LEPROSY REVIEW

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EDITORIALS

Professor Heaf, in his recent lecture to the British Medical Association,* gives four cardinal points of the compass as our guide to the eradication of tuberculosis. These are: tuberculin-testing, miniature radiography, BCG vaccination and antibiotics. "But," he adds, "the compass must be firmly based and binnacled by sound public health measures." He goes on to emphasise the importance of the primary infection "for the initial reaction of the tissues to this invasion influences the subsequent course of the disease." It may be useful to seek a guide to the eradication of leprosy on parallel lines.

In leprosy there is nothing comparable with the tuberculin test for indicating previous infection with *Myco. leprae*; though under two circumstances the lepromin test may help in the diagnosis of leprosy: (a) in a lesion where leprosy is suspected, but which, if leprosy, could only be of the lepromatous type, a strongly positive lepromin reaction would contraindicate leprosy; (b) when a clinically doubtful lesion appears, which if caused by leprosy would undoubtedly be of the tuberculoid type, then a negative lepromin reaction would contraindicate leprosy.

In diagnosis of leprosy there is nothing comparable to radiography in pulmonary tuberculosis, but neither is there need for such a guide; the evidence—whether in the form of smears, biopsy sections, thickened and tender nerves, clinical appearances, changes in sensation or secretion—is on the surface of the body.

The third point of the compass in tuberculosis is BCG vaccination; can we hope that BCG vaccination gives resistance in leprosy? It took many years before the value of this prophylactic measure was generally adopted in tuberculosis. It may need as many years to decide on its value in leprosy. No aspect of leprosy has raised more interest and controversy among specialists in both diseases, than this question of cross-relationship between tuberculosis and leprosy.

In reference to antibiotics or chemotherapeutics, leprosy stands in an interesting relationship to tuberculosis, that of a grateful junior partner. In the future as in the past the leprologist keeps at least one eye on what is happening in the tuberculosis laboratory and ward.

Regarding the basing and binnacling of the leprosy compass, this also depends on the sound education of public opinion, and above all on early diagnosis through examination of contacts, and early institution of treatment.

* Brit. Med. Jl., 1956, Dec. 15th, p. 1383.

The control of leprosy has one disadvantage as compared with that of tuberculosis—the repugnance of its name and the consequent dearth of workers. Leprosy has also an outstanding advantage over its partner, that it tends to go out by the back door as tuberculosis enters by the front.

* * * * * *

With this issue of LEPROSY REVIEW the Acting Editor lays down his pen, or rather hands is over to Dr. James Ross Innes, the new Medical Secretary of BELRA. Dr. Innes, who is 53, graduated M.B., Ch. B. (Hons.) in Edinburgh. He went to Itesio in November, 1953, when plans had been completed to build a Leprosy Research Centre there. Previously, Dr. Innes, who arrived in East Africa in 1947 as Inter-Territorial Leprologist, following a short tour of Nigeria, made a series of surveys in East Africa to find the incidence of leprosy and co-ordinate leprosy control work.

From 1947 to 1952 he travelled extensively in these territories, and he was also invited to carry out leprosy surveys in Northern Rhodesia, Nyasaland and Zanzibar. Dr. Innes served in India as a medical officer from 1928 until 1946, except for a period during 1938 when he carried out a leprosy survey in the Solomon Islands.

Dr. Innes is succeeded at Itesio by Dr. J. M. B. Garrod, who for the last four years has specialised in leprosy in Northern Rhodesia.

* * * * * *

The VII International Congress of Leprology

The International Leprosy Association at its General Meeting held in Madrid on October 11th, 1953, after the closing of the VI International Congress of Leprology, accepted the invitation of the Government of India to hold the 1958 Congress in India.

The preparations for the Congress have now been taken in hand. The Government of India has appointed an Organizing Committee with Lt.-Col. C. K. Lakshmanan, Director General of Health Services, as Chairman, Dr. Dharmendra as Secretary, and about a dozen other members. It has been decided to hold the Congress at New Dehli (India) from December 8th to 15th, 1958

The details of technical aspects of the Congress will be worked out by the Organizing Committee in consultation with the International Leprosy Association. In light of the experience of the previous Congresses, the Association has under contemplation the introduction of some new procedures, both before and at the Congress itself. The contemplated changes will have a bearing, amongst other things, on the nature of Scientific Sessions, and on

the procedure for setting up Technical Committees of the Congress. When an agreement is reached on these matters, the accepted procedures will be duly announced.

