THE DIPHTHERIA TOXOID TREATMENT OF LEPROSY

Final Report

by

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So broad have been the claims on the therapeutic action of diphtheria toxoid in the treatment of leprosy that scientific interest on the subject has not as yet subsided. Our preliminary paper (4) and McKean's latest article (5) do not seem to have entirely counteracted the favorable impression created by the previous enthusiastic reports. Numerous letters received at the National Leprosarium, both professional and non-professional, inquiring as to the current status of this therapeutic agent in leprosy attest this fact. It is regrettable that such premature publications on so-called new specifics for leprosy continue to appear in print before they have been verified by other workers. This is what has been so discouraging to patients with leprosy in the past, since it raises their hopes only to dash them down again and may ultimately destroy their faith in all new drugs.

Sufficient data have at present accumulated and sufficient time has elapsed to warrant a final, more conclusive report on the therapeutic trial of diphtheria toxoid at the National Leprosarium. A complete exposition of our extensive experimental work on the subject is here given, together with case histories and photographs, that the reader may see for himself how the claims for this new therapy have failed of fulfillment at the U. S. Marine Hospital, Carville, Louisiana.

As recorded in our previous report, the experimental study undertaken at the National Leprosarium was an impartial one and was carefully controlled in order that the true value of this new treatment might be ascertained. The experiment can be divided into three groups of patients. The first group comprised patients subject to frequent lepra reactions, who were considered as suitable cases to test the claimed abortive effects of diphtheria toxoid on acute lepra reactions (1). The second experiment included 70 patients who volunteered for treatment with diphtheria toxoid; these were divided into two closely matched groups of 35 patients each. The patients of one of these groups were given diphtheria toxoid, and those of the other, or control, group were given similar amounts of the broth from which diphtheria toxoid is made. All of the patients of both groups were under the impression that they were being treated with toxoid. Finally, when the enthusiasm of the patients was so aroused by the visit of Dr. D. R. Collier to the National Leprosarium that there was a great demand for the new treatment, an additional group of 183 patients was started on diph-

theria toxoid therapy. This third group of patients was given the routine course of toxoid treatment but was not checked by another control group.

Method of Treatment

The method of administering the toxoid was that used by Collier (2). The initial dose was 1 cc. of diphtheria toxoid given subcutaneously. This injection was repeated every two weeks, increasing each time by 0.5 cc. until a dose of 3 cc. was given. Thereafter the injections were continued at monthly intervals, and the dose was reduced to 1 cc.

Test for Serum Antitoxin Concentration

One of the arguments in support of the rationality of the diphtheria toxoid therapy of leprosy is the supposed close biologic relationship between leprosy and diphtheria. Collier (3) thought that the diphtheria toxoid injections would stimulate the production of diphtheria antitoxin in the patient and that this antitoxin would react by neutralizing leprosy toxin. He reports that almost every patient tested at the Chiengmai Leprosarium (there was only one positive reactor among 120 patients tested) was found to be Schick negative. Through the courtesy of the Eli Lilly Laboratory a study was undertaken at the National Leprosarium to determine the serum diphtheria antitoxin titer of a number of the patients who had volunteered for the toxoid treatment. As controls a number of the patients with latent or arrested leprosy and a group of healthy employees of the leprosarium were also tested. The blood specimens were collected at the leprosarium and sent with identifying numbers to the Lilly Laboratory, where the tests were run without knowledge of which blood samples were from patients and which were from employees. The results, shown in the following table, are very interesting.

Table I. *Serum antitoxin units*

	.001	.002	.005	.01	.02	.05	.1	.2	.5	1.	2.	5.	10.	Total
Active leprosy.....	—	—	—	—	—	—	—	11	11	3	7	1	1	34
Latent or arrested leprosy.....	—	—	1	—	—	—	1	3	2	1	—	—	—	8
Healthy adults..... Controls	—	5	—	1	1	3	2	5	—	1	—	—	—	18

This table conforms with the experience of Collier in that it shows that the lepra patients as a group have a higher diphtheria antitoxin blood titer than healthy adults. All of them exhibit a

serum antitoxin concentration sufficiently elevated to produce a Schick negative reaction, whereas many of the healthy adults have such a low antitoxin titer that they would react positive to the Schick test.

In order to ascertain the degree of stimulation of antitoxin production by the diphtheria toxoid injected in the patients with leprosy, additional antitoxin titrations were made on some of the patients after a period of treatment. The table below demonstrates that there was a substantial rise of diphtheria antitoxin in the blood stream, showing that the toxoid therapy was adequate as far as the production of antitoxin was concerned. Table 2 also contains antitoxin titers of some of the patients of the control group, both prior to and after the administration of the toxoidless broth.

TABLE 2

Diphtheria toxoid group				Broth control group		
	Serum antitoxin units				Serum antitoxin units	
Cases	Before treatment	After 7cc toxoid	After 10cc toxoid	Cases	Before treatment	After 10cc broth
1375	—	200	100	1347	0.5	0.5
1261	—	—	50	1399	0.5	0.5
1356	—	—	50	1369	0.2	0.5
1232	0.2	—	50	823	0.5	0.5
943	0.5	10	—	1401	10.0	20.0
1050	0.2	20	—	—	—	—
1046	0.5	20	—	—	—	—
1403	0.5	20	—	—	—	—
1391	0.5	20	—	—	—	—
1417	2.0	20	—	—	—	—
918	0.2	50	—	—	—	—
1257	0.2	50	—	—	—	—
1203	1.0	50	—	—	—	—
899	0.5	300	—	—	—	—

The antitoxin produced by diphtheria toxoid in patients with leprosy does not seem to neutralize the toxins of leprosy. This is evident in each of the three groups of patients treated at this leprosarium.

