

Result of Marianum Antigen in the Treatment of Leprosy

ARTEMIO BAGALAWIS, M.D., ELIZABETH OH, M.D.
(the late) MARGARET WHANG, M.D.
Catholic Leprosy Service, Seoul, Korea

INTRODUCTION

We present a report on patients who were treated principally with Marianum Antigen at eight small leprosaria and 70 treatment stations in six provinces of Korea at least once a month by stationary and mobile clinics.

The total number of patients was over 11,000 listed by seven doctors, among whom 6,605 were registered by Drs Bagalawis, Oh and Whang, who worked a much longer term than our other doctors, but for this paper only 2,869 were selected who came regularly for treatment and observation up to 7½ years. Of the 2,869 treated, 2,502 had M.A. therapy and the other 367 cases were divided into two therapy groups for comparison. The great majority omitted from this report were inmates of leprosaria given over to other control, or wandering patients, forced from place to place by the public or the police, of whom track was lost. Many expecting too rapid a cure came and went then disappeared; and some died.

Except 687 living in leprosaria nearly all of the 2,869 were home patients. They were treated at 70 stations; many of them had no shelter except bridges and crematoria, so that often the patients were exposed to bad weather and to the curiosity of passers-by. Advanced patients usually could not use public transport some having to walk up to 10 miles. But all cited here were faithful in meeting our clinics at fixed places, days and hours.

The majority had no previous care from any doctor and had only self-treatment, if any. Few have means to support themselves. Some work hard as day-labourers, some have to beg for their living. Without the monthly food supply, which we try to distribute, about 20 lbs of grain, many would verge on starvation.

Most of the wandering patients had been in leprosaria under sulphone therapy. Some were discharged as negative patients and nearly all were stationery patients but often needing care for concurrent diseases. Some had narcotic or alcoholic habits and had gone off as wandering beggars. Home patients in fear of segregation shun government officials.

Mobile clinics seem to be the best means of taking care of these patients, to examine their contacts in view of early treatment, to follow up suspicious cases and to prevent the spread of the disease.

METHOD EMPLOYED

- Group A* . . M.A. – Marianum Antigen
- Group B* . . DDS – sulphone
- Group C* . . M.A. + DDS – Marianum Antigen and sulphone.

The usual dose of Marianum Antigen was from 0.03 to 0.1 ml, given by intradermal injection in the deltoid region of the shoulder, once a month for periods of six months, and occasionally stopping for a month.

In Group B and C the initial dose of DDS was 50 mg a week given orally for the first two weeks; 100 mg a week for the second two weeks, with a gradual increase until the maximum dose of 600 mg a week was reached.

Clinical examinations, dermatological and neurological, were made by the doctors once a month, while bacteriological examination, generally, was made only in the lepromatous type by the modifications of Wade's method two to four times a year.

TABLE I

Classification of Patients by Clinics

Group	No. of Patients Participating			Total
	Dr Bagalawi's Clinic	Dr Oh's Clinic	Dr Whang's Clinic	
Group A on M.A.	509	1,548	445	2,502
Group B on DDS	196	71	17	284
Group C on M.A. plus DDS	83	—	—	83
<i>Total</i>	788	1,619	462	2,869

Of the total number of patients in the three clinics, approximately two-thirds were males; most of the patients were between 10 and 50 years of age. The ratio of lepromatous to tuberculoid types was 1.3 to 1.

CLINICAL RESULTS

The clinical results were summarized as 'Improved' (arrested, markedly or moderately), 'Stationary' or 'Worse'.

In the above table the respective proportion

TABLE II

Therapy Group and Type of Disease	No. of pts.	Dr Bagalawi's Clinic			No. of pts.	Dr Oh's Clinic			No. of pts.	Dr Whang's Clinic			
		Impr.	Stat.	Worse		Impr.	Stat.	Worse		Impr.	Stat.	Worse	
A	L	311	72%	17%	11%	758	69%	29%	2%	288	67%	30%	3%
	T	198	60.6%	31.8%	7.6%	790	66%	33%	1%	157	51%	49%	
	Total	509	67.8%	22.6%	9.6%	1,548	68%	31%	1.0%	445	61%	37%	2%
B	L	126	66%	25%	9%	44	63.6%	31.8%	4.6%	14	57%	43%	—
	T	70	49%	47%	4%	27	52%	48%	—	3	67%	33%	—
	Total	196	60%	33%	7%	71	59%	38%	3%	17	59%	41%	—
C	L	68	72%	16%	12%								
	T	15	73%	20%	7%								
	Total	83	72%	17%	11%								

classified as 'Improved', 'Stationary' and 'Worse' is about the same in each clinic, according to the mode of therapy. On the average 66.5 per cent of the patients were improved in Group A. 59.5 per cent of the patients were improved in Group B, while in Group C, 72 per cent of the patients were improved. The difference of improvement

between Group A and B averages approximately at 7 per cent — Group A — Marianum Antigen — was more effective than Group B on DDS.