The present preliminary announcement is being made to provide early information about the venue and dates of the Congress. Further information regarding the membership fees, accommodation, and travel arrangements, official subjects for discussion at the Congress, and the last date for receipt of application for membership and for submitting papers, etc., will be published later in the form of a descriptive bulletin.

The Congress Members may attend under official or institutional auspices, or on a private basis. Official invitations to various governments, requesting them to appoint official delegates to the Congress, will be sent through the Ministry of External Affairs, Government of India. Apart from the official invitations, the Organizing Committee has pleasure in extending invitations to all members of the International Leprosy Associations, members of the Leprologist Associations in the various countries, and all others interested in the study of leprosy. There is likely to be a difference between Members of the International Leprosy Association and non-members with respect to the Registration Fee. Persons who are not already members of the Association may now join it.*

DHARMENDRA,
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India.

* For this purpose, the membership fee of U.S. $7 should be remitted to Dr. Huldah Bancroft, Assistant Editor, International Journal of Leprosy, 1430 Tulane Avenue, New Orleans 12, Louisana (U.S.A.), or the sterling equivalent (£2 10s. 0d.) may be sent to the Secretary-Treasurer of the International Leprosy Association, at 8 Portman Street, London, W.1. The amount will cover one year's subscription to the International Journal of Leprosy, with membership in the International Leprosy Association.

THE TREATMENT OF LEPROSY WITH DIAMINO-DIPHENYL SULPHOXIDE: A PROGRESS REPORT

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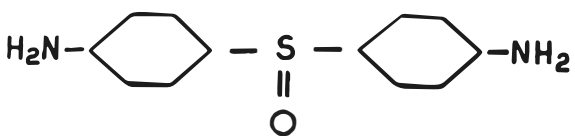
Introduction

During the last few years the great achievements of the sulphones in leprosy treatment have tended to discourage the search for new anti-leprosy drugs. While in a majority of patients sulphone therapy may provide all that is necessary, there remains a sizeable minority, susceptible to one or other of the complications of sulphone treatment, for whom the existence of an effective alternative would be an advantage. Among possible groups of compounds worth studying, those closely related to the sulphones invite interest, and of these the sulphoxides, and in particular, diamino-diphenyl sulphoxide may claim priority. Buu-Hoi and his co-workers have reported on a short term trial of this substance in 34 leprosy patients, and found it comparable in activity with DDS itself. (Buu-Hoi, Nguyen-Ba Khyen and Nguyen-Dat-Xuong, 1955). Through the kindness of Professor Buu-Hoi and of Dr. F. Hawking of the Medical Research Council, supplies of this drug were obtained for a trial in Nigeria, and a progress report is here presented after the trial has been in progress for 15 months. During recent months additional supplies of the drug have been provided by Imperial Chemical (Pharmaceuticals) Ltd.

Chemistry and Dosage

The molecular structure of diamino-diphenyl sulphoxide is very similar to that of DDS, and may be represented as follows:



It is a white or greyish powder, and was received in the form of compressed tablets of 100 milligrammes.

With a molecular weight not far removed from that of DDS, it would appear reasonable to use diamino-diphenyl sulphoxide in a dosage similar to that employed for the parent sulphone. Buu-

Hoi used a dose of 100 mg. daily and it was decided to make this the maintenance dose in adults in this trial. Experience with DDS prompted the starting of treatment at a lower level than this, and 50 mg. was used as the routine initial dose, with an increase to the standard maintenance dose in from three to four weeks from the onset of treatment. Children received an initial dose of 25 mg. daily, raised later to 50 or 75 mg. according to age. All patients had a rest from treatment on one day a week. This system proved entirely satisfactory in practice.

Choice of Patients

A small group of seven patient volunteers was first selected for preliminary trial. All were able bodied, the group consisting of four active tuberculoid cases, one of borderline, and two of indeterminate type. None had had any previous chemotherapy. Under careful laboratory cover these were given treatment with diaminodiphenyl sulphoxide in the dosage indicated above. The drug was well tolerated, and within one month all seven patients showed signs of resolution in their leprosy. On this evidence that the drug was not unduly toxic and was not without activity against *M. Leprae*, the group was expanded as suitable patients became available to form the main trial group of 24 patients, the maximum possible with the supplies available. The 17 patients added were all of lepromatous type, and were representative of this type of leprosy. They included some very severe infections. The group included three children, and neither these nor any others of the patients had had any previous treatment.

