

TREATMENT OF LEPROSY WITH DIPHTHERIA TOXOID*

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In the treatment of leprosy, a problem which still awaits a satisfactory solution, it is of the utmost importance that any new medication or new therapeutic method should be received with an open mind, especially if it should originate in a scientific center. At the same time it should be tested quietly and meticulously in other centers in order that agreement may be reached regarding its value.

The experiments of Oberdoerffer and Collier on the treatment of leprosy with diphtheria antitoxin and toxoid, a preliminary report of which was published by Collier and McKean (1), were given much publicity in the United States and also awakened public interest in this country. We had resolved therefore to repeat them in the Carrasco Leprosy Service so that our opinion on the subject might be based upon personal experience. But it was the later report of Collier (2) with such encouraging results, superior to those obtained with any other type of medication, according to the author, which caused us to postpone no longer a repetition of the experiments.

The work of Oberdoerffer and Collier: Space will not be taken for an extensive analysis of the theories of these authors and the results which they have reported as these have been discussed recently in the JOURNAL (3). We will limit ourselves to the following points:

(a) Treatment with diphtheria toxoid is based upon the hypothesis of Oberdoerffer that in leprosy there is a functional deficiency of the adrenals. It is well known that in diphtheria the toxin damages these glands. Therefore diphtheria antitoxin conceivably might prevent this deficiency, perhaps by neutralizing "leprosy toxin."

(b) A number of patients who had been having severe lepra

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reactions were treated with antitoxin with results considered to be beneficial. Since, in diphtheria, antitoxin produces only temporary immunity, active immunization with toxoid was regarded as even more promising.

(c) Diphtheria toxoid therefore was used in treatment, commencing with a dose of 0.5 cc., increasing to 2.0 cc. and continuing every two weeks with this dosage.

(d) Results followed which are described as "startling," superior according to Collier, to those obtained with any form of treatment previously employed; results based upon a large series of 600 cases treated at the Chiengmai Leprosarium in Thailand. Among other indications of success let us mention the following:

1. Clinical and bacteriological improvement after six months of treatment in 50 per cent of early cases, including those of type L1.
2. Beneficial effect on nervous disturbances (sensation, neuralgias, atrophies), on the lepra reaction and on the iritis.
3. In advanced lepromatous cases even better evidence was obtained than in early, a higher percentage showing improvement.
4. Action on the bacilli, consisting first in fragmentation and evident diminution and later in disappearance.

It was especially these latter points (beneficial effect in advanced lepromatous cases and the bactericidal action) which influenced us to undertake our experiments without further delay.

EXPERIMENTAL

Our experimental work was initiated in May, 1941, with a group of 11 patients, purposely kept small so that they could be followed in greater detail. If favorable results were obtained it was our intention to increase the number.

Selection of cases: To appraise the therapeutic value of a remedy in leprosy it is of primary importance that the cases to be subjected to the treatment must be selected and classified with great care. At the outset, "tuberculoid" cases should be rejected. These tend to improve spontaneously. In the favorable evolution of these the factor of human resistance is more important than medication. Only lepromatous cases should be included. These are cases with low resistance which have a tendency to progress and which influence greatly epidemiological, prognostic and therapeutic viewpoints on leprosy. This selection should be founded upon a rigorous classification, clinical, bacteriological and histopathological, and above all immunological; that is, they must be cases with a negative Mitsuda reaction.

Our first group of patients included ten of the lepromatous type (3 L1; 3 L2; 4 L3) and one of the tuberculoid, the latter included merely for comparison.

Material employed: Diphtheria toxoid was furnished by the National Department of Health. It was injected intramuscularly.

commencing with one cc. and increasing rapidly to a dose of three cc. which was repeated weekly. Tolerance was perfect, even though we gave larger and more frequent doses than those administered by Collier. All 11 patients were treated for approximately five months and each received from 15 to 17 injections and a total of 45 to 50 cc. of toxoid.

Results: Clinical and bacteriological examinations of the patients were made every two weeks. Scrapings were taken from the same sites on each occasion in order to secure evidence of fragmentation and diminution in numbers of bacilli. To save space we shall limit ourselves to descriptions of the condition before and after the five months of toxoid treatment, without recording the results of intervening examinations.

