

Clinical and Immunological Results obtained with the *Marianum* Antigen after more than Ten Years of Therapeutic Use

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In 1952 the experimental study of the *Marianum* antigen was begun at the St. Michel Leprosarium, Nden by DR. M. BLANC. His first report was on 457 patients in 1954. The results being satisfactory the antigen was applied in therapy for all new patients of the leprosarium. Since that time we estimate that about 1,500 patients have derived benefit from this therapy.

The present paper comprises a detailed report on the results obtained with combined treatment with sulphone and *Marianum* antigen over ten years.

The Mitsuda test is carried out on every patient before the treatment is begun, and the test repeated every year. Every six months bacteriological examinations are made. Using the customary technique, the patients every month receive one intradermal injection of 0.10 ml. of the *Marianum* antigen. This goes on for six months and is followed by a rest period of three months and then another course of injections is begun. The therapy is really a combined one with sulphone or other anti-leprosy drug, such as Ciba 1906, or Sultirene.

The results mentioned in this paper are expressed as such:

‘Arrested’ – no clinical nor bacteriological activity for one year;

‘Much improved’ – the clinical improvement is great, and the bacteriological examinations are negative for one year;

‘Improved’ – there is clinical improvement and bacteriological findings are still undecided;

‘Stationary’;

‘Worse’.

The reactions to the Mitsuda are described in the usual way:

Negative (—), Slightly positive (+), Positive (++),

Highly positive (+++).

1.—Results with 266 Actually Inmate Patients of the Leprosarium

These consisted of 57 Lepromatous,

64 Tuberculoid,

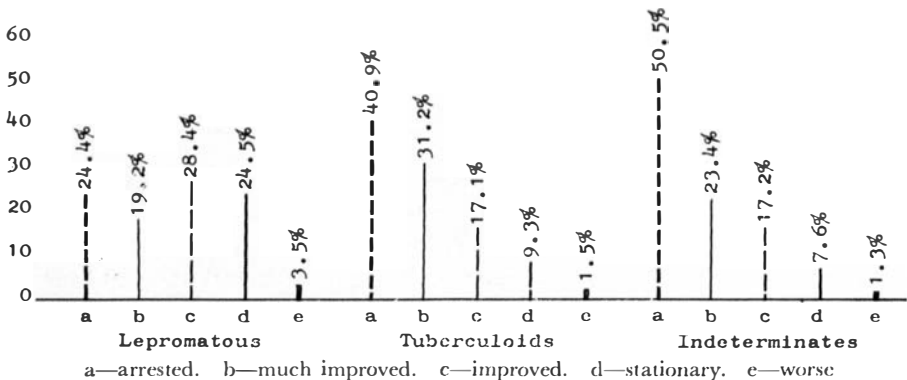
145 Indeterminate,

and their classification of leprosy was seen and adjusted by DR. MARTINEZ, of WHO in March 1961

The present clinical results are:

		<i>L.</i>	<i>T.</i>	<i>I.</i>		
'Arrested'		14	26	73	=	113
'Much improved' ..		11	20	34	=	65
'Improved'		16	11	25	=	52
'Stationary'		14	6	11	=	31
'Worse'		2	1	2	=	5

In relation with the type of case percentages are: (1)



Results can be summarized as follows:

Lepromatous = 72.1 per cent have benefited of the treatment, against 28 per cent without effect;

Tuberculoids = 89.2 per cent have benefited of the treatment, against 10.8 per cent without effect;

Indeterminates = 90.9 per cent have benefited of the treatment, against 8.8 per cent without effect.

For each of the above groups, the results are shown in relation with the number of injections received.

To achieve this result, we point out that in the three first groups of 'Arrested', 'Much improved,' and 'Improved', higher percentages are obtained from a large number of injections (between 30 and 40).

