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DIPHTHERIA TOXOID IN THE TREATMENT OF LEPROSY

CLINICAL AND IMMUNOLOGICAL INVESTIGATIONS

A. R. DAVISON AND E. GRASSET

In the Thai Science Bulletin, April 1940, Collier¹ reported on the use of diphtheria toxoid in the treatment of leprosy and this has been followed by a second report in the International Journal of Leprosy January-March 1941². His results were very encouraging and in an effort to duplicate them we selected 100 cases in July 1940 and placed them under observation while undergoing treatment by diphtheria formoltoxoid.

The investigation was approached from (1) the Clinical and (2) the Immunological aspects.

1. *Clinical:* Forty cases—European and Bantu, were set aside for special study. They comprised a selection of every type and stage of the disease. Sixty cases, mostly Europeans, of the L₂ and L₃ type completed the series. A monthly record was kept of the weight, bacillary condition and clinical changes of all cases. The special study group were Schick tested and a monthly record was made of their sedimentation index. They were further divided into four groups of which three received accessory treatment.

2. *Immunological:* A series of special study cases were Schick tested before treatment. Sixteen representative cases had a titration of diphtheria antitoxin done before and after treatment with a view to the possible correlation between the clinical results and the immunological findings.

SCHEME OF IMMUNIZATION AND NATURE OF THE REACTIONS FOLLOWING DIPHTHERIA TOXOID INJECTIONS.

(I) The diphtheria formoltoxoid used for immunization was prepared in the Serum Department of the South African Institute for Medical Research and was taken from the stocks issued to the public for anti-diphtheritic immunization. It originated from several batches, all prepared from the P.W.No.8 B. Diphtheria strain.

The immunizing properties of the product are tested in accordance with the Union's Therapeutic Substances Regulations.

(II) *Dosage*: The injections were given subcutaneously every fortnight. The dosage was commenced at $\frac{1}{2}$ cc. then 1 cc. then $1\frac{1}{2}$ cc. followed by 2 cc's. As at this stage there was no sign of any clinical or bacteriological effect the dosage was raised by 1 cc. at each subsequent injection until a maximum of 10 cc's was reached.

(III) *Reactions following Diphtheria Toxoid*: The local reactions were slight. In most cases there was slight tenderness at the site of the injection for 48 hours. Others showed a zone of erythema around the site—this also faded rapidly. The reactions were only slightly more severe with the larger than with the smaller doses.

General reactions: Following the injection a slight elevation of temperature occurred and complaints of insomnia with pains in the head and shoulders were sometimes received. These complaints increased as the dosage increased above 5 cc's. One case only, No. 541, had severe reactions with each injection. The erythema here sometimes encircled the arm and extended from the shoulder to the elbow. The final injection of 10 cc's. was followed by the reactionary phase with an acute outcrop of nodules—located almost exclusively to the sites where she had previously received intradermal ethyl esters of hydnocarpus.

(IV) *Grouping*: As we have been investigating group antigen therapy we took the opportunity to try the effect of combined therapy and the cases were, therefore, divided into 4 groups.

Group I. Diphtheria toxoid alone.

- ,, II. Diphtheria toxoid plus an emulsion of the whole diphtheria bacillus (1,000 millias p.c.c.) the latter given bi-weekly in 1-10 cc. doses.
- ,, III. Diphtheria toxoid plus T.B. Endotoxoid, given as above.
- ,, IV. Diphtheria toxoid plus a killed emulsion of a T.B. culture which had lost its acid-fast properties (hereafter called N.A.C.) given as above.

TABLE I.

Tables of Clinical Findings: The following tables show the type of the disease (N=neural, L=lepromatous), the registered number of the patient and the clinical and bacillary condition before and after the course of treatment.

GROUP I.

DIPHTHERIA FORMOLTOXOID.

July, 1940.

February, 1941.

		Worse.		
L3. 475.	New nodules on legs	L.B. +	Acute reactionary phase	L.B. +
L3. 476.	Flat infiltration face	L.B. +	New infiltration buttocks	L.B. +
L3. 536.	Slight early infiltration	L.B. +	Infiltration worse	L.B. +
L3. 541.	Slight early infiltration	L.B. +	Infiltration worse	L.B. +
L2. 543.	Slight early infiltration	L.B. +	Reactionary phase	
L3. 519.	Absorbing infiltration face	L.B. +	Infiltration worse	L.B. +
		Total 7.	Face—no change.	L.B. +
			Erythematous	
			nodules	limbs

No Change.

L1. 506.	Diffuse infiltration face and trunk	L.B. +	No Change	L.B. +
L1. 507.	Erythematous infiltration eyebrows	L.B. +	"	L.B. +
L3. 532.	Diffuse infiltration face	L.B. +	"	L.B. +
L3. 539.	Slight infiltration trunk	L.B. +	"	L.B. +
L3. 540.	Infiltration face. Erythema Nodosum leproticum	L.B. +	"	L.B. +
L3. 551.	Firm infiltration	L.B. +	"	L.B. +
L1. 530.	Scarlet plaques	L.B. +	"	L.B. +
L3. 520.	Infiltration face, back and arms	L.B. +	"	L.B. +
L3. 513.	Infiltration face. Plaques body	L.B. +	"	L.B. +
L3. 486.	Subsiding plaques	L.B. +	"	L.B. +
L3. 483.	Erythematous infiltration	L.B. +	"	L.B. +
L3. 464.	Erythematous infiltration	L.B. +	"	L.B. +
N1. 454.	No lesions but nasal smear	L.B. +	Nasal smear	L.B. +
L3. 452.	Erythematous infiltration	L.B. +	No Change	L.B. +
L3. 449.	Heavy infiltration	L.B. +	"	L.B. +
L3. 446.	Scarlet infiltration	L.B. +	"	L.B. +
L3. 344.	Diffuse infiltration	L.B. +	"	L.B. +
L3. 314.	Erythematous plaques	L.B. +	"	L.B. +
L2. 550.	Infiltration face	L.B. +	"	L.B. +
N2. 549.	Erythematous macules	L.B. —	"	L.B. —
L3. 7788.	Heavy infiltration	L.B. +	"	L.B. + +
N2. 7817.	Raised margins macules,	L.B. —	Macules flatter but new outcrop of macules	L.B. —
L3. 7232.	Erythematous infiltration, no rugae	L.B. +	No Change	L.B. +
L3. 6750.	Face infiltration	L.B. +	"	scanty L.B. + +
		Total 24.		