In ten cases biopsies were taken to remove any doubt as to classification and to provide a check on progress.

Controls

In a trial of this nature the basis for the assessment of the activity of the new drug is that provided by the expected response of the patients concerned to standard sulphone treatment. The choice of controls is therefore important, but is not an easy matter. A random selection based on the consecutive choice of patients exhibiting the main types of leprosy will almost certainly lead to error. Within the framework of its three or four main types, leprosy presents a variety of forms which differ from one another in the speed with which they exhibit a response to chemotherapy. In view of this fact it appears desirable to choose controls on an individual basis, matching each trial patient as exactly as possible with a control presenting the same type and subtype of leprosy, of

similar duration and extent, and having a comparable Bacterial Index and reaction to lepromin.

In this trial, controls were chosen on such a basis. Some were admitted at approximately the same time as trial patients, found to correspond, and were selected and placed on routine DDS treatment. Others were patients already receiving DDS treatment who at the start of their treatment had fulfilled the necessary conditions. Three had completed their course of treatment, but all the remainder continued under constant observation throughout the period of the trial.

Toxicity

In dealing with a substance closely related to DDS some degree of toxic action was to be expected, and careful and continuous laboratory control was therefore exercised from the start.

The drug has been well tolerated both by adults and by children. There have been no complaints of any gastro-intestinal disturbance or of any other symptom suggestive of toxic action, and all the patients concerned have been able to continue their treatment throughout the period of trial without interruption. At the dosage tested the toxicity of diamino-diphenyl sulphoxide has thus been of a low order, though abnormalities have been detected by routine examination which might very well become serious at higher dose levels. These call for further comment.

Anaemia

A fall in haemoglobin levels occurred during the early stages of treatment in 13 out of the 24 patients. It was never severe, varying between 10% and 20%, and by the fourth month the loss had been regained in all cases. Thereafter no sign could be detected of any disturbance in normal haemopoiesis. During the first three months moderate doses of iron were given orally to some patients as a precautionary measure, but none was given after the third month, and none was needed, several patients later repeatedly giving values of 100% or a little more, as read by the Grey Wedge Haemoglobinometer.

Leucopenia

In Nigeria, under the influence of such conditions as filariasis and virus infections, white cell counts in apparently healthy individuals are subject to wider variation than is covered by the normal physiological range. This exaggeration of the normal was encountered in several of the trial patients, and would not have deserved mention but for the fact that it was more noticeable

among them than among patients taking part in the trial of thiocarbanilide compound SU1906 which was running concurrently, and also because in three individuals it took the form of a mild but definite leucopenia which occurred between the second and fourth months of treatment. In these patients the white cell count fell to the neighbourhood of 3,000, polymorphonuclears being more affected than the other varieties of cell. Once again, the effect was only temporary and did not demand the cessation of treatment.

Drug fever, hepatitis

No case of dermatitis or drug fever was seen among these patients, and no evidence was obtained of any significant toxic action either on the liver or kidneys. Slight degrees of liver enlargement were encountered in two patients at the second and eighth months respectively during routine examinations, but both then and at other times, tests for urobilinogen were normal.

The impression remains that at the level of dosage used in this trial the toxic effects of diamino-diphenyl sulphoxide were insignificant, but that tendencies were revealed which would call for caution in raising the dosage above that used here. The study of a much larger group is, of course, necessary before any authoritative statement can be made on these matters.

Progress of Leprosy: Comparison with Controls

Of the 24 patients available for study, 18 have had treatment with diamino-diphenyl sulphoxide continuously for 12 months or longer, 22 for 8 months or longer, and all for more than 5 months. The progress made by the various groups is as follows.

(a) *Tuberculoid cases*

All four patients have shown satisfactory clinical improvement and all are now in a residual condition. The time taken for resolution to occur can be compared with that exhibited by controls as follows:

	DDSO	DDS
Becoming residual		
Within 9 months ...	1	2
12 months ...	3	2

(b) *Indeterminate and Borderline cases*

The single borderline case in this series has made very satisfactory progress. After 15 months' treatment skin lesions have become clinically residual and bacteriological improvement has also been marked, with disappearance of bacilli in the nose and in sites in the skin where they were formerly numerous, a few granulated

bacilli persisting at only one of several sites examined. This result is at least as good as that seen in the control patient.