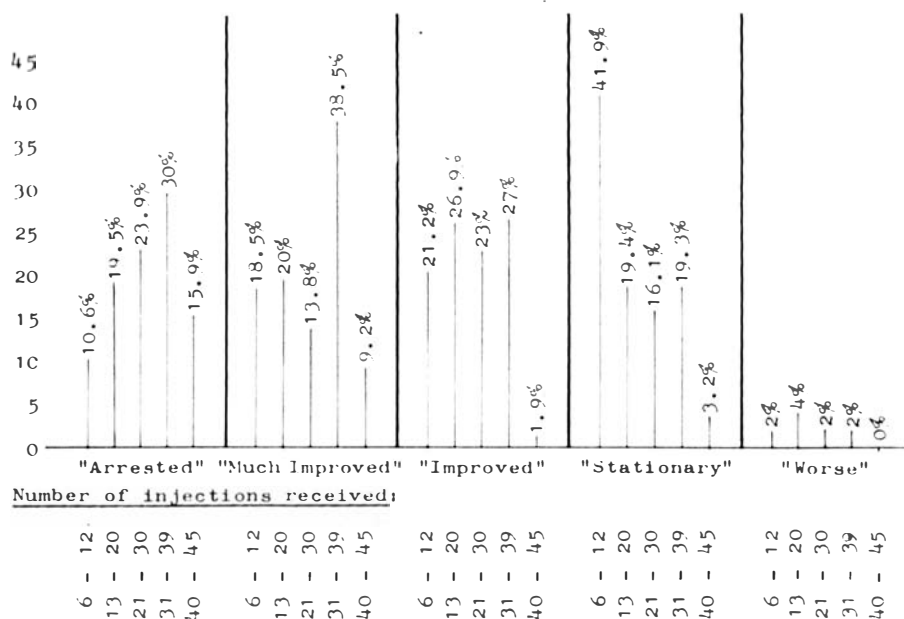
Immunological results — The regular giving of the Mitsuda test at the beginning of treatment and once a year enabled the study of the action of the Marianum antigen according to the type of the disease. The results mentioned hereto were checked at the end of 1962 or beginning of 1963.

To summarize; those who were positive before treatment (83 patients) remained positive in 97.5 per cent. Among the 117 negative before treatment, 101 cases became and remained positive, giving a percentage of 86.3 —. This figure corresponds with the clinical results where the number of 'Arrested' and 'Improved' cases gives 86.5 per cent. For most of the cases, positivation of the Mitsuda test is observed at the end of the

Summary of the Mitsuda modifications (I)

	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>			<i>Before</i>	<i>After</i>		
	++	++	+	—	+	++	—	—	+	++
Lepromatous										
57	5	5 = 100%	6	■	■	4 = 66.6%	46	3	2	39c = 84.8% 2v
Tuberculoid										
64	37	37 = 100%	24		4	20 = 83.4%	3			3 = 100%
Indeterminate										
145	41	39c = 95.1%	36	3	5	28 = 77.7%	68	4	2	59c = 86.8% 3v
Total	83	81c = 97.5%	66			52c = 78.7%	117			101c = 86.3%

(I) c = constant v = variable



second course of Marianum antigen, which consists of 12 injections, and maintained with a prolonged treatment.

2° - Results with 53 patients of Sangmelima Leprosarium, who had previously the Marianum antigen: these patients were four lepromatous, 10 tuberculoid, and 39 indeterminate.

The results were that 34 per cent were 'arrested', 39.5 per cent 'much improved', and 30.1 per cent improved.

The Mitsuda changes to positivation were 67 to 77 per cent to definite positive (++), and 28 negatives to positive (++) were noted. These results had been obtained on six to 12 injections in 47 patients, and 12 to 24 injections in six patients. A greater percentage of positive Mitsuda test might have been obtained with more courses of Marianum injections.

3° - Results with 30 patients, inmates of Nden Leprosarium, previously contacts of the patients. Of these contacts there were 11 children and 19 adults, of whom six children born at the leprosarium had received the Anti-Lepreux Vaccination (prepared with *Mycobacterium marianum*).

The group includes eight tuberculoid and 22 indeterminate.

The general results are 23.3 per cent 'arrested', 36.6 per cent 'much improved', and 40 per cent 'improved'. For the six children previously vaccinated four had no clinical nor bacteriological activity, one had no clinical activity, but variable bacteriology, and one still suspicious activity of patches.

The changes in the Mitsuda were that all six were positive (++) before, remained positive (++). Of seven who were mildly positive before (+), six became definitely positive (++), and of 17 who were negative, 13 became definitely positive (++).

4°—Considering results with 124 patients who received this treatment but left the leprosarium a short time ago, studying their condition at departure and assuming that their lack of returns signifies that their leprosy condition has not changed. The group includes: 18 lepromatous patients, 29 tuberculoid, and 77 indeterminate.

The clinical changes were 29 per cent much improved, 27.4 per cent improved, 40.4 per cent stationary and 3.2 per cent worse. About half of these patients had been treated for one to six years.