Slight Improvement.

L3. 499.	Multiple erythematous lepromatous lesions	L.B. +	Lesions flatter and browned	L.B. +
L2. 529.	Trace erythematous infiltration face	L.B. +	Less erythema	L.B. +
N1. 548.	Raised erythema macules	L.B. —	Macules red but flat	L.B. —
L2. 546.	Subcutaneous nodules	L.B. +	Nodules absorbed but skin shows	L.B. +

L2.	535.	Infiltration ear lobes and buttocks	L.B. +	Infiltration ab- sorbed buttocks	L.B. +
L3.	527.	Trace infiltration face	L.B. + scanty	Infiltration less	L.B. +
L3.	524.	Slight infiltration	L.B. +	Infiltration less	L.B. +
L2.	515.	Trace flat erythematous lepromata on arm	L.B. +	Erythema fading	L.B. -
L3.	492.	Slight rugae forehead	L.B. +	Skin more pliable	L.B. +
N1.	473.	Pink raised macules	L.B. -	Less raised	L.B. -
L3.	479.	Generalised infiltration trunk	L.B. +	More pliable	L.B. +
N2.	6965.	Erythematous macules raised	L.B. -	Flatter and less erythematous	L.B. -
N2.	7739.	Spongy tuberculoid minor macules	L.B. -	Less raised	L.B. -
N2.	7713.	Spongy tuberculoid minor macules	L.B. -	Less raised but	L.B. +
			Total 14.		

Marked Improvement.

N1.	342.	New macules	L.B. +	26/2/41. No ac- tivity	N.S. -
N1.	552.	Early maculo-anæsthetic pink macules	L.B. -	No activity	L.B. -
N2.	7842.	Dusky red raised macules	L.B. -	Macules flat in- active	L.B. -
N2.	378.	Outcrops of new macules	L.B. -	Macules gone	L.B. -

Total 4.

Conclusion:

Only four cases out of 48 showed marked improvement. These were all neural cases who would have responded equally well to intradermal ethyl esters of hydnocarpus.

GROUP II.

DIPHTHERIA FORMOLTOXOID PLUS EMULSION B. DIPHTHERIA.

July, 1940.

February, 1941.

Worse.

N2.	407.	New maculae back and abdomen	L.B. -	New maculae face, others persist	L.B. +
N3.	7851.	Trace erythema of some macules others healed	L.B. -	Infiltration fore- arms	L.B. +
L3.	6663.	Small 6d. sized plaques	L.B. +	Multiple new plaques	L.B. +

Total 3.

No Change.

N1.	544.	Slight erythema maculae	L.B. -	No Change	L.B. -
L1.	547.	Slight infiltration face	L.B. +	"	L.B. +
N2.	7853.	Tuberculoid minor maculae	L.B. -	"	L.B. -
N2.	7855.	Flat pale macules	L.B. -	"	L.B. -

Total 4.

Slight Improvement.

L1.	538.	Erythematous macules with one plaque	L.B. +	Macules fading. Plaque persists	L.B. +
N2.	7738.	Slightly erythematous raised margins	L.B. -	Less raised and red	L.B. -
N2.	7838.	Raised brown macules	L.B. -	Less raised more granular	L.B. -
L1.	7847.	Raised erythematous plaques	L.B. +	Plaques flatter	L.B. -

Total 4.

Conclusion :

The addition of emulsion of B.Diphtheria did not favourably influence the effect of diphtheria toxoid.

GROUP III.

DIPHTHERIA FORMOLTOXOID PLUS GRASSET'S TUBERCLE ENDOTOXOID.

*July, 1940.**February, 1941.*

		Worse.	
L3. 7438.	Small plaques	L.B. +	Infiltration worse
N1. 7608.	Flat pale macules	L.B. -	Raised red new macules
			Total 2.
		No Change.	
L3. 381.	Diffuse infiltration trunk	L.B. +	No Change
L3. 7601.	Diffuse infiltration face	L.B. +	"
			Total 2.
		Slight Improvement.	
N2. 6852.	Raised margins to maculae	L.B. -	Less raised
N2. 6247.	27/8/40. Reactionary phase, macules very raised. Two nodules on face	L.B. +	No nodulae, Margins
			Total 2.
		Marked Improvement.	
N2. 7872.	Very raised black mar- gins to maculae	L.B. -	No activity in residual maculae
			Total 1.

Conclusion :

Only one case showed marked improvement under diphtheria formoltoxoid plus Grasset's tubercle endotoxoid. The small number of cases does not permit a true appreciation of the value of this combined treatment.

GROUP IV.

DIPHTHERIA FORMOLTOXOID PLUS N.A.C.

*July, 1940.**February, 1941.*

		Worse.	
		Nil.	
		No Change.	
L3. 7105.	Early infiltration. Chronic reactionary phase	L.B. -	No change
N2. 6607.	Raised dusky spread- ing macules	L.B. -	"
L3. 7645.	Slight erythematous in- filtration face	L.B. -	"
N2. 7365.	Raised erythematous pea-sized macules	L.B. -	"
			Total 4.
		Slight Improvement.	
N3. 7667.	Grey granular macules	L.B. +	Now macules are flat and pale
			Total 1.
		Marked Improvement.	
		Nil.	

Conclusion:

The combined treatment by diphtheria formoltoxoid plus N.A.C. is not of obvious value, but the number of cases is small.

TABLE II.
RESULTS OF TREATMENT OF 71 CASES ACCORDING TO TYPE OF THE DISEASE.