The two indeterminate cases have become residual, one after 10 months, one after 12 months, and in this respect they have resolved more speedily than their controls.

(c) *Lepromatous cases*

The 17 cases may be classified as follows:—

Advanced diffuse or nodular leproma ...	2
Moderately advanced ditto	5
Early diffuse leproma	5
Lepromatous macules	5

Both advanced cases were longstanding and of unusual severity. All the remainder were typical, firmly established examples of their respective types, and all were in a very active progressing phase of their disease. The group included three young children with rapidly advancing infections, and their inclusion brought the average age of the group to the low figure of 23 years.

During the period of treatment all the lepromatous cases without exception have shown satisfactory clinical signs of resolution, with flattening of nodules, reduction in infiltration, and loss of erythema and thickening in macules. Clinically their progress as a group has been as good as would have been expected under DDS treatment, and equalled that displayed by their controls. In a number of cases it has been very gratifying.

Clinical improvement is also reflected in the histological findings. The resolution occurring in two cases in this group, one adult and one child, is illustrated in Figures 1 to 4.

Bacteriological progress: Comparison with controls

A decline in numbers of bacilli in routine smears has occurred in every case, and has been accompanied by the changes in morphology of bacilli now familiar in satisfactory chemotherapy. In Tables I and II bacterial indices are presented for each trial patient and the corresponding control, calculated at three monthly intervals. Each figure is the average of all smear results obtained on that individual during each period of three months, the maximum in all cases being 4.0. This provides a satisfactory basis of comparison both between individuals and between groups, and was found useful in a similar trial of this nature. (Davey and Currie, 1956.)

TABLE I

BACTERIAL INDEX: TREATMENT WITH DIAMINO-DIPHENYL SULPHOXIDE

Maximum 4.0

Trial Patient Ref. No.	Months of Treatment						Decrease
	0	3	6	9	12	15	
1	3.5	2.5	1.9	1.0	1.0	1.0	2.5
2	2.8	2.0	2.0	2.0	1.8	2.4	0.4
3	1.8	1.5	1.8	1.5	2.0	1.7	0.1
4	4.0	2.8	3.1	2.5	2.8	2.6	1.4
5	0.7	0.3	0.2	0.2	0.4		0.3
6	2.5	2.3	1.7	1.3	1.8		0.7
7	2.6	2.7	1.7	2.0	2.1		0.5
8	1.4	1.0	0.6	0.3	0.6		0.8
9	0.8	0.8	0.6	0.2	0.1		0.7
10	1.7	0.7	0.6	0.9	0.8		0.9
11	0.5	0.1	0.1	0.1			0.4
12	3.0	2.0	1.0	1.0	0.9		2.1
13	3.0	2.7	2.0	2.7	1.9		1.1
14	2.8	2.0	2.8	2.6			0.2
15	1.7	1.5	0.7	1.0			0.7
16	3.4	2.4	2.6	2.5			0.9
17	3.0	2.0	1.5				1.5
						Group decrease	15.2
Group average	2.3	1.7	1.5	1.4			

TABLE II

BACTERIAL INDEX: CONTROLS ON DDS TREATMENT

Maximum 4.0

Control Patient Ref. No.	Months of Treatment						Decrease
	0	3	6	9	12	15	
1	3.3	2.8	2.8	2.5	2.3	2.0	1.3
2	2.5	2.5	2.5	2.0	2.0	2.0	0.5
3	1.8	1.3	1.0	0.5	0.3	0.3	1.5
4	4.0	4.0	3.3	3.5	3.5	2.5	1.5
5	1.1	1.1	1.2	0.4	0.7		0.4
6	2.5	2.5	1.5	2.0	1.5		1.0
7	2.2	2.5	1.8	1.8	1.5		0.7
8	1.2	1.2	1.0	0.8	0.5		0.7
9	0.9	1.0	0.8	0.6	0.8		0.1
10	1.8	2.5	2.0	2.0	1.0		0.8
11	0.6	0.4	0.2	0.2			0.4
12	3.0	3.2	2.3	2.3	1.3		1.7
13	3.0	3.3	1.5	2.5	2.0		1.0
14	2.5	2.5	2.3	1.8			0.7
15	1.7	1.0	0.4	0.2			1.5
16	3.5	4.0	3.5	3.0			0.5
17	2.5	1.9	2.0				0.5
						Group decrease	14.9
Group average	2.2	2.2	1.8	1.6			

The improvement in bacterial index displayed by the trial patients as a group is thus a little better than that shown by their controls.