We should emphasize that at no time did we observe any improvement, but we endeavored to continue for a sufficient period before expressing an opinion. Analyzing now the results after five months of treatment with toxoid we regret to state that they were completely negative. None of the patients has shown the slightest improvement; three have remained stationary (Nos. 1, 2, and 6) and eight others have evidently become worse. This progression was manifested clinically by infiltration, increase of old lesions and appearance of new (Nos. 9 and 10), and bacteriologically by frank increase in the quantity of bacilli and globi.

Among our patients there are three (Nos. 2, 5, and 10) who had not received any previous treatment. Experience has taught us that lepromatous cases treated for the first time almost always are benefited by the first series of chaulmoogra. We sought to discover if the same occurs with diphtheria toxoid. Apparently this is not so, as these patients evidently became worse, especially No. 10.

Neither did we obtain satisfactory results in any patients with the lepra reaction nor in the neurological aspects of the disease (disturbances of sensation, neuralgias and atrophies).

Conclusions: We failed with diphtheria toxoid in all our patients, even in one of the tuberculoid form as well as in all of the lepromatous cases. Instead of regression, we observed progress, appearance of new lesions and increase in numbers of bacilli. For these reasons we decided to terminate the experiment and to continue with chaulmoogra medication.

SUMMARY

1. Having become interested in recent favorable reports by other workers on treatment of leprosy with diphtheria toxoid we subjected a group of 11 patients, ten lepromatous and one tuberculoid, to this treatment over a period of five months.

2. None of the patients improved, three remained stationary and eight became worse, clinically and bacteriologically. We therefore decided not to pursue the investigation further.

CLINICAL HISTORIES

The patients for which details are given were treated for five months (May 26th to October 26th, 1941), by means of weekly injections of diphtheria toxoid. The average number of injections was 18 and the average total quantity was 50 cubic centimeters.

CASE No. 1. A. Bor. 55 yrs. Form L3N1.

Clinical condition

May 26, 1941

Patches on the back, color of *café con leche*. Papules and tubercles on both upper and lower limbs. Atrophy of interossei of hand.

October 26, 1941

The same elements, patches, papules, and tubercles persist in the same areas. No clinical change in lesions or in atrophies.

Bacteriological condition

Many bacilli and globi in all fields. Streptococcoid and diplobacillary forms predominate, but there are also uniformly stained bacilli.

No change. Abundant bacilli and globi persist. Streptococcoid forms predominate. Uniformly stained bacilli persist. No diminution in numbers of bacilli.

Result: *Stationary.*

CASE No. 2. M. Giu. 58 yrs. Form L2N1 (no previous treatment).

Clinical condition

May 26, 1941

Average number of tubercles on chest, back, abdomen, arms, some on face. Some show central ulceration. Erythematous spots, both feet.

October 26, 1941

Tubercles persist but give impression of reduction in size. Some tubercles show cicatrization.

Bacteriological condition

Many globi and bacilli in all fields. Predominately diplobacillary and streptococcoid in form, but there are uniformly stained bacilli.

Large numbers of bacilli and globi fill the microscopic fields.

Result: *Stationary; slight clinical improvement; decided bacteriological progression.*

CASE No. 3. (Photographs Nos. 1, 2), (Plate 1), F. Fa 20 yrs. Form L3N1.

Clinical condition

May 26, 1941

Light brown erythematous spots, flattened and some infiltrated, on thighs and buttocks. Legs completely covered by tubercles of various sizes, some the size of a large pea. Inguinal adenopathy both sides.

October 26, 1941

Spots on buttocks and thighs are more deeply infiltrated and tubercles seem to have increased in size.

Bacteriological condition

Quantities of bacilli and globi in all fields. Streptococcoid forms predominate but there are solidly stained bacilli present.

Large numbers of globi and bacilli in all fields. Predominately streptococcoid. Solidly stained bacilli also present.

Result: *Condition worse (clinically and bacteriologically).*

CASE No. 4. Al. Fi. 16 yrs. Form L1.

Clinical condition

May 26, 1941
Erythematous spots, brownish, flattened, on back, thighs, and legs. No tubercles.