First Experimental Group

In our preliminary report it was shown that recurrent attacks of lepra reactions in the patients of the first group were unabated by the diphtheria toxoid injections. In four of the five cases of this group no lessening of the severity or the frequency of lepra reactions was noted. The experience in this group of patients does not substantiate the claim that the new therapy usually causes rapid subsidence in lepra reactions and prevents their recurrence.

Seven additional patients were added to the first group before the second experiment was started. It is interesting to note the present condition of these 12 patients; in two the disease is considered stationary, eight are in worse condition, one has absconded and one is dead.

CONTROL CASES—(BROTH INSTEAD OF TOXOID)

Case No.	Place of Birth	Color	Sex	Age	Year of Admission	Type of Leprosy	*Treatment Prior to 1941	Toxoid in c.c.	Length of Toxoid Treatment (Months)	Weight Change		Skin Smears			Sedimentation Rate (m.m.)			Change in Lesions		Change in Anesthesia		Clinical Evaluation	
										Mar. 1941 to Dec. 1941	Dec. 1941 to July 1942	Mar. 1941	Dec. 1941	July 1942	Mar. 1941	Dec. 1941	July 1942	Mar. 1941 to Dec. 1941	Dec. 1941 to July 1942	Mar. 1941 to Dec. 1941	Dec. 1941 to July 1942	At Start of Treatment	At End of Treatment
1005	Mexico	W	F	23	1934	L_2	3	18	11	○	−1.5	+	+	+	24	28	26	○	+	○	○	Stat.	Worse.
1347	Mexico	W	F	22	1939	L_2	3	18	11	−5	○	+	+	+	24	26	24	○	+	○	+	×	Worse.
821	U. S. A.	W	F	63	1931	L_3	3	14	7	+9	−15	+	+	+	27	24	27	○	+	○	+	Prog.	Worse.
890	U. S. A.	W	F	41	1932	L_3N_3	3	18	11	○	+6.5	+	+	+	27	29	30	○	+	±	○	Prog.	Worse. Completely blind.
833	U. S. A.	W	M	51	1932	L_3	2	18	11	+12	−8	+	+	+	20	22	21	○	○	+	○	Prog.	Stationary.
1405	Mexico	W	M	51	1940	N_t	2+	18	11	+2.5	+0.5	+	+	+	9	6	15	±	—	○	○	Imp.	Stationary.
1202	Cuba	C	F	25	1937	L_3	2	12	7	−1	+4.5	+	+	+	28	28	28	○	○	±	○	Prog.	Stationary.
1401	U. S. A.	W	M	18	1940	L_2	3	19	12	+6	−2.5	+	+	+	22	24	25	○	○	○	○	Prog.	Stationary. Had first lepra reaction following 5th broth injection.
1399	U. S. A.	W	M	18	1940	N_t	2+	17	10	+14	+5	+	+	+	10	7	5	±	±	○	○	Stat.	Stationary.
1063	U. S. A.	W	F	35	1935	L_3N_2	3	15	8	○	○	+	+	+	27	28	29	○	+	○	+	Prog.	Worse.
823	U. S. A.	W	M	20	1931	L_2	3	17	10	−8.5	−14.5	+	+	+	21	26	29	+	+	±	×	Prog.	Worse. Rhinitis and laryngitis advancing.
1352	Mexico	W	M	40	1939	L_2	1	19	12	−2	−1	+	+	+	23	21	23	○	○	±	±	Stat.	Stationary.
1193	U. S. A.	W	F	32	1937	L_1	3+	19	12	+10	−1	+	—	—	24	13	20	○	—	—	×	Stat.	Improved.
1369	Mexico	W	F	50	1940	L_2	3	19	12	+3	−8	+	+	+	25	27	25	—	—	±	×	Stat.	Improved.
1431	U. S. A.	C	F	56	1940	N_2	2	16	9	○	×	—	—	×	24	×	×	—	×	—	×	Impr.	Improved. Paroled Nov. 26, 1941.
1147	Mexico	W	M	38	1936	L_2	3+	18	11	+13	−12	+	+	+	21	23	25	—	○	×	+	Impr.	Worse. Completely blind.
836	U. S. A.	W	F	45	1932	L_3N_2	1	14	7	−4.5	+17.5	+	+	+	×	×	26	+	—	○	○	Prog.	Worse. Emergency tracheotomy.
1295	U. S. A.	C	F	53	1939	L_3N_3	3	17	10	+3	+2	+	+	+	26	27	25	○	○	×	○	Prog.	Stationary. Two severe lepra reactions 1st period.
1289	Mexico	W	M	26	1938	L_2	3	18	11	−3	○	+	+	+	20	×	22	—	+	○	○	Imp.	Worse.
1174	U. S. A.	W	M	48	1937	L_2	1+	18	11	○	−9	+	+	+	22	21	24	—	+	○	○	Prog.	Worse.
1148	U. S. A.	W	M	37	1936	L_2	3	15	8	−2	−7	+	+	+	21	17	21	—	○	×	○	Prog.	Stationary.
862	Montenegro	W	M	56	1932	L_3	×	17	10	−7	−10	+	+	+	20	21	21	+	+	○	○	Stat.	Worse.
1097	Mexico	W	M	40	1935	L_1	3	14	7	+2	−1	+	+	+	23	20	22	○	+	○	+	Impr.	Worse. Several lepra reactions 2nd period.
1390	Mexico	W	F	50	1940	L_1	3	17	10	+1.5	×	+	+	×	29	28	×	—	×	○	×	Impr.	Stationary. Died intercurrent septicemia March 2, 1942.
1362	Mexico	W	M	38	1940	L_2	3+	18	11	−7	+5	+	+	+	26	24	26	○	+	○	+	Impr.	Worse. Lepra reaction 2nd period.
1299	Mexico	W	M	38	1939	L_2N_3	3	19	12	+3	+3	+	+	+	16	17	17	○	○	○	○	×	Stationary.
1249	P. I.	O.R.	M	23	1938	L_2	2	17	10	○	+4	+	+	+	24	17	19	+	+	○	○	Impr.	Worse. Nasal occlusion.
888	U. S. A.	W	M	58	1932	L_2	3	19	12	+6	×	+	+	+	23	21	23	○	+	×	+	Stat.	Worse. Severe lepra reaction; too ill to cooperate.
1376	U. S. A.	W	M	58	1940	L_2	1+	14	7	−4	−2.5	+	+	+	25	26	25	○	○	○	○	Impr.	Stationary.
1420	Mexico	W	M	43	1940	N_3	3	17	10	+12	−5	+	+	+	26	22	22	○	○	○	○	Stat.	Stationary.
1384	Mexico	W	M	36	1940	L_2N_1	2+	19	12	+3	+2	+	+	+	11	12	17	+	+	×	○	Impr.	Worse. Many lepra reactions.
1423	U. S. A.	C	M	53	1940	L_1	3	19	12	+1	−3	+	+	+	25	23	22	○	○	○	○	Stat.	Stationary.
1430	U. S. A.	C	M	7	1940	N_1	1	19	12	+4	+0.5	+	+	+	11	13	13	○	+	○	○	Stat.	Worse.
1415	U. S. A.	C	F	27	1941	L_1	3	19	12	+1	+9	+	+	+	23	25	26	—	+	○	○	Stat.	Worse.
1251	Mexico	W	M	59	1938	L_2	2	18	11	+2	−1	+	+	+	19	17	18	○	○	○	○	Impr.	Stationary.