Clinical and histological improvement was thus borne out by bacteriological progress, but similarities and differences between Tables I and II should not be pressed too far. No matter how accurate the technique of bacteriological examination may be, there remains an element of uncertainty which cannot be overcome. In the advanced florid lepromatous case the skin may be sufficiently saturated with bacilli everywhere to make it immaterial where smears are taken, and in such a patient if multiple sites are selected on each occasion, consecutive smears will give a fair picture of progress. In all other cases, although bacilli may be very numerous, the skin is not uniformly invaded by them. At the onset every site examined may display innumerable bacilli, but as treatment progresses, the decline in bacilli first makes itself felt at sites where their density was least. Such sites may be small and scattered all over the body, and cannot be detected clinically until the process of resolution is gaining momentum. An element of luck in the choices of sites for bacteriological examination therefore exists, and although it is minimised by making multiple smears, it is not overcome. As a result, even though a patient may be making steady progress, some irregularity may appear in successive bacteriological findings, according as to whether sites of great or lesser bacteriological density happen to have been chosen.

This accounts in part for the variations in the progress of individuals in these Tables. The difference in progress between one individual and another is also noticeable. It serves to emphasize the care needed in the choice of controls, and is also a reminder that in any case there is an element of irregularity in the progress of leprosy patients, the causes of which still need to be clarified. In this trial there was a definite seasonal variation in progress, noticeable both among trial patients and among controls. One other feature needs comment. Although clinically and histologically there was little to choose between the progress shown by children and by adults, where bacteriological progress was concerned adults were at an advantage. At a later stage in the trial this finding may no longer apply, but it has applied during the first year.

Complications during Treatment

Erythema Nodosum Leprosum

Erythema nodosum occurred in one individual, a severe

nodular case, at the twelfth month. It was not sufficiently severe to interrupt treatment.

Neuritis

Three lepromatous cases experienced neuritis for short periods after treatment had been in progress for from nine months to one year. One tuberculoid case experienced neuritis of moderate severity at the fifth month. In none of these cases was neuritis of sufficient severity to interrupt treatment. All four of them had extensive nerve involvement before treatment was started. Others, also with marked nerve involvement, had no neuritis, and at this stage of the investigation it may be said that neuritis has not been a prominent feature.

Increased activity in lesions

None of the trial patients has so far exhibited any change in the form of the disease.

Complications of treatment have thus been few and unimportant.

Discussion

The findings in this trial confirm and extend those of Buu-Hoi and his colleagues. On its showing during the first fifteen months of observation there is evidence that diamino-diphenyl sulphoxide possesses activity against *M. Leprae* of the same order as that displayed by DDS, and that at a dosage of 100mg. daily it has been found safe to use.

Wider and more prolonged trials will be needed before any realistic assessment can be made of the place of this drug in leprosy treatment. Much will depend in the first place on whether its administration on a twice weekly basis is practicable. Its toxicity obviously calls for further study. The remarkable improvement shown by individiual patients, and the general freedom from complications shown by the trial patients as a group are, however, facts of interest. The drug is not a proprietary preparation and may possibly be manufactured quite cheaply. It therefore invites further study, and if progress is maintained, and late complications do not arise, it may very well be a potential rival to the sulphones.

Summary

A progress report is presented of a clinical trial in leprosy treatment of diamino-diphenyl sulphoxide.

This substance was administered in doses of 100 mg. daily to a representative group of 24 leprosy patients, none or whom had had any previous chemotherapy. Patients were matched individually against controls receiving routine DDS treatment, and a