Percentages of 'Arrested' patients out of the 'Improved' — in relation with the length of time of treatment in Dr Oh and Dr Whang's clinics are as follows:

TABLE III

Duration of Treatment (Year)	Dr Oh's Clinic		Dr Whang's Clinic	
	No. of improved	No. of arrested (per cent)	No. of improved	No. of arrested (per cent)
1st Year	220	—	48	—
2nd Year	235	0.4%	58	1.7%
3rd Year	198	20.2%	43	27.9%
4th Year	151	51.1%	51	56.9%
5th Year	133	83.7%	37	67.6%
6th Year	85	88.2%	34	94.1%
7th Year	25	92.0%	2	100.0%
Total	1,047	25.1%	273	37.0%

(Arrested patients were defined according to the description of the 'Inactive' cases adopted by the VIIth International Congress on Leprology in Tokyo).

Although the proportion of 'Arrested' patients is remarkably increased after 2½ years treatment, there is a big difference of percentages obtained in the two clinics — 25 per cent of Dr Oh's

patients, against 37 per cent for Dr Whang's. Such difference may be related to the stage of the disease among the selected patients.

Table 4 shows percentages of improvement obtained among Dr Bagalawis's patients, according to the duration of treatment (three years) in the different therapy.

TABLE IV

Therapy Groups

Duration of Treatment	A. on M.A.		B. on DDS		C. on M.A. and sulphone	
	No. of patients	No. of Impr. (per cent)	No. of patients	No. of Impr. (per cent)	No. of patients	No. of Impr. (per cent)
1st Year	316	62.0%	80	53.7%	29	58.6%
2nd Year	122	71.3%	76	59.2%	31	71.0%
3rd Year	35	77.1%	39	71.8%	14	85.7%
Total	473	65.5%	195	59.5%	74	68.9%

In the above Table, improvement is obtained more rapidly in Group A than in Group B, in the first three years of treatment; but Group C shows a higher percentage of improved cases, than the other two groups for the same length of time.

Leprosy reaction was present during the course of treatment in 20.7 per cent (E.N.L. 25.2 per cent, and 16.3 per cent of reaction in tuberculoid cases) of Dr Oh's clinic; and 32.1 per cent of Dr Whang's clinic in Group A; they occurred more frequently in the first to second years of treatment, without any clear relationship to the therapy group.

Ocular complications were present on preliminary examinations in 158 patients in Dr Oh's clinic, and 58 patients in Dr Whang's clinic.

The clinical results of these patients were as follows:

DR OH'S

66 improved; 79 stationary; 13 worse

DR WHANG'S

8 improved; 35 stationary; 15 worse

The loss of eyebrows was commonly seen in lepromatous patients; among the patients classified as 'Arrested' in Group A, 63 patients in Dr Oh's clinic, and 41 patients in Dr Whang, had

their eyebrows grown again, while none was observed in Group B patients.

Gynaecomastia was recorded as healed in four patients out of 12, by Dr Oh; and 10 patients out of 13 by Dr Whang, in Group A, without any sexual hormone treatment.

The general condition of the patients remained good in all therapy groups, even among those classified as 'Stationary' in all the clinics.

For the bacteriological examinations of lepromatous patients, smears were taken from both sides of the nasal septum, both earlobes, and other optional skin sites, and subsequent smears were from approximately the same areas. The present

analysis deals only with Group A, in the preliminary and final results.

Three grades in a positive finding were designated as follows:

- Negative .. no bacilli found in 100 fields.
- One-plus .. rare, one or less than one bacillus in each microscopic field.
- Two-plus .. numerous, bacilli found in all field.
- Three-plus .. abundant, many bacilli in all field.

