discussed with them last year, agreed to provide translations of the publications on the subject. That of Mitsuda's article is reprinted in full in this issue; that of Hayashi is included in a Letter to the Editor also in this issue. In view of the importance of the Mitsuda, or lepromin reaction these historical documents are regarded as of exceptional interest. As Mitsuda said in his covering letter—and the same would apply to Hayashi's material—the opinions expressed are those held at the time, and some have changed with the passing of time and with progress in knowledge of leprosy and of this reaction. —H. W. W. *ade*

² MITSUDA, K. On the value of a skin reaction to a suspension of leprosy nodules. *Hifuka Hinyoka Zasshi (Japanese J. Dermatol. & Urol.)* **19** (1919) 697-708 (in Japanese).

³ HAYASHI, F. Mitsuda's skin reaction in leprosy. *Internat. J. Leprosy* **1** (1933) 31-38; *Leprosy Rev.* **4** (1933) 159-165.

⁴ MITSUDA, K. Les lépreux maculo-nerveux, d'une part, les tubéreux, d'autre part, se comportent différemment à la suite d'une inoculation d'émulsion de tubercle lépreux. III^e Conf. Internat. Lèpre, Strasbourg, 1923; Paris, Baillière et Fils, 1924, pp. 219-220.

⁵ MARIANI, G. Osservazioni sopra una forma speciale di allergia cutanea nella lebbra (lepra tuberculoide sperimentale nell'uomo). *Pathologica* **16** (1924) 451-477. Nuove osservazioni sulle reazioni provocate sperimentalmente con materiale lebbroso nell'uomo. *Gior. taliano Dermat. e Sifil.* **66** (1925) 402-426.

⁶ BARGEHR, P. Künstliche lepraspezifische Allergie und aktive Immunisierung gegen Lepra. *Ztschr. Immun. u. Exp. Theraf.* **49** (1926) 346-353. Spezifische Hautreaktionen bei Lepra. *Ibid.* pp. 529-531.

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