October 26, 1941
Spots on back with the same appearance, although some show more infiltration. A few tubercles on thighs and legs.

Bacteriological condition

Average number of bacilli in all fields. Occasional globi.

Large numbers of bacilli in all fields. Many globi.

Result: *Condition worse (clinically and bacteriologically).*

CASE No. 5. J. Le. 21 yrs. Form Nt (no previous treatment).

Clinical condition

May 26, 1941
On the forehead, both sides of nose, contiguous portions of the cheeks, and lower maxillary regions, violet-colored erythematous plaques, raised, infiltrated, with well-defined edges and smooth surfaces.

October 26, 1941
The congestion has lessened, but infiltration is greater. The surface of the plaques is now scaly.

Bacteriological condition

No bacilli.

No bacilli.

Result: *No improvement.*

CASE No. 6. Am. P. 21 yrs. Form L1.

Clinical condition

May 26, 1941
Brown erythematous spots on the thighs and buttocks, flattened, which tend to coalesce. Some small papules observed.

October 26, 1941
Spots are paler and the papules less prominent.

Bacteriological condition

Few bacilli and very rare globi.

Average number of bacilli and globi.

Result: *Stationary. Slightly better clinically; bacteriologically there is progression.*

CASE No. 7. N. C. 49 yrs. Form L3.

Clinical condition

May 26, 1941
Diffuse infiltration on face. Patches on limbs and trunk, bronze in color. Numerous papules and tubercles on these patches.

October 26, 1941
No improvement clinically. Lesions appear unchanged.

Bacteriological condition

Abundant bacilli and globi in all fields. Streptococoid and diplobacillary forms predominate.

Abundant bacilli and globi in all fields. Same bacillary forms predominate.

Result: *Stationary.*

CASE No. 8. F. So. 61 yrs. Form L2.

Clinical condition

May 26, 1941

Large bronze-colored spots cover a large part of the skin surface. On these are papules and tubercles of various sizes.

October 26, 1941

No change. Spots and tubercles persist without sign of improvement.

Bacteriological condition

Large numbers of bacilli in all fields and globi.

Large numbers of bacilli and globi in all fields.

Result: *Stationary.*

CASE No. 9. A. Te. 50 yrs. Form L2.

Clinical condition

May 26, 1941

Copper-colored spots cover the major part of the body, mostly flat and some infiltrated. There are papules and tubercles about the size of a grain of corn.

October 26, 1941

The lesions persist without change. New tubercles have appeared as well as some nodules.

Bacteriological condition

Numerous bacilli and a few globi in most of the fields. Predominating are solid-staining and streptococoid forms.

Average number of bacilli and numerous globi in many fields. Streptococoid forms predominate but solid-staining bacilli persist.

Result: *Worse.*

CASE No. 10. J. Tr. 40 yrs. Form L1. (no previous treatment).

Clinical condition

May 26, 1941

Copper-colored erythematous patch in lumbar region and upper buttock, flattened in all its surface except supra-external. One tubercle on forehead; one on upper lip. Nothing on rest of body.

October 26, 1941

Patch on the thigh is more prominent. The tubercles greatly enlarged. Erythematous spots and papules have appeared on abdomen, back and upper limbs.

Bacteriological condition

Average number of bacilli in most of the fields, streptococoid forms predominating. Occasional globi.

Very great abundance of bacilli in every field and globi in the majority.

Result: *Clinically and bacteriologically worse.*

CASE No. 11. (Photographs Nos. 3 and 4), (Plate 1). B. Me. 51 yrs. Form L2.

Clinical condition

May 26, 1941

Bronze-colored erythematous spots on the limbs and trunk. The majority are flat and a few infiltrated in the center.

October 26, 1941

The spots are more infiltrated over all the limbs.

Bacteriological condition

Bacilli in all fields and globi in some. Streptococoid forms predominate but there is an average number of uniformly stained bacilli.

Numerous bacilli and globi in all fields. Streptococoid forms predominate but there is an average number of uniformly stained bacilli.

Result: *Clinically and bacteriologically worse.*



May, 1941

October, 1941

CASE No. 3



May, 1941

October, 1941

CASE No. 11

PLATE I

REFERENCES

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