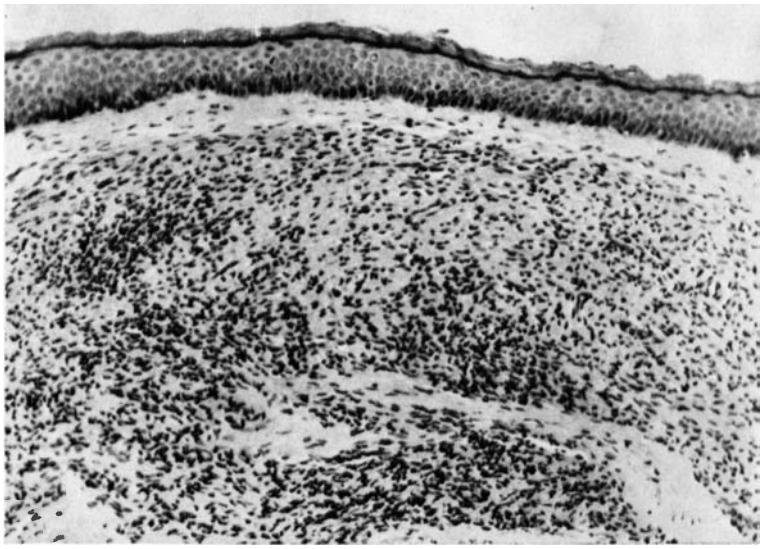


Fig. 1.—Trial Patient No. 1. Moderately severe lepromatous leprosy in a middle aged adult male. The section shows the typical features, flattened epidermis, subepidermal clear zone, and fairly extensive infiltration in the corium lepromatous in nature. The foamy appearance of the infiltration can be seen. X 195. Slide H75/55.

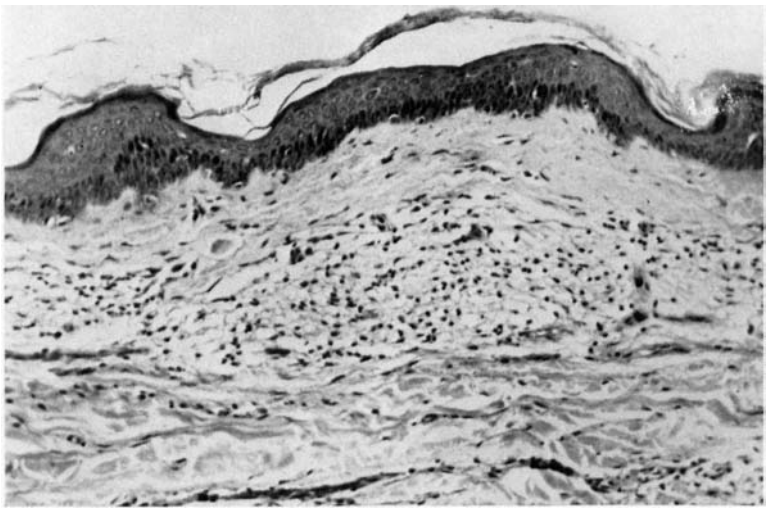


Fig. 2.—Trial Patient No. 1. Section from a site immediately adjacent to that shown in Fig. 1, and taken seven months later. Resolution is apparent. The epidermis is regaining its normal contour, and marked shrinking has occurred in the area of infiltration, with loss of cellularity, a vacuolated appearance, and dilatation of capillaries. X 195. Slide H24/56.

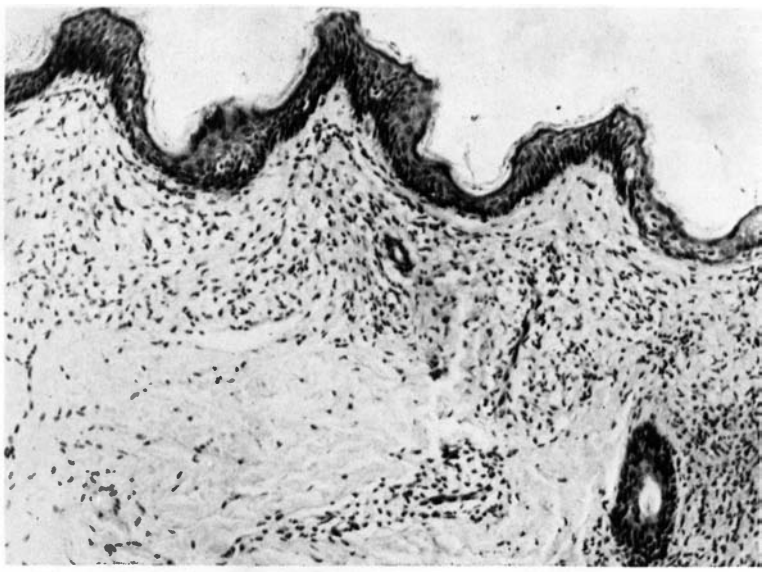


Fig. 3.—Trial Patient No. 3. Rapidly advancing lepromatous leprosy in a young child of six years, showing the typical features of a lesion of recent origin. The foamy nature of the infiltration can be seen especially in relation to a hair follicle. X 195. Slide H85/55.