CASES	N ₁ 7	N ₂ 17	N ₃ 2	L ₁ 6	L ₂ 6	L ₃ 23	Totals 71
BACTERIOLOGY							
Negative throughout ...	5	14	—	—	—	—	19
Positive to Negative ...	1	1	1	1	1	—	5
Negative to Positive ...	—	2	1	—	—	3	6
Persistently Positive ...	1	—	—	5	5	30	41
SKIN LESIONS							
Improved ...	4	10	1	1	4	5	25
No change ...	2	6	—	5	1	21	35
Worse ...	1	1	1	—	1	7	11

Clinical Investigation. Treatment was naturally voluntary and the first significant fact which emerges is that only 71 patients completed the seven months course. It is no doubt the common experience that leprosy patients will persist with any treatment, however painful, where they can observe any improvement. In the 25 cases who showed improvement in the final assessment it was noted that improvement had occurred in the early months, but the changes were slight and were probably not obvious except to a leprologist. Changes recorded were "maculæ flatter and paler," "erythema less in infiltrated areas," "maculæ healing in centre," "maculæ not so spongy" and "infiltrated skin more pliable." Such changes of course occur as natural fluctuations of the disease and occur whether a patient is under treatment or not. But it is encouraging that these changes persisted. The only clinical changes of real significance are the five cases recorded as "Marked Improvement."

Weight—no changes were observed which did not conform to ordinary seasonal changes, i.e., during the winter football season our patients show, on an average, a lower weight.

Sedimentation Index—our sedimentation index is read at the end of one hour—the blood having been mixed with potassium oxalate. We do not regard the index as showing any direct relation to the leprotic condition but it does reflect intercurrent infections, or causes of debilitation, e.g., septic feet or fingers. The average sedimentation index of these cases under treatment showed no alteration one way or the other.

Bacillary condition—not only the presence or absence of bacilli was noted but the degree of fragmentation or clubbing of the

bacilli. During the period of observation we were cheered to note fragmentation occurring in many cases but were again disappointed to find these cases at later dates showing normal bacilli. Only five of the cases previously showing bacilli are now negative, but on the other hand six cases previously negative are now showing bacilli.

IMMUNOLOGICAL INVESTIGATIONS.

As stated above, a series of sixteen patients was selected for these investigations. Five were European, all adult females, and eleven were natives, of whom nine were males, including eight adults and a child of nine years and two adult females.

These patients were Schick tested and the diphtheria antitoxin content of their blood was titrated before and after immunization.

Schick Test.

The Schick test material used was prepared at the South African Institute for Medical Research. The toxin was a matured diphtheria toxin prepared in 1937 from the P.W. No. 8. *B.diphtheria* strain. Glenny's modified buffer solution was used for the dilutions. This Schick test material is controlled in accordance with the Union Therapeutic Substances Regulations.

0.2 c.c. of the Schick test material was injected intradermally in the right forearm in a non-affected area; 0.2 c.c. of the control heated Schick solution was similarly injected in the left forearm. The reactions were read after 24, 48, 62 and 86 hours.

Results of Schick tests before Immunization.

The results are given in column 5 of Table III. They show that three out of five of the European patients exhibited a positive Schick reaction, one after 24 and the second after 48 hours; the third showed a less typical, delayed reaction, which appeared only on the third day. All the natives proved to be non-reactors, i.e., Schick negatives. This last finding agrees with the observations referred to in previous immunological studies on the anti-diphtheritic immunity among Bantus (E. Grasset and others, 1933)³, that a considerably higher rate of Schick non-reactors is shown among South African Natives than among Europeans.

Antitoxin Titration.

The antitoxin titration of the serum of these patients *before immunization* was carried out by means of the Römer method modified by Zingher⁴, by intradermal injections of toxin-antitoxin mixtures in guineapigs, which allows the determination of minute amounts of antitoxin. The titrations were done within wide limits, from 1/500 antitoxin unit to 1/100 u., 1/50 u., 1/25 u.,

$1/10$ u., and $1/2$ antitoxin unit per cc. These results are to be found in column 5 of Table III.

Titration of diphtheria antitoxin was again carried out on the serum of the same patients *after a course of 6 months of diphtheria toxoid immunization*. Blood was taken from thirteen patients on the 11th February, 1941, i.e., 3 weeks after the last toxoid injection, but from three patients (Nos. 407, 499 and 7847) samples of blood could only be taken on the 7th May, i.e., about 4 months after immunization.

Preliminary titrations covering a wide range indicated a considerable increase of the antitoxic contents of most of the sera. Further titrations by means of the Ehrlich method, using one guineapig per mixture, were carried out to end titre for each serum from a minimum of $1/2$ unit to a maximum of 50 units, according to the following increasing dosage: 0.5 u., 1 u., 5 u., 10 u., 20 u., 30 u., and 50 antitoxic units per cc. of serum.

The results of these titrations are indicated in column 6 of Table III. In only one case was the antitoxic titre found to be less than $1/2$ u. It corresponds to one of the two Schick positive European patients, whose titre before immunization was below $1/500$ u. per cc. By contrast the titre of the second case—also Schick positive originally, and less than $1/500$ per cc.—reached $10 < 20$ units per cc. after immunization.

Classification of the antitoxic contents of the series of sera into groups corresponding respectively to < 1 u.; 1 to 5 u.; 5 to 10 u.; 10 to 20 u.; 20 to 30 u.; and > 30 u., is shown in Table IV.

Table III—see next page

TABLE IV.

Antitoxin titre in units per c.c.	1 u.	1-5 u.	5-10 u.	10-20 u.	20-30 u.	30 u.
Number of Sera	2	3	1	7	2	1

It can be seen that the group containing the highest number of cases is that corresponding to $10-20$ units, represented by 7 cases, i.e., 43.75 per cent of the total of the cases. Although the number of cases included in these titrations is small, and has no statistical value, some interesting observations can nevertheless be drawn from these investigations.

On the whole the immunity response to diphtheria toxoid is

TABLE III.

RESULTS OF TITRATION OF DIPHTHERIA ANTITOXIN IN LEPER CASES IMMUNIZED WITH DIPHTHERIA FORMOL TOXOID (ANATOXIN).