The changes in the Mitsuda were that of 29 who were positive before, 27 remained positive (+ +). Of 32 who were mildly positive before (+), 29 became positive (+ +), and of 63 who were negative before, 56 became positive (+ +); therefore percentages vary between 88 to 92.7 per cent in the various groups of the three main types.

5°—An extra study of the Mitsuda reaction was made in 412 patients who had received benefit from the Marianum therapy, but who left the leprosarium at an early date. This group included 75 lepromatous, 94 tuberculoid, and 243 indeterminate.

Results of the positivation of Mitsuda test summarize as follows:

	Before	After
Lepromatous:	71 —	61 + + = 85.9 per cent
(75)	4 +	4 + + = 100.0 per cent
Tuberculoid:	93 + +	85 + + = 91.1 per cent
(94)	1 —	1 —
Indeterminate:	155 —	133 + + = 85.8 per cent
(243)		25 — = 14.2 per cent
	88 + +	82 + + = 93.1 per cent
		6 — = 6.82 per cent
Total:	227 —	194 + + = 85.4 per cent
		33 — = 14.5 per cent
	185 + +	171 + + = 92.4 per cent
		14 — = 7.5 per cent

6°—Results obtained with the Anti-Lepreux Vaccin (prepared with *Mycobacterium marianum*) on 'contacts' living at the leprosarium. There were 92 children living in permanent contact with their parents and other inpatients of the leprosarium. These were all examined, as all of them had one or more courses of the Anti-Lepreux Vaccin; since 1960, on the suggestion of DR. GAY PRIETO, they also had been given prophylactic sulphone. Study was made of 73 children and the others discarded, as they were only a few months old, and had had too short a prophylactic treatment, although none showed any sign of leprosy. Most of the children in the group studied had been born at the leprosarium; 13 only were aged 7, 8, 10 or 12 years at the time of their admission with their parents. Although they already had a few years contact with their parents, they showed no difference from the others in respect to changes in the Mitsuda reaction.

After six to 30 injections of Anti-Lepreux Vaccin this group showed considerable modification of the Mitsuda:

<i>Before</i>	<i>After</i>
65 —	54 ++ = 83.0 per cent
	5 +
	6 —
1 +	1 +
7 ++	7 ++

Eighty-eight of these children show no clinical sign of leprosy; four only have a suspicious patch with no clinical or bacteriological activity.

Twenty-four adults 'contacts' have also been examined. Contrarily to the children we notice that 11 of them had a Mitsuda (++) before vaccination, which was a sign of acquired immunity. Eight were slightly (+) and five (-). On these 13 'contacts' the positivation of Mitsuda is 76.9 per cent.

In comparison, data from Bafia Leprosarium was studied concerning child contacts, and it was found that over nine years the percentage of infection was 4.75 per cent.

The children were given B.C.G. a few weeks after birth, as well as prophylactic sulphone (Disulone). As is seen in Section 3 of this paper, six children vaccinated with the Anti-Leprosy Vaccin out of 30 contacts developed Leprosy. In fact out of 225 child contacts observed over 10 years to whom the Anti-Leprosy Vaccin was given, the percentage of infection was 2.6 per cent.

SUMMARY

This paper reports on the records of 885 patients treated with the Marianum antigen. Of 349 inpatients of the leprosarium, 86.5 per cent received benefit from this therapy as 'arrested' or 'improved'; 12.1 per cent remained 'stationary', and 1.4 per cent 'worse'.

Concomitant study of the Mitsuda reaction showed that in 349 inpatients a previously negative Mitsuda became positive in 81.7 per cent (there were originally 159 negative Mitsudas) and remains positive to date; 10 per cent attained a positive but unstable Mitsuda. Most of the conversion of the Mitsuda was noted after 12 injections of Marianum antigen, and remained constant.

Of the 536 patients studied, there were 357 with a negative Mitsuda. These became positive in a percentage of 85.9 per cent.

In contrast with the general opinion of leprologists that the first few years of sulphone therapy results only in a low percentage of positive Mitsuda, the present study has shown that even in 1½ years, a high percentage is obtained. This means at the end of the second course of injections of Marianum antigen.

The authors think that this antigen is a good adjuvant in therapy, which reinforces the resistance of the patient, and permits a better and safer response to chemotherapy. The absence of relapse over 10 year period is most striking, and is attested by MISS M. TH. PROST, Directress of St. Michel Leprosarium.

From the point of view of prophylaxis, the authors draw attention to the low percentage of infection among permanent contacts, and cite the 92 children, who might have been considered to have a high susceptibility to infectious diseases.

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