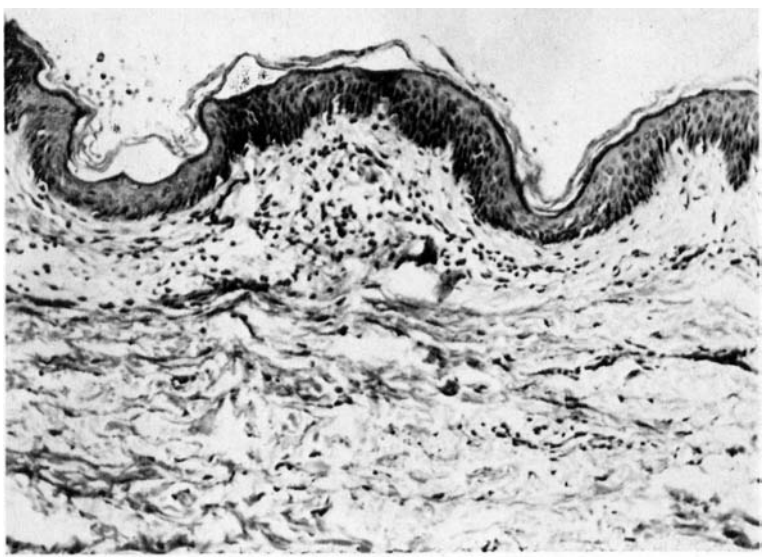


Fig. 4.—Trial Patient No. 3. Section from a site immediate adjacent to that shown in Fig 3, and taken seven months later. The features of resolution are again evident, with shrinking in the area of infiltration, a vacuolated appearance and loss of cellularity in the lesion, and dilatation of capillaries. X 195. Slide H33/56.

progress report written when the trial had been in progress for 15 months, by which time 18 of the patients had received the drug for one year or longer.

The drug was found to be active during the first year against *M. Leprae*, and to be comparable in this respect with DDS itself. The findings of Buu-Hoi and his colleagues are thus confirmed. Clinical progress was satisfactory in all cases, and indeed very gratifying in some. Decline in bacilli as evidenced by routine tests took place in all cases, but was irregular in degree, adults on the whole showing more progress than children. Toxicity was not of a high order at the dosage used in this trial. A mild degree of anaemia encountered in the early stages of treatment was self-limiting and called for no interruption in the treatment schedule. Complications of treatment were insignificant. The drug is considered worthy of wider trials.

Acknowledgements

This trial was suggested by Dr. F. Hawking of the Medical Research Council, and thanks are due to him for his encouragement and assistance in obtaining supplies of the drug used and in the preparation of photomicrographs. Thanks are also due to Professor Buu-Hoi, who obtained supplies of diamino-diphenyl sulphoxide before the drug was available in Britain, and also to Imperial Chemical (Pharmaceuticals) Ltd. for generous supplies later.

Grateful thanks are also due to Mr. S. E. Drewett, F.I.M.L.T., Laboratory Superintendent, and the laboratory staff of the Unit, especially Mr. G. Okezie, Senior Technician. The laboratory cover of this trial has so far called for over 2,000 laboratory procedures, and the promptitude and complete reliability with which these have carried out have been extremely valuable.

It is a pleasure to acknowledge the assistance given by the patient staff of the Research Unit, and also the patients themselves who cheerfully volunteered to take part in the trial and thus exposed themselves to many tests and no little inconvenience.

Thanks are also due to Dr. Onwu, Acting Director of Medical Services, Ministry of Health, Eastern Region, Nigeria, and to Dr. A. Zahra, Acting Leprosy Adviser, for permission to publish.

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CHLORPROMAZINE IN THE "PAINFUL" COMPLICATIONS OF LEPROSY

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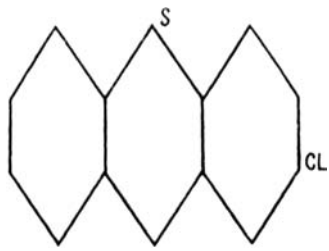
Introduction

Consequent on the favourable results obtained with Chlorpromazine in the relief of pain-producing conditions, the clinical trial with "Largactil" brand of Chlorpromazine in the treatment of painful complications of leprosy was initiated at the Government Silver Jubilee Children's Clinic, Saidapet, in April 1955. This being an out-patient clinic, a close watch could not be kept on the condition of the patient. However, except for a few instanecs, the patients were fairly regular in reporting at the clinic as and when instructed to do so. The assessment of the results of treatment was largely based upon what the patient said about his symptoms from day to day, and also, to some extent, on his clinical condition.