Patient's Number.	Race.	Age.	Schick Test.	Titration in units per c.c. of serum.				Amount of Diphtheria Toxoid Injected in c.c.	Clinical Results.
				Before Immunization.		After Immunization.			
547	European	23 yrs.	-	1/10	< 1/2	20	< 30	65	No change
538		36 yrs.	+		< 1/500		< 1/2	17.5	Slight improvement
407		25 yrs.	+	1/50	< 1/25	1/2	< 1	37.5	Worse
499		32 yrs.	-	1/10	< 1/2	10	< 20	39	Slight improvement
378		25 yrs.	+		< 1/500	10	< 20	50	Worse
6965	South African Bantu	43 yrs.	-	1/2	>	10	< 20	66	Slight improvement
7838		19 yrs.	-	1/50	< 1/25	10	< 20	78	Slight improvement
7739		9 yrs.	-	1/25	< 1/10	1	< 5	42	Slight improvement
6663		61 yrs.	-	1/25	< 1/10	40	< 50	67.5	Worse
7855		41 yrs.	-	1/2	>	1	< 5	72	No change
7851		25 yrs.	-	1/10	< 1/2	20	< 30	75	Worse
7847		66 yrs.	-	1/100	< 1/50	1	< 5	67	Slight improvement
6750		26 yrs.	-	1/100	< 1/50	10	< 20	37	No change
7817		46 yrs.	-	1/10	< 1/2	10	< 20	55	No change
7788		28 yrs.	-	1/100	< 1/50	10	< 20	67	No change
7842		20 yrs.	-	1/10	< 1/2	5	< 10	56	Marked improvement

satisfactory. Individual differences like those recorded are similarly observed among series of normal immunized subjects. They are also liable to include exceptional instances of individuals who respond poorly to active immunization.

The two instances given by serum No. 538 and No. 407 of our series, with a respective titre of less than $1/2$ unit and of $1/2$ unit, nevertheless represent an appreciable proportion for a small number of cases; i.e., 12 per cent, a percentage higher than would be normally expected. (No. 538 received only 17.5 cc. of Toxoid.)

Finally, if we attempt to correlate the rate of antitoxin contents of the respective sera with the clinical condition of the patients, as compared with before and after immunization, we come to the conclusion that no relation can be established between the antitoxin titre reached after treatment, and the clinical changes observed in those patients. As indicated in the last column of Table III only one case, No. 7842, of the 16 patients of this series has shown a marked improvement after treatment. His antitoxin titre was determined originally as $1/10$ u., and reached 5 u. after immunization.

On the other hand, the antitoxin titre of the four patients whose condition is indicated as "worse," are to be found from the lowest to the highest titres observed, respectively, $1/2$ u. for Ser. No. 407, 10 u. for Ser. No. 378, 20 u. for No. 7851, and 40 u. for No. 6663.

With regard more particularly to the two patients originally Schick positive, and with a titre of less than $1/500$ u. before treatment, one, as mentioned above, gave a very poor immunity response with less than $1/2$ u. after immunization, accompanied nevertheless by a "slight improvement" of his condition. In the second case the antitoxic titre reached 10 units after immunization, without however any appreciable clinical change. With regard to the third patient, who showed a delayed Schick reaction with antitoxic contents of $1/50$ u. before immunization, his titre, after toxoid injections, remained low— $1/2$ u. per cc.—and his condition became worse.

From the therapeutic point of view, Collier's suggested line of treatment, based on a suprarenal stimulation, does not appear to have attained the expected results in our series, in spite of repeated and increasing doses of diphtheria toxoid spread over a period of several months.

Regarding the hypothesis of an eventual group neutralisation of the leper toxin by diphtheria antitoxin, the rate of circulating antitoxin after active immunisation, would appear sufficient in the larger number of cases of our series, to exert such action.

Out of 72 cases who completed the course of treatment, 12 became worse, 34 showed no appreciable clinical change, 21 showed a slight improvement, and 5 a marked improvement. The proportion of our cases who appear to have really benefited by the treatment is only 6.94 per cent, compared with 50 per cent or more as reported for Collier's series.

We are unable to propose any reason for the differences between the clinical findings observed in our series, and the results claimed in a great majority of the cases treated by Dr. Collier using a similar diphtheria toxoid treatment in Thailand.

Discussion :

Collier's theory that suprarenal inefficiency was a necessary predisposing cause of leprosy seemed strange to us as in reviewing the cases which had passed through our hands, a total of nearly 5,000, not one case of gross deficiency could be traced, and if every leprosy case had some deficiency it seemed natural to expect that some would have shown extreme degrees of deficiency at least such as would be clinically discernable. In further investigations a hundred cases were selected at random and their blood pressures recorded. These were found to be entirely within the normal range. Eight successive post-mortem of non-treated cases had their suprarenals examined and no anatomical degeneration could be discovered.

During the period of toxoid immunization no evidence of suprarenal deficiency was evoked such as collapse, or a sudden fall in the blood pressure or any undue systematic reaction following the injection even of the larger doses. Only one case, already referred to, showed severe local reactions.

Conclusion :

According to Collier's suggested line of treatment, 100 leper patients were submitted to diphtheria formol toxoid immunization, in increasing doses from 0.5 cc. to 10 cc. spread over a period of seven months. The results were assessed nine months after beginning the treatment, and were based on clinical changes, weight, bacteriological examinations and sedimentation rate.

Of the 72 cases who completed the treatment, 12 became worse, 34 showed no appreciable change, 21 showed a slight improvement and 5 (6.94 per cent) a marked improvement.

A series of 16 patients were Schick tested before immunization and the antitoxin of their blood was titrated before and after treatment. The immunity response was found to be satisfactory in the majority of cases. 62.5 per cent of the patients showed an anti-toxin titre of 10 units or more per cc. of serum. No relation could

be established between the antitoxin titre reached after toxoid treatment and the clinical changes observed in these patients.

We cannot suggest any reason for the very limited therapeutic results observed in our series, as compared with those claimed in the majority of cases submitted to a similar treatment by Collier.

Acknowledgments :

We wish to thank Professor A. Sutherland Strachan and Dr. F. W. Simson of the Department of Pathology of the South African Institute for Medical Research, for their much appreciated contribution to these investigations in the examination of *post-mortem* specimens, and Mr. A. W. Schaafsma (Senior Technician, Serum Department) for his valuable assistance with titration of the sera. Also we have to thank Dr. Peter Allen, Secretary for Public Health and for the Union of South Africa, for authority to conduct this investigation.

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THE OJI RIVER SETTLEMENT AND CLINICS REPORT ON THE YEAR 1940

T. D. F. MONEY

1. POLICY.

There has been no change in general policy and steady progress has been made towards the completion of the plan of development outlined in the meeting presided over by His Honour the Chief Commissioner at the Settlement on 15th September 1938. The aim remains to control, that is progressively to reduce the incidence of, leprosy in the community over as wide an area of the Onitsha

Province as possible, and in doing so to afford the maximum of relief possible to those already suffering from the disease.