*Coded as follows: Chaulmoogra oil—1 by mouth, 2 by injection, 3 by mouth and injection. Plus (+) sign following code indicates additional treatment as follows: Cases 899, 1359 and 1174 hydnocarpus oil; cases 1376, 1385, 1396 and 1399 alfon; cases 1028, 1147 and 1384 sulfanilamide; case 1405 alfon and sulfanilamide; case 1362 Fowler's Solution; case 1090 fever therapy and case 1193 Vitamin B_1. × Indicates unknown throughout the entire table.

TABLE 3.—SUMMARY OF CASE HISTORIES FOR PERSONS TREATED WITH TOXOID AND FOR CONTROLS GIVEN BROTH.

Case No.	Place of Birth	Color	Sex	Age	Year of Admission	Type of Leprosy	*Treatment Prior to 1941	Toxoid in c.c.	Length of Toxoid Treatment (Months)	Weight Change		Skin Smears			Sedimentation Rate (m.m.)			Change in Lesions		Change in Anesthesia		Clinical Evaluation	
										Mar. 1941 to Dec. 1941	Dec. 1941 to July 1942	Mar. 1941	Dec. 1941	July 1942	Mar. 1941	Dec. 1941	July 1942	Mar. 1941 to Dec. 1941	Dec. 1941 to July 1942	Mar. 1941 to Dec. 1941	Dec. 1941 to July 1942	At Start of Treatment	At End of Treatment
1203	U. S. A.	W	F	35	1937	L_2	3	17	10	+3.5	—5	+	+	+	25	26	25	+	+	+	+	Stat.	Worse. (See photograph.) Repeated lepra reactions.
1046	Mexico	W	F	25	1935	L_2	2	16	9	+2	—4	+	+	+	24	26	28	+	+	+	±	Prog.	Worse. (See neurological chart.)
1224	U. S. A.	W	F	45	1937	L_3	3	16	9	+2.5	—5.5	+	+	+	25	26	24	+	+	±	+	Prog.	Worse. Vision frailing; progress of leprous keratitis.
691	Hawaii	W	F	42	1930	L_3N_3	3	16	9	O	×	+	+	×	29	34	×	+	×	+	×	Prog.	Worse. Died March, 1942.
899	Greece	W	M	47	1933	L_3	3+	17	10	—2.5	—18.5	+	+	+	27	26	35	O	+	+	+	Prog.	Worse. Increase in lepra reactions.
1438	U. S. A.	W	M	61	1941	N_t	1	18	10	+17	+2	—	—	+	18	18	26	—	+	+	+	Stat. or Impr.	Worse. (See photograph.) Conjunctivitis and photophobia.
1428	Bahama	C	F	41	1940	L_2	2	19	12	+2.5	O	+	+	+	30	28	28	—	—	—	O	Stat.	Improved.
1257	U. S. A.	W	M	18	1938	L_2	2	15	8	—7	+7	+	+	+	19	27	23	+	+	+	+	Stat.	Worse. Dizziness and weakness after toxoid.
1403	U. S. A.	W	F	18	1940	N_t	3	19	12	—2	—7	+	+	+	11	15	13	—	—	O	—	Impr.	Improved.
1234	U. S. A.	W	F	25	1937	L_2N_2	3	16	9	—3	+3.5	+	+	+	24	24	25	+	O	O	×	Prog.	Worse.
1028	Mexico	W	M	24	1934	L_2	3+	16	9	—5	O	+	+	+	25	26	25	+	+	+	+	Prog.	Worse. Several attacks of leprous neuritis.
1385	Mexico	W	M	53	1940	L_2	3+	19	12	—4.5	—7	+	+	+	25	27	28	O	+	—	+	Impr.	Worse. Patient's first lepra reaction followed 3rd toxoid.
1359	Mexico	W	F	48	1940	L_1	+	15	8	×	×	+	×	×	25	×	×	×	×	×	×	Impr.	Stationary. July, patient appeared worse; absconded in Oct., 1941.
1375	U. S. A.	W	F	55	1940	N_2	3	19	12	+11	—3	+	+	+	24	22	18	O	O	+	O	Impr.	Stationary. Had first lepra reaction during treatment.