TABLE V

Bacteriological Findings on Preliminary Examination

<i>Results</i>	<i>Dr Oh's Clinic</i>	<i>Dr Whang's Clinic</i>
Negative	168 (22%)	55 (19%)
Positive +	332 (44%)	112 (39%)
Positive ++	175 (23%) 590 (78%)	74 (26%) 233 (81%)
Positive +++	83 (11%)	47 (16%)
Total	758 (100%)	288 (100%)

Seventy-eight per cent of all lepromatous patients were positive at the outset as by Dr Oh, compared to 81 per cent by Dr Whang. Of all positive patients who completed treatment, the proportions becoming negative were 83.6 per cent (493) by Dr Oh and 82.8 per cent (193) by Dr Whang. The remaining patients were never heavily positive except 12 of them by Dr Oh and nine of them by Dr Whang.

DISCUSSION

In the treatment of leprosy, Marianum Antigen was given for large scale trials by stationary and mobile clinics, while the other two groups (Group B on DDS and Group C on M.A. plus DDS) were used for control.

Comparing the results in the three therapy groups, Group C on M.A. plus DDS which was experimented by Dr Bagalawis, has shown better results than the other two therapy groups, however the number of selected patients was too small and no significant control group was made by any doctor. Therefore, it may be advisable to have more experimental study in the future.

The results between Group A on M.A. and Group B on DDS Group A was slightly better benefit than Group B. On the average 66.5 per cent of the patients were clinically improved in Group A, against 59.5 per cent in Group B.

The proportions recorded as stationary were relatively high at all clinics. The reason seems due to the different concept of the doctors for the state of the disease and also there are many difficult problems to judge clinical change in patients. These patients who were classed as stationary may be either improved or arrested.

The present paper includes some inmates of the leprosarria treated by Dr Bagalawis and most of them received prior to sulphone therapy. Thus clinical changes were recorded considerably more frequent in patients with prior sulphone treatment than in others.

During the treatment at the stationary and mobile clinics, 25 patients who had gynaecomastia were treated on M.A. alone without any sexual hormone. Out of 25, the symptoms of 14 patients were healed or disappeared, however it is doubtful whether the improvement was attributed to therapy or not.

In the majority of the patients who received M.A. treatment, there appeared at the injection site an erythematous papule (sore). After that, it showed an ulcer sometimes due to secondary infection, but it healed with scar within the month. A few patients had lymphangitis in the local area and a less number had general reactions such as: fever, headache, dizziness and rarely pruritis, etc., but these usually disappeared after a few days to two weeks.

The patients have been supplied with food and relief goods when possible. It would be very helpful for patients to be treated regularly.

It was found that M.A. therapy is more effective for patients visited once or twice a month by mobile clinics than sulphone drugs administered orally, because M.A. is non-toxic and the doctor controls the exact dosage.

SUMMARY

- (1) This is a controlled study of leprosy patients which was carried out by stationary and mobile clinics using the antigenotherapy of Marianum Antigen. Among 6,605 registered by three of seven doctors, 2,869 were selected for the report. Out of 2,869, 2,502 were treated with M.A. up to 7½ years in standard dosage, 287 with only DDS and 83 received M.A. plus DDS for comparison.
- (2) Both M.A. and DDS therapies were well tolerated. In this study the Group on M.A. showed slightly better clinical improvement than the Group on DDS. The clinical effect of M.A. is seen in the following results: 4.2 per cent did not benefit; 30.2 per cent remained stationary; and 65.6 per cent continued to improve in general conditions and in specific lesions such as: infiltration, nodules, ulcers, maculae, nerve enlargement and others until arrested.
- (3) The lepromatous type showed higher proportion of improvement than tuberculoid type. To the patients who became arrested after 2½ years on M.A. a maintenance dose was given for the next three or four years. *No relapse occurred.*
- (4) No evidence was obtained that clinical improvement may be related to age or sex.

- (5) In the lepromatous type 83.4 per cent among the patients who were bacteriologically positive were converted to negative.

- (6) Patients with leprosy reaction or ocular complications received about a half the standard dosage of M.A. or DDS with symptomatic treatment, usually with beneficial effect.

This report was compiled and edited by Shi Riong Choi, M.D. and D.P.H. Leprologist of R.O.K. Ministry of Health and Social Affairs, after careful study of the voluminous reports of Drs Bagalawis, Oh and Whang, and of thesis charts on individual patients.

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