2. CLINICS.

In accordance with this policy, existing clinics have been maintained, the numbers served thereby showing increases in every case (in one up to fifty-one per cent). These clinics, four in number, serve patients in the Awka, Awgu and Udi Divisions and in some areas bordering on these. In the course of the year a clinic in the Onitsha Division was opened at Orifite, but, owing to opposition which was confined to Orifite Town, the clinic had to be closed after five weeks in operation. Immediately requests flowed in from patients and councils for the re-establishment of the clinic at another site in the area. Eventually it was decided to operate a morning clinic at Amichi and an afternoon clinic at Uke. The attitude of the councils concerned was entirely different from that at Orifite. The reason given by the Amichi council for desiring a clinic was that they had seen the good results from Agulu. Amichi lies nearer to Agulu than does Orifite. The two new clinics have to some extent relieved the great pressure on the Agulu clinic, owing to considerable numbers of patients transferring to them. Despite this the Agulu clinic has, at the close of 1940, twenty per cent more patients on the register than at the beginning of the year.

3. THE SETTLEMENT AS A BASE.

The Settlement has emerged more clearly than ever as the essential base from which clinics are operated. Six of its functions as such may be mentioned.

- (a) From the patients resident in the Settlement are selected those suitable for training for clinic work.
- (b) In the course of treating in-patients and local out-patients at the Settlement, training is given to clinic assistants under close supervision.
- (c) The records of the clinic patients, approaching ten thousand in number, are classified, filed and issued as required for use in the clinics.
- (d) The oil required for injection (averaging approximately forty pints a week) is taken from bulk, treated, sterilised and issued in suitable containers.
- (e) The bacteriological preparations made from patients (approximately 8,500 in the year) are examined in the laboratory.
- (f) Out-patients are treated in the hospital.

4. STAFF.

The staff falls into three sections, namely European, African non-patient, and African patient. The European staff are largely trained for the particular branches of the work which are allotted to them. On the other hand, with but few exceptions, the African non-patient staff are young and unqualified and still in process of training. This is even more true of the African patient staff which, being selected from the patients, is drawn from a body in which even moderate educational attainments are rare. The general plan of the organisation is, therefore, to divide the whole work into departments, the functions of each of which are limited, and as simplified as possible. Each department has, with few exceptions, at least two Africans, the senior of which is responsible to the European member of the staff in charge of his department. Each member of the European staff has charge of several departments. Some such method is essential if the work, which is both extensive and technical, is to be carried on with a staff of which such a small proportion has technical qualifications.

5. THE SETTLEMENT.

(i) *Population.* The Settlement may now be likened to a small town made up of several quarters or villages. In one part there live the men, in another the women, in another the married couples, in another those under observation, in another the staff, in another those concerned in the market or with contracts in the Settlement. The in-patients have increased by 75% and the staff by 54%. In addition, relatives and servants of the staff permitted to live in the Settlement are a considerable number. Fifty new houses were built in 1940. In all, it is calculated, the community at Oji River now numbers 621. With church, schools, market, councils, court, hospital, dispensary and playing fields, a life that may compare not unfavourably with that which they have left is lived by farmers, nurses, clerks, blacksmiths, brickmakers, watchmen, teachers, school children and many others.

(ii) *Public Health.* Sanitation by means of Otway pits is generally used throughout the Settlement and is most satisfactory, being both simple of construction and effective. A notable step forward has been the acquisition of land along the whole of the south border of the Settlement. A number of undesirable dwellings had begun to appear on this land which is now brought under control. This was most desirable as the land in question is adjacent to the African and European staff reserves in the Settlement. There were no major epidemics of disease in the Settlement during the year.

(iii) *Market.* The establishment of a market (Oye), arranged suitably for use by both patients and others, is proving of benefit to those resident in the Settlement, as well as to those from the surrounding country.

(iv) *Schools.* Three advances have been made in the year. (a) In January a school was opened for the children of the staff. This school has grown steadily through the year from one teacher, two classes and twelve pupils, to two teachers, four classes and forty pupils. (b) An industrial school was started in April. The place of bookwork in the education of many of the children is limited and in some cases very limited. At the same time both their present happiness and future needs are well served by giving them training in various forms of handwork, in which they may become proficient and by which they earn a living, while taking pleasure in their craftsmanship. In the Industrial School the children are taught farming; the growing of cotton, spinning and weaving; dyeing; mat, basket and sandal making; selection and preparation of wood and carpentry; pottery; sewing; and laundry work. A number are crippled in various ways by their disease and are more fitted for one occupation than another, but all do something. (c) A hostel for boys was opened in August. Previously all the boys lived with the adult patients who acted as guardians and exacted service. Now these boys, who are supported either by private subscription or the Settlement, live in the hostel. This is designed so that boys work and cook by groups of five or six. The main feature of the building is that the boys live always out of doors, on an outer verandah by day and an inner verandah by night. They are never "indoors"—there are no doors except to each group storeroom. Supervised in this way, the boys have more time for play, more ordered discipline and make better use of the food issued to them.

(v) *The Hospital.* With the strengthening of the medical staff more surgical work has been undertaken. A beginning has also been made with physiotherapeutics and some good results obtained in otherwise severely disabled patients. The nursing staff (patients) has been much increased, largely to allow individual members more time to attend classes of instruction. A school for nurses is in operation each afternoon.

(vi) *The Prison.* By arrangement with the Prisons Department of the Government a prison has been built and in it are lodged leprous prisoners from Enugu gaol. Warders are supplied by the Prison Department and the prison routine is much as in the gaol with modifications to allow of prisoners receiving treatment.

(vii) *Casualty Department.* Inevitably when accident befalls, the people of the countryside look to the Settlement for assistance. Snake bites, more or less severe injuries due to falls from palm trees, and difficult maternity cases are the commonest troubles. Such cases cannot be dealt with alongside the leprosous patients and for long there has been no better accommodation than a bench on a verandah or a partially cleared store. Now, by rebuilding St. Francis Chapel elsewhere, a casualty room has become available to the benefit of accidents from without and sick members of the staff within the Settlement.

(viii) *Other Departments.* Minor improvements have been effected in the working of most other departments not specifically mentioned. Their work is partly apparent in the statistical section of this report.