1417	Mexico	W	F	44	1940	L_2	1	19	12	+3	+3	+	+	+	27	25	25	—	—	O	O	Impr.	Improved. (See photograph.)
1090	U. S. A.	W	F	24	1935	L_2N_2	3+	18	10	+1.5	+1	+	+	+	25	29	28	+	O	×	+	Impr.	Worse, increase in lepra reactions.
275	Greece	W	M	48	1924	L_3N_2	3	16	9	+1	×	+	+	×	29	31	×	+	×	×	×	Prog.	Worse. Death, suicide.
650	U. S. A.	W	F	46	1929	L_3N_3	×	14	6	—10	—3	+	+	+	27	33	31	+	+	+	+	×	Worse. General health and eyesight more impaired.
1050	Mexico	W	M	36	1935	L_2	3	19	12	+1	—1	+	+	+	24	24	25	+	+	O	+	Stat.	Worse. (See photograph.)
1232	U. S. A.	W	M	29	1937	L_3	3	16	9	O	O	+	+	+	21	16	18	+	+	+	×	Prog.	Worse. Neuritis for first time.
1110	U. S. A.	W	M	24	1925	L_2	3	14	8	+2.5	—6.5	+	+	+	20	26	23	+	+	+	—	Prog.	Worse. Extensive leprous laryngitis also recent keratitis.
1018	Mexico	W	M	53	1934	L_3	3	19	12	+3	—7	+	+	+	25	26	27	—	O	×	O	Prog.	Stationary.
943	Mexico	W	F	67	1933	L_2	3	18	11	+1	—3	+	+	+	20	20	21	—	+	O	+	Stat.	Worse. Severe lepra reaction.
1374	U. S. A.	W	M	65	1940	L_2	3	18	11	—4	+6.5	+	+	+	25	24	23	+	O	×	+	Impr.	Stationary. Lepra reaction for first time; none since Dec., 1941.
982	Mexico	W	M	53	1934	L_2	3	19	12	+3	—1	+	+	+	20	15	20	O	+	×	+	Impr.	Worse.
964	U. S. A.	W	M	39	1934	L_2N_2	3	14	8	—13	×	+	+	+	27	30	34	O	×	×	×	Impr.	Stationary. Died nephritis July, 1942.
918	P. I.	O.R.	M	17	1923	L_2	3	15	8	—2.5	—15	+	+	+	22	21	28	+	+	×	+	Prog.	Worse. Numerous lepra reactions.
1396	Mexico	W	M	53	1940	N_1	1+	18	11	+3	O	+	—	+	10	11	18	O	O	+	±	×	Stationary.
1380	Mexico	W	M	33	1940	L_1	1	18	11	+2	—3	+	+	+	31	24	25	O	O	O	O	Stat.	Stationary.
1273	U. S. A.	W	M	50	1928	N_2	1	16	9	+14	—8	+	+	+	21	18	23	+	+	O	O	Stat.	Worse. (See photograph.)
1391	U. S. A.	W	F	15	1940	L_2N	3	18	11	+2	+3	+	+	+	24	25	26	+	+	+	+	Stat.	Worse. (See photograph.)
1339	U. S. A.	C	M.	26	1929	L_2	3	16	9	—3	O	+	+	+	17	22	25	+	+	×	+	Impr.	Worse. (See photograph.)
1149	U. S. A.	C	F	35	1933	L_1	3	17	10	+1	—4	+	+	+	28	28	26	O	+	O	O	Impr.	Worse.
1429	U. S. A.	C	F	11	1940	N_2	1	14	8	+1	+7	—	—	—	27	11	11	O	O	+	+	Stat.	Stationary.
1300	U. S. A.	W	F	67	1939	L_1	1	17	10	+3	—3	+	+	+	14	13	5	+	+	+	+	Stat.	Worse. (See photograph.)

*Coded as follows: Chaulmoogra oil—1 by mouth, 2 by injection, 3 by mouth and injection. Plus (+) sign following code indicates additional treatment as follows: Cases 899, 1359 and 1174 hydnocarpus oil; cases 1376, 1385, 1396 and 1399 alfon; cases 1028, 1147 and 1384 sulfanilamide; case 1405 alfon and sulfanilamide; case 1362 Fowler's Solution; case 1090 fever therapy and case 1193 Vitamin B_1. × Indicates unknown throughout the entire table.

Second Experimental Group

As recorded in the preliminary report, in the second controlled experiment the patients of the treated and those of the control group were all carefully examined before and after 10 months of treatment. Since then all of them were given a final reexamination five months after the termination of one year of treatment. This period is considered sufficient time for the development of any change which could be attributed to the treatment. Case reports for all patients of the second experiment, toxoid treated and controls, are summarized in Table 3. For those patients for whom photographs are shown the histories are given below.

Selected Reports

Case No. 1203. (Plate 1)

March, 1941.

White, female, American; 35 years of age; admitted June 29, 1937.

Lepromatous leprosy, moderately advanced (L2).

Weight 132½ lbs. Skin smears positive. Sedimentation rate 25 mm.

Treatment has consisted of chaulmoogra oil by intramuscular injection and by mouth.

Disease stationary. Numerous small, discrete lepra nodules on face, ears, back, chest and limbs. Areas of anesthesia on hands and feet and distal halves of forearms and legs.

Has taken 17 cc. of toxoid during period of 10 months.

December, 1941.

Weight 136 lbs. Skin smears positive. Sedimentation rate 26 mm.

Has had repeated acute lepra reactions with chills, fever and areas of acutely inflamed skin. Attacks have been more frequent than before institution of treatment. Anesthesia more extensive in both forearms and in left leg.

July, 1942.

Weight 131 lbs. Skin smears positive. Sedimentation rate 25 mm.

During latter months of treatment new crop of nodular lesions noted over upper part of back. Believing condition worse, patient decided to discontinue treatment in December, 1941. Areas of anesthesia more extensive and cover entire upper and lower extremities with exception of small areas in anticubital and popliteal spaces.

Impression: worse.

Case No. 1046. (Plate 3)

March, 1941.

Female, Mexican; 25 years of age; admitted May 24, 1935.

Lepromatous leprosy, moderately advanced (L2).

Weight 103 lbs. Skin smears positive. Sedimentation rate 24 mm.

Has received treatment with chaulmoogra oil by intramuscular injections fairly regularly for period of 6 years. Disease has slowly advanced in this time.

Lepromatous nodules on upper face, ears, breasts, buttocks, upper and lower extremities. Minimal amount of anesthesia found on right little and ring fingers and on dorsa of feet and front of ankles.

Has taken 16 cc. of toxoid during period of 9 months.

DECEMBER, 1941.

Weight 105 lbs. Skin smears positive. Sedimentation rate 26 mm.

A few new nodules have developed on chin. Some of older lesions are larger or more prominent. Areas of anesthesia now extend up posterior forearms to elbows and over lower ulnar surface in front. Anesthesia of lower extremities has also advanced to knees in front and covers calves behind.

JULY, 1942.

Weight 101 lbs. Skin smears positive. Sedimentation rate 28 mm.

New nodules on chin more numerous and larger. Other nodules have formed on back. Progressive induration of lower legs has occurred. Considers herself definitely worse. In November, when she felt her legs and forearm becoming numb, decided to discontinue treatment. Areas of anesthesia have progressed only slightly since last examination.

Impression: worse.

Case No. 1438. (Plate 1)

MARCH, 1941.

White, male, American; 61 years of age; admitted February 19, 1941.

Maculo-anesthetic or tuberculoid leprosy (Nt).

Weight 118 lbs. Skin smears negative. Sedimentation rate 18 mm.

Chaulmoogra has been given orally. Disease is stationary or improving.

Large reddish-brown macules on face, body, arms, thighs and buttocks. Some of these have infiltrated borders and anesthetic centers. Ulnar nerves are palpably enlarged. Areas of anesthesia are found over back of left hand and dorsal surface of right little and ring fingers. Anesthesia extends along ulnar side of lower forearms. Feet and lower two-thirds of legs are also anesthetic.

Has taken 18 cc. of toxoid over period of 10 months.

DECEMBER, 1941.

Weight 135 lbs. Skin smears negative. Sedimentation rate 18 mm.

Macules are paler and borders less infiltrated. Those of face have faded almost completely. Is improving. However, there has been extension of anesthesia in lower extremities.

JULY, 1942.

Weight 137 lbs. Skin smears have become positive since February, 1942. Sedimentation rate 26 mm.

New macules developed over upper arms during December and January. All older macules have flared up anew, with intensification of erythematous borders; some macules appear larger. Although he considered himself improved at first, now finds himself much worse than before starting treatment. Has also had several attacks of conjunctivitis and photophobia. Areas of anesthesia in both lower and upper extremities have again increased in size.

Impression: worse.

Case No. 1417. (Plate 2)

MARCH, 1941.

Mexican, female; 44 years of age; admitted October 3, 1940.
Lepromatous leprosy, moderately advanced (L2).
Weight 97 lbs. Skin smears positive. Sedimentation rate 27 mm.

Does not know just how long she has had leprosy. Has taken only small amount of chaulmoogra oil by mouth over short period of time, and at present leprosy is improving. General health excellent. Over both cheeks and both forearms are discrete brownish-colored nodules. Diffuse thickening of skin over nose, cheeks, chin and forearms. Some muscular atrophy of interosseous muscles of both hands. Anesthesia on legs and feet to just below knees and on ulnar surface of both forearms.

Has taken 19 cc. of toxoid during period of 12 months.