6. FINANCE.

At the close of the year 1939/1940 there was a small credit balance on the Native Administrative subscribed funds. This, and sundry other small balances, have been carried forward to help in meeting the effect of the rise of prices in the present financial year, the Native Administrations contributing the same sum as in 1939/1940. Without budgetting for any marked expansion in 1941/42, the estimated expenditure on general maintenance (European and African non-patient staff excluded) amounted to a sum of 38% above the Native Administration grant for 1940/41. (The increase to some extent was accounted for by the auditors' recommendations for further provision for replacements.) On the other hand, the Resident decided that the contribution from the Native Administrations would have to be reduced to a sum 58% below that for 1940/1941. Eventually arrangements have been made by which the Nigerian Branch of the British Empire Leprosy Relief Association will contribute £1,000 and the Native Administrations an approximately similar sum. A difference between estimated expenditure and revenue for 1941/42 amounting to £1,676 has been reduced to £400. The greater part of this will be met by making no provision in 1941/42 for replacements—a departure from the "sound financial principles" commended by the auditors only to be justified as a temporary emergency measure. The remainder of the difference is under consideration. The proportions of the contributions in 1939/40 by the Native Administrations (for general maintenance) and by the voluntary bodies concerned in the Settlement (for European and African non-patient staff) remained as in 1938/39, that is by the Native Administrations 45% and by voluntary bodies 55% of the total recurrent costs.

7. AGRICULTURE AND INDUSTRIES.

Two far-reaching innovations were made after last year's farming season. The first concerned the conditions of patients' admission and their work on the Settlement farms. The previous system was as follows. Patients contributed £2 annually to the Settlement general funds. They were then employed at a living wage by the Agriculture and Industries Department of the Settlement. It was realised that the average capacity for work of the patients is considerably below that of average normal labourers. Nevertheless, wages are paid on the basis of what a normal labourer would earn in the same time, because a diseased man cannot work extra time to make up for his physical incapacity. Thus the foodstuffs grown cost more to produce than if normal labour was employed. But they could only be sold at open market rates. It therefore was necessary to subsidise the Agriculture and Industries Department from general funds. The amount of the subsidy approached the sum contributed by the patients to general funds. In other words the net contribution of the patients to the Settlement was small. It was further realised that the agricultural produce of the country is largely the result of family or communal work which is not valued in terms of money, and for which no cash wages are paid. Such agricultural produce can come on the market at lower rates than if the labour involved were on a cash basis. (This might not apply to large scale scientific agricultural methods but these are not applicable at the Oji River Settlement.) It was therefore decided (a) to abolish the payment of £2 by patients to general funds; (b) to abolish wages; and (c) to demand a contribution in unpaid labour from all patients, at the same time setting up a "Works Committee" of four senior patients to distribute and supervise the execution of the work set. The whole scheme was explained to the patients and their co-operation invited. The results have been (a) that patients now only have to find £2 to bank for their first year until established on their private farms, and are no longer faced with the often impossible task of raising £2 in cash in the second and subsequent years; (b) that there is a considerable reduction in book-keeping; and (c) that the Agriculture and Industries Department requires no subsidy from general funds, while its profit exceeds the net contribution by patients under the old arrangement. Secondly; a system of crop rotation on a four year cycle has been adopted and all agricultural land in the Settlement is divided into four units. Patients and staff for their individual farms, and the Settlement for its communal farm, have a stake in each of the four units, in any one of which only certain crops may be grown in any particular year. Building, brick-

making and numerous other works have been carried out as usual by this department.

8. TRAINING.

(i) *External.* During May the District Officers of the Province attended a two-day course at the Settlement. A brief outline of the disease in its various forms was given, followed by an explanation of the significance of these for the individual and the community. This led on to consideration of measures of control and the part of the Administration in these. It should be recorded that if the talks and discussions were as valuable to the Administrative Officers as they were to him who gave the course, the time spent was not lost.

(ii) *Internal.* The school for nurses has been referred to above (paragraph 5 (v).). Out-patients who show promise in minor posts at the clinics are brought into the Settlement for courses of training fitting them to work as local clinic assistants.

9. RELIGIOUS LIFE OF THE SETTLEMENT.

Religious observance is entirely voluntary. Christians and pagans worship together in the Church of Our Saviour of the Transfiguration, while Anglican and Roman priests visit the Church at intervals to administer the Sacraments to those of their own flock. The system of class teaching of the Diocese is in use for Anglicans and pagans whose interest in the Faith has been aroused and who wish to be instructed. The teaching in the classes is distinctively Anglican and those who can read are encouraged in the public and private use of the Prayer Book. Members of the Roman Church do not attend such classes. The preaching in the Church remains on the large area of ground common to all Christians present. Emphasis is laid upon respect for the seasons and festivals due to be observed by all Christians. In a community such as that at the Settlement, where members of both the Anglican and Roman obedience are present in considerable numbers, it would be idle to pretend there are no deep differences of belief, and it behoves those with responsibility in the religious life of the Settlement to understand something of the different standpoints of the two bodies. The occasion of a man's physical distress is not made the occasion for pressing him to change his allegiance as a Christian. It is realised that, to those of the Roman obedience, without any sacrifice of charity, the Anglicans must seem as mistaken and outside the body of the Church but also that they may perhaps be seen as Christians and of the soul of the Church. The exclusive element in this the Anglicans cannot accept, but they, on their

part, may see and respect their fellow Christians as members of the largest branch of the Catholic Church. Good will on both sides amongst those responsible has led to a modus vivendi, and, deep though divisions may be, there is an outward harmony based upon a fellowship born of common suffering and common work in the life together. *Deo gratias.*

10. ACKNOWLEDGMENTS.

His Honour the Chief Commissioner (G. G. Shute, Esq.) paid three visits to the Settlement and Clinics and, having obtained a mastery of the system in operation and its financial implications, presented in person the case of the Settlement to the Executive Committee of the Nigerian Branch of the British Empire Leprosy Relief Association with the result described in paragraph 6 above. The Resident (Captain D. P. J. O'Connor) acquainted himself in detail with the financial position and has made every attempt to increase the original Native Administration estimates for the Settlement and Clinics. In addition his efforts have been untiring to settle local objections at the Ozubulu and Awwa Clinics, in the latter case successfully. District Officers have continued their co-operation in sundry ways, especially in connection with the Clinics. The Senior Health Officer (Dr. N. S. Turnbull) has, as usual, assisted in various matters. The Rev. Father Nwanigbo has ministered to those of the Roman Church in the Settlement. Within the Mission assistance has been received from many. The Bishop has given freely his ministrations through the year. His advice has also been sought and obtained on a number of occasions. The Archdeacon has assisted likewise. Several of the clergy of the Diocese have also given their services. The new farming policy owes much to the Mission Agriculturist (K. H. Prior, Esq.). At a time when the Agulu Clinic was overwhelming the staff, Mrs. Prior gave great assistance. The Superintendent of Iyi Enu Hospital (Dr. Batley), to provide a relief, released a Sister (Miss Simmons) who gave much needed help. On behalf of the patients and staff of the Settlement and Clinics warm thanks are expressed to all of these.