DECEMBER, 1941.

Weight 100 lbs. Skin smears positive. Sedimentation rate 25 mm.

Patient shows improvement. Slight diminution in size of nodules over all areas of face and forearms. Diffuse thickening about same. Anesthesia has not progressed.

JULY, 1942.

Weight 103 lbs. Skin smears positive. Sedimentation rate 25 mm.

Shows about the same amount of improvement as of December of last year. There is improvement in general health. All lesions have subsided, and patient states that she has improved. Anesthesia about same.

Impression: improved.

Case No. 1391. (Plate 2)

MARCH, 1941.

White, female, American; 15 years of age; admitted May 24, 1940.
Mixed leprosy, moderately advanced (L2N).
Weight 94 lbs. Skin smears positive. Sedimentation rate 24 mm.

Has had disease about three or four years. Has taken chaulmoogra oil by mouth for several months, also intramuscularly. Disease at present is stationary. There are lepromata over ear lobes and both hips, also diffuse thickening over both cheeks. Over back are several small brown patches. Atrophy of interosseus muscles of both hands. Contraction of little finger of right hand is present. Anesthesia includes feet to just above ankles, also ulnar surface of forearms, including little finger of each hand.

Has taken 18 cc. toxoid during period of 11 months.

DECEMBER, 1941.

Weight 96 lbs. Skin smears positive. Sedimentation rate 25 mm.

Progressively becoming worse. Numerous new nodules over face and ears. Diffuse thickening over cheeks has extended. Also there is extension of anesthesia to upper legs and forearms.

JULY, 1942.

Weight 99 lbs. Skin smears positive. Sedimentation rate 26 mm.

Leprous lesions much more extensive over entire face, ears and body, in-

cluding legs and arms. Widespread anesthesia of legs, and new anesthetic areas on thighs and arms.

Impression: worse.

Comments

It is generally recognized that improvement in a patient under treatment cannot be attributed entirely to the drug used. Under favorable conditions leprosy has a tendency towards self-healing, and improvement may be due to proper diet, better hygienic surroundings, or other conditions incidental to leprosarium care. This fact should be remembered in considering the above cases, especially those who have been more recently institutionalized.

The aggregate of the final impressions of the examiners recorded in the above cases indicates that diphtheria toxoid cannot be regarded as a specific remedy for leprosy. This is brought out in Table 4.

Table 4. *Aggregate of final impressions of examiners.*

	Improved	Stationary	Worse
Toxoid group	3	8	24
Control group	3	14	18

In evaluating his results, Collier (3) took the following factors into consideration:

1. Bacteriologic examinations of the skin and nasal mucous membrane.
2. Determination of the erythrocyte sedimentation rate.
3. Blood counts and urinalyses.
4. Recording of weight.
5. Charting of areas of anesthesia.
6. Record of lepra reactions before and during period of treatment.
7. Photographs of leprous lesions before and after treatment.

All of these factors were taken into account in arriving at the final impression in each of the case records. These various factors may now be considered separately to note how they have been influenced by the toxoid and the broth injections.

Bacteriologic Examination of the Skin and Nasal Mucosa

It will be observed from the case records that with only five exceptions all of the patients were bacterioscopically positive throughout the experimental study period.

Three of these exceptions were in the toxoid-treated group. One is a patient whose skin smears remained negative through the whole course of treatment and are still negative at present. Another is a

patient whose originally positive skin smears became temporarily negative during the middle of the treatment period but reverted to positive towards the end and have remained so to the final observation. The third is a patient who showed negative skin smears at the outset of treatment which returned to positive before the end of the course, persisting positive to the final observation.

In the control series of cases there were only two exceptions to the rule of continuously positive bacteriologic reports. One patient, having started with negative skin smears, was reported negative throughout the period of observation. Another, whose skin smears were originally positive, became negative during treatment and remained so to the end, although a nasal smear taken in June, 1942, proved positive for *M. leprae*.

Determination of the Sedimentation Rate

The Cutler technic recording the fall in the erythrocyte column at the end of one hour was the method employed. In the majority of cases little, if any, change in the sedimentation rate was noted during the entire period of observation. Only an increase or a decrease of 3 mm. or over in sedimentation rates was regarded as of sufficient significance to denote possible improvement or retrogression in the disease. In the following table cases showing differences of less than 3 mm. in a sedimentation test compared with the one at the outset of treatment are listed as stationary. Those showing a decrease of 3 or more millimeters are recorded as improved, and those showing an increase of 3 or more millimeters as worse.

Table 5. *Changes in sedimentation tests*

	Toxoid group			Control group		
	Improved	Stationary	Worse	Improved	Stationary	Worse
10 months' treatment.....	5	20	8	8	22	2
5 months' post-treatment.....	5	14	12	5	20	7

The results shown in this table are in favor of the control over the toxoid-treated group.

Blood Counts and Urinalyses

These laboratory procedures were frequently performed on all patients during the observation period. Although they are valuable indicators of the patient's general condition, there occurred no changes in any patient's blood picture or urinary findings which could be attributed in any way to the toxoid or broth injections. They are therefore not discussed further here.

Recording of Weight

Each patient's weight was recorded prior to and during the course of treatment and at the final observation period. The following table gives the results of these findings, a difference of less than three pounds above or below the original weight being listed as a stationary weight.

Table 6. *Changes in weight*

	Toxoid group			Control group		
	Increase	Stationary	Decrease	Increase	Stationary	Decrease
10 months' treatment	9	19	6	13	15	7
5 months' post-treatment	8	12	11	15	7	10

From this table it can be seen that the general health of the control group of patients, as indicated by their weight, was better than that of the toxoid group both during and after the experimental treatment.

Charting Anesthetic Areas

It was found at the final examination that in the toxoid-treated cases areas of anesthesia had increased in 20, were stationary in 5, and had decreased in 2. In the control group there was an increase of anesthesia in 10, a stationary condition in 17, and a diminution of anesthesia in 3.

Record of Lepra Reaction before and during Period of Treatment

It was found that instead of abolishing lepra reactions, the toxoid injections seemed to initiate lepra reactions in 4 patients. In an additional 5 cases, lepra reactions seemed more severe or more frequent during the course of toxoid treatment than they had been prior to that time. In 3 cases lepra reaction continued unabated during the treatment course. In only one case did lepra reactions cease on the institution of this therapy; Collier's contention, then, that the cessation of lepra reactions was one of the treatment's important results, is not corroborated at the National Leprosarium.

In the control group by comparison it is found that initial lepra reactions were experienced by two patients, a greater severity or more frequent attacks occurred in four patients, a continuation of lepra reactions of equal severity in two, and a decrease or abolition of lepra reactions in three.

One of the favorable actions of diphtheria toxoid reported by Collier (3) was the prompt relief of lepra neuritis. This was not

observed in our cases and, on the contrary, three patients complained of severe lepra neuritis during the course of treatment. In the control group there was relief of lepra neuritis in one case and production of lepra neuritis in one case.

Photographs of Leprous Lesions before and after Treatment

During this experimental study 276 photographs were taken. Only a few of those demonstrating the changes which occurred in leprous lesions are included in this report. Others showing equally outstanding unfavorable developments are in the files at the U. S. Marine Hospital, Carville, Louisiana, for future reference.

Third Experimental Group

A third group of patients who eagerly requested this new treatment was started on it in June, 1941. There were 183 patients in this group, and they were given the diphtheria toxoid by the method already described. Most of them took the treatment for nine months. Only six of these patients show any definite improvement at the present time. Four of these six are of the tuberculoid type, in which type spontaneous improvement is common; the other two were already improving and were bacterioscopically negative at the outset of this treatment. One hundred twenty-one are definitely worse and have shown new lesions or evidence of an extension of the old lesions. Fifty-six are classified as stationary with no material change in their condition at the present time. A majority of the 183 patients blame the treatment for the aggravation of their disease.

During the course of treatment of this last group of patients it was noted that acute lepra reactions were frequent. In none of these patients was a lessening of areas of anesthesia demonstrated, whereas an extension of the zone of anesthesia was not an unusual finding.

Conclusions

From close observation of 35 patients treated with diphtheria toxoid for one year under carefully controlled conditions and from the observation of 195 other patients treated with diphtheria toxoid from 6 to 15 months, it is concluded that this treatment has no beneficial therapeutic action in leprosy.

It is the unanimous opinion of the medical staff of the National Leprosarium that diphtheria toxoid is productive of no good and is fraught with danger for the patient with leprosy.

Acknowledgments

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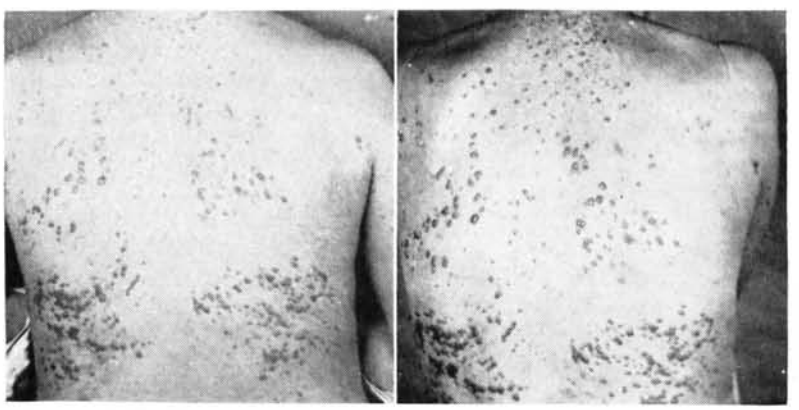
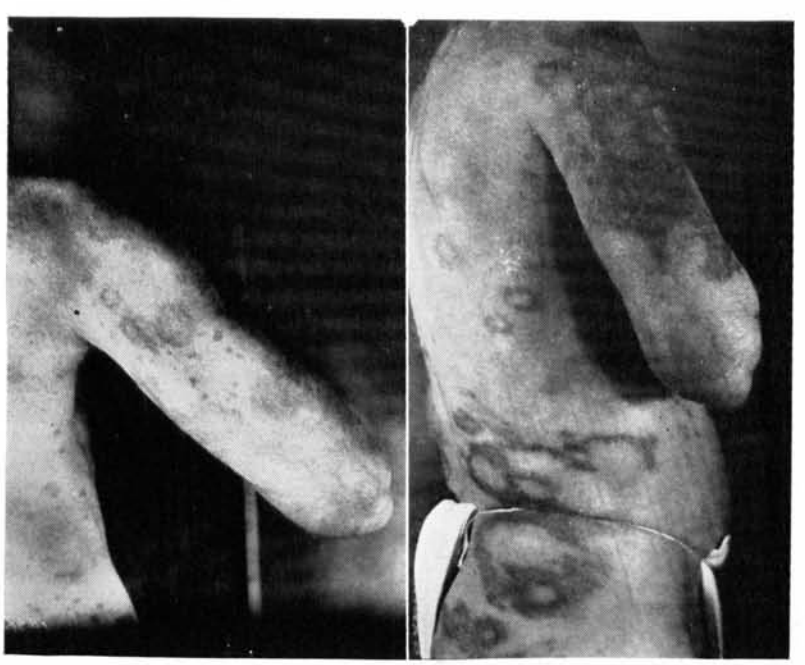