11. STAFF ACKNOWLEDGMENTS.

Record should be made of the consistently steady work of the staff, European and African, patients and non-patients, which has operated every clinic due to be operated and turned away no patient seeking help. Two severe losses call for mention. In July the Chief of the patients, Solomon Ugwuoka died. He was a man beloved, respected and of ability. After lying in the Church

that all in the Settlement might pay their respect, he was received with honour by the Christian community of his own town and was buried by the Church which he had done so much to establish. In October H. P. Pedrick left the Settlement to join the army in response to a call for recruits from the Mission. Since August 1937 his increasing ability had been devoted to the Settlement and many marks of his work as Manager will long remain.

12. GENERAL SUMMARY.

The number of patients on the registers has increased by seventy-three per cent. The number of clinics has increased from four to six (fifty per cent). The area of the Province served (allowing a 15 mile radius from a clinic) is now approximately two-fifths of the whole, but as it is the most densely inhabited area, a larger proportion of the population is served. On the other hand, the European staff has increased only from four to five (twenty-five per cent). There has therefore had to be (a) an increase in the African staff and (b) an increased efficiency of organisation. The Settlement and Clinics may now be regarded as a somewhat finely balanced machine with a cycle of seven days.

13. THE FUTURE.

Any remarks under this head postulate a continuance of supplies without any great increase in cost. It also postulates the maintenance of the European staff at the present level. And here attention must be drawn to the fact that every member, in the ordinary course of events, would be due for leave before the end of October, 1941. Even if all can sustain an appreciable extension of service, which is very open to doubt, the question of reliefs will arise with increasing frequency and insistence before the end of the coming year. As there are no members of the staff on leave, the solution of the problems is not immediately to hand. There remain, to complete the scheme of development under the Three Year Plan, three pieces of work. (a) The establishment of a clinic in the Nsukka Division is necessary. For some time the matter has been under arrangement with the people of Nsukka and it is expected the clinic will open very shortly. (b) African Preventive Officers must be trained and attached to clinics from which they will work to arrange the segregation of those infectious cases brought to light by the clinic. They will also spread information about leprosy in the community. The training quarters for these men are nearing completion. (c) Much information has been collected in the records of the patients and requires collation. This work has been begun but much remains to do. With these things

there must always be a striving for improvement in technical efficiency. But beyond everything mentioned there still lacks detailed survey work occupying itself with forms of the disease in relation to environment. Such survey work on any adequate scale will probably always remain a dream until there is created for it a Research Unit with a staff not responsible for routine administration and treatment. In an area of the Empire as large as the West African Colonies, where the numbers of persons affected by leprosy are so high, probably at least as high as anywhere in the world, there should surely be a central Leprosy Institute for training and research. When finally the Empire is free from the present man-made distraction of destruction and the time to build anew has come, it is to be hoped that the eyes of men will be open to the age-long destruction which nature has not ceased to inflict, and compared to the suffering of which death in war would be to many a boon.

STATISTICS FOR 1940.

SUMMARY.

	31.12.40.	31.12.39.	Difference
Patients in the Settlement ...	491	281	+ 210 (+ 75%)
Patients on the Clinics Registers	9,506	5,502	+ 4,004 (+ 73%)
Attendance at Clinics	158,336	116,676	+ 41,660 (+ 36%)
Treatment with Hydnocarpus Oil, Settlement and Clinic cases	170,937		

(Note: A patient may receive treatment by intramuscular or intradermal injection or by both in a week. All treatment, by either method or both in the course of a single week, is reckoned as one treatment in these statistics.)

Of these 491 patients 291 were males, 103 females and 97 children.

The staff consisted of 5 Europeans and 32 Africans, including 19 doing clerical or technical work. The average number of patients in hospital was 39, and the babies in the home for the infants of infectious cases numbered 9. The laboratory carried out 8,695 bacteriological and 343 other examinations during the year. The hydnocarpus oil prepared and issued in sterile containers amounted to 2,051 pints. The treatments of Settlement patients with hydnocarpus oil were estimated at 18,349.

The Works Department constructed from native materials 50 houses, a staff school, an industrial school, a hostel for schoolboy patients, a prison, which only had 10 occupants in the year, and a market. A brick and concrete chapel was also built.

The patients registered during the year at the six clinics, two of which were only opened in October, 1940, totalled 9,506. Of these

7,540 were treatment cases, 1,331 observation ones and 635 cases for diagnosis. The total number was 73% higher than in 1939. Treatment attendances amounted to 152,588 and the total attendances to 158,336, an increase of 36%.

REVIEWS

Leprosy in India, 1941. Vol. XIII, No. 2. April, 1941. **Studies of the Lepromin Test** by Dharmendra and S. S. Jaikaria.

The authors report that positive lepromin reactions have been obtained in persons in whom the chances of exposure to leprosy are very remote. It does not therefore appear to be one of specific allergy. No direct evidence was obtained for or against the theory that the positive test is dependent on the resistance of the tissues. The increased number of reactions with increasing age is compatible with either theory. The incidence and degree of reactions is more marked in endemic than in non-endemic areas. Thus exposure to infection and increasing age influence the number of reactions.

A note on Leprosy in the Kangra District of the Punjab. There is little leprosy in most parts of the Punjab but more in Kangra than elsewhere. Its elevation varies from a few hundred to over 10,000 feet and it is sparsely inhabited. The known cases number 803, or 0.1%. The disease is uncommon at altitudes under 2,000 feet and most common between 4 to 6 thousand feet. The neural and lepromatous cases are about equal in number, but the lepromatous type is the more frequent at over 2,000 feet. The proportion of cases under the age of 15 is under 5% and of above 35 is 56%, which is unusual for lepromatous cases. Further studies are being made.