March, 1941 CASE NO. 1203 July, 1942

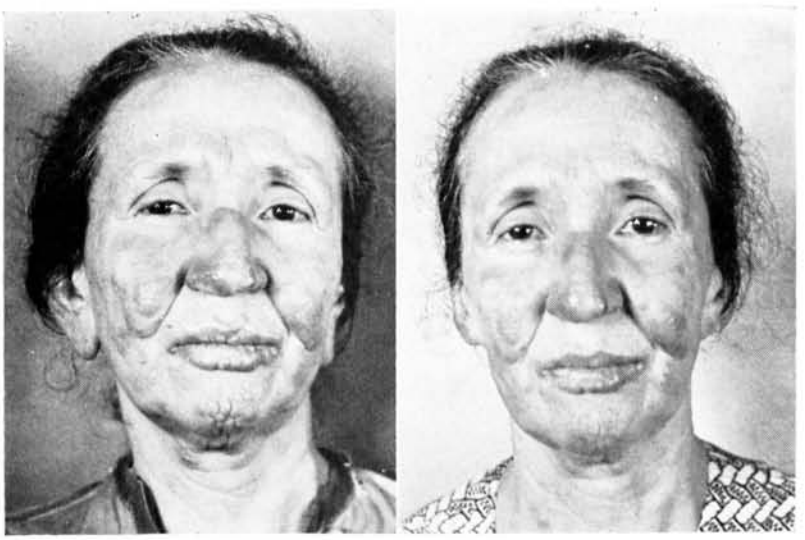
TOXOID GROUP



March, 1941 CASE NO. 1438 July, 1942

TOXOID GROUP

PLATE 1



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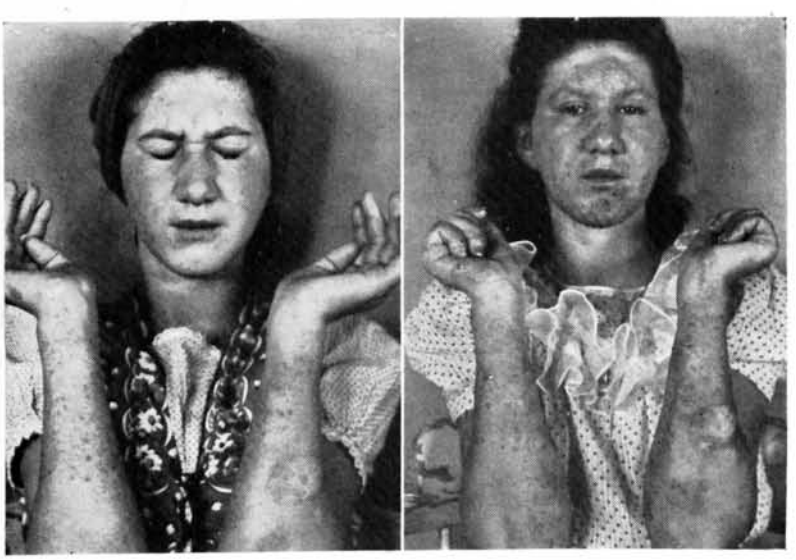
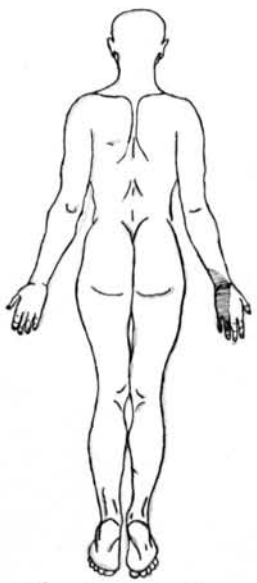


March, 1941 CASE NO. 1391 July, 1942

TOXOID GROUP

PLATE 2

Case 1046 ~ Toxoid Group

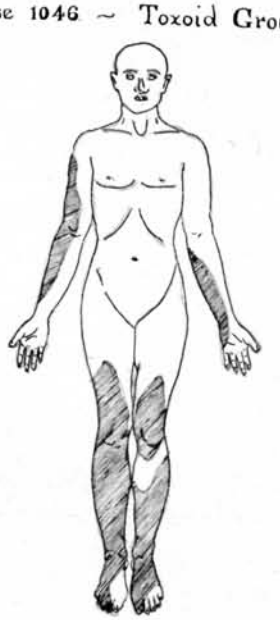


Area of Anesthesia to Pain ~ March 1941

Case 1046 ~ Toxoid Group

Areas of Anesthesia to Pain ~ March 1941

Case 1046 ~ Toxoid Group



Areas of Anesthesia to Pain ~ July 1942

Case 1046 ~ Toxoid Group

Areas of Anesthesia to Pain ~ July 1942

CASE NO. 1046

PLATE 3