A note by Dharmendra states that the chaulmoogra oil of ancient Hindu medicine is *Hydnocarpus Wightiana*.

They Walk Alone. A Leper's Life. By Perry Burgess. (Dent 12/6.)

Our readers will know well the name of the author of this book. Dr. Burgess, after a distinguished career in other fields of social service, was from 1925 to 1930 the National Director of what

is now the Leonard Wood Memorial (American Leprosy Foundation) and since 1930 has been its President. In these capacities he has studied lepers and leper institutions throughout the world and has done work of the greatest value in the organisation of leprosy work in the United States and elsewhere.

He has now written a remarkable and moving book which will appeal to the general reader and the expert alike. The writing is simple and direct for the most part, but in its descriptions of scenery it is graphic and colourful. It is admirably fitted to convey, as it does, the essential truth of the tale it tells.

This is the life history of a leper as narrated by himself. His name and the names of others have been altered, but the experiences ascribed to them are vouched for as true.

"Ned Langford" was infected with leprosy when serving as an American soldier in the Philippines. Only after many years did the disease declare itself and only gradually did he realise the tragic possibility and, later, certainty. With the help of a brother it was arranged that he should be reported as dead from a motor accident and so he disappeared from his family and country.

The main part of the story is concerned with his life in the Leper Colony at Culion where he spent some 25 years. There, after a time of mental struggle, he succeeded in rising above the horror of his fate. He never recovered but nevertheless created and lived a new life, one full of interest for himself and of benefit for his fellow-patients.

Ned Langford's work consisted in teaching the lepers self-help, and in organising and leading them in co-operative enterprises which provided for the needs of their community, fish, electricity, light and power and the like. It is an inspiring record of what the lepers of Culion accomplished for themselves. Its value is summed up in the words of a visitor from Calcutta who says: "Nothing is more important, few things are, in fact, so important, as instilling some degree of cheer, hope and the consciousness of being useful into the head of people who must be shut away. I expect to carry back to India with me word of what has been done here, and I am certain that your work will bear fruit not only on Culion but in many places which you will never see or know about. Good luck, and thank you for letting me see what a man can do who refuses to be defeated."

Mr. Burgess's name and position are sufficient guarantees for the accuracy of the medical details of the book. It is not a treatise but much may be learned from it by anyone who is not a specialist. At its end there is a useful appendix giving answers to some of the questions commonly asked about leprosy.

REPORTS.

Annual Report for 1940 of Indian Council of B.E.L.R.A.

This full report records that the war had so far had only a limited influence on anti-leprosy work in India. The number of leprosy clinics is fairly stationary, although a few new centres have been opened in several provinces. A few more leprosy institutions for in-patients have been opened and a colony established by the Asansol Leprosy Relief Association. Another feature is the increase in the amount of accurate survey work carried out, and the Indian Research Fund Association has appointed a committee to draw up proposals for such surveys to enable the incidence of leprosy in one part of India to be compared with that in another area. The usual post graduate leprosy courses at the School of Tropical Medicine, Calcutta, were attended by 52 doctors from different parts of India, and special courses were also organised in Bengal and the Central Provinces with 19 and 37 attendances respectively.

The Leprosy Research Department of the School of Tropical Medicine, Calcutta, has published work on the action of methylene blue in the leprosy organism, leprosy and dermal leishmaniasis, negative results of attempts to infect Syrian hamsters with human leprosy, an epidemiological study in North Bengal, the preservative effect of cresote on hydnocarpus oil, and studies of the lepromin test. Work is also being done on the regional variations in leprosy, the course of the disease, the immunological significance of the lepromin test, the histology of different types of leprous lesions and the possible bactericidal action of sulphonamide preparations on the bacillus of rat leprosy. Dr. Santra is now devoting most of his time to the study of regional variations in leprosy and their causation. The results of epidemiological inquiries in four areas, shown in the following table, illustrate the great variations in the proportion of different types of leprosy in different regions, the explanation of which is not at present known.

Country.	Area.	Popula- tion exam. ined.	Per- centage of L. cases.	Per- centage of cases below 15.	Author.
India ...	Santalpur (Bengal)	3,600	7.4%	4.1%	17% Lowe & Santra
Do. ...	Bankura (W. Ben- gal) ...	10,011	4.38%	18%	26% Lowe
Do. ...	Saidapet (Madras)	2,040	6.7%	25%	49% Cochrane
Do. ...	Madras Rural area) ...	2,007	4.3%	25%	36% Cochrane

**Report of the Director of Medical Services for the Year 1939
(Hongkong).**

Neither the title page nor the introductory paragraphs of this report state the country to which it refers, but further search reveals that it relates to Hongkong. Leprosy is dealt with briefly on page 21 and records that the former smallpox hospital was acquired by the Government in 1938 for the accommodation of lepers. At the end of 1938 133 patients remained, and in 1939 295 were admitted, 165 were transferred to Sheklunl, Swatow and Pakhoi, 67 escaped, 21 died, 3 were discharged and 172 remained at the end of 1939. A barbed wire fence patrolled by police has now been provided. Two male and one female patient have been chosen as paid heads to maintain discipline and cleanliness with good results. The conditions of life have been greatly improved by the provision of treatment, beds; a balanced diet, games, newspapers, etc.. and wandering in the streets of possibly dangerous lepers is prevented.

Annual Report of the Dichpali Leprosy Hospital for the year 1939-40.

The admissions numbered 695. The discharges included 71 symptom free, 242 disease stationary and non-infective, 200 improved but left before completion of treatment, 132 discharged otherwise and 12 died; a total of 657. The cases treated during the year numbered 1,452 and 795 remained at the end of the year. Applicants who had to be refused admission numbered 712. The war, epidemics and famine made things difficult and raised the cost of maintenance. The cases refused admission were mostly referred for treatment to centres near their homes. The usual course of instruction on leprosy for the students of the Hyderabad Osmania Medical College aroused keen interest. Land cultivation to provide food and educational work were other important features of this flourishing and successful leprosy institution.

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