Pharmacology

Chlorpromazine is a new synthetic, non-barbiturate, central nervous system depressant. It is derived from the alkylamine derivatives of phenothiazane and has the following formula:



It is a whitish, odourless, slightly granular powder, with a melting point of 180° C. It is freely soluble in water and alcohol, and on exposure to light it tends to change colour.

Although chemically related to antihistaminics like promethazine and diethazine hydrochloride, it has a relatively weak antihistamine action. It has been described as a "young near-relation of the antihistaminic substance."[1] It appears to be a drug with diverse and useful pharmacological action, and has been described as vagolytic, sympathicolytic, spasmolytic, antipyretic, antiemetic and sedative. It also has a potentiating effect on hypnotics, narcotics, anaesthetics and analgesics. At present it is being used in the control of vomiting, management of mental and emotional disturbances, and relief of severe or intractable pain.[2]

It is this last mentioned pharmacological action that forms the theme of the present study.

Chlorpromazine in Leprosy

It was felt worthwhile investigating the use of " Largactil " brand of chlorpromazine in some of the " painful " or pain-producing complications of leprosy, such as acute neuritis, chronic persistent joint pains met with in lepromatous cases, acute painful condition of the eye (for instance, iritis) and general bodily pain of a severe nature seen during and after lepra reaction. It was clearly understood before the initiation of the present investigation that Largactil was not being offered as a treatment for leprosy, but that the drug might be tried by itself or in conjunction with the usual treatment offered for the painful complications of leprosy indicated above.

Dloch,[3] working on three cases of leprosy, a leproma, a tuberculoid and an undifferentiated, administered chlorpromazine either orally or parenterally. In the leproma which was treated with injections of DDS and Largactil orally 25 mgm. per day, remarkable improvement in the lepromatous condition was noticed. He himself expresses the doubt regarding the actual value of Largactil as an anti-leprotic drug. The second case, a tuberculoid with " neural reaction " did well with 12 injections of Largactil, there being complete subsidence of " reaction."

The Present Investigation

1. **The Material:** The painful complications of leprosy in which Largactil was tried were as follows:—

(1) Neuritis, acute and chronic.
(2) Joint pains, acute and chronic.
(3) Generalised bodily pain of lepra reaction along with nerve pain, joint pain and bone pain.

For purposes of this study the bulk of cases were drawn from those suffering from neuritis of varying severity. A few cases with joint pains alone and a small group of cases in lepra reaction with generalised pain were also included. Out of a total of 47 cases taken for investigation, 16 cases dropped out for reasons best known to themselves. The remaining 31 cases were treated for the following painful complications:—

Neuritis	21 cases
Joint pains	3 ,,
Neuritis and joint pain	2 ,,
Generalised bodily pain	5 ,,

2. **The Method:** At this clinic, the routine treatment for the painful complications of leprosy has been the intravenous adminis-

tration of Potassium Antimony Tartrate in doses of 0.02 gm. for three days and 0.04 gm. for the next three days. In addition Mist. Sodi Salicylas 1 oz. t.d.s. is given. The results have been uniformly good in neuritis, joint pains and classical lepra reaction.

When Largactil was offered as a drug that will induce a state of indifference to pain, the investigation was undertaken with a twofold purpose: (a) Whether Largactil could conveniently replace the other forms of pain relieving measures in practice, which are rather messy, needing more attention and care, and (b) whether combined Largactil and the usual pain-relieving measures in practice was more beneficial to the patient in so far as the rapid amelioration of his painful symptoms was concerned.

Largactil was administered orally in doses of 25 mgm. twice or three times a day in addition to the usual Sodi Salicyl Mixture. After some time, a stage was reached when the patients (who, being chronic sufferers, are in the habit of suggesting the line of treatment that should be adopted for the relief of their symptoms) were not quite taken up with the " tablet " treatment but demanded Potassium Antimony Tartrate injections also. Hence in order to satisfy the psychology of the patient and at the same time keeping a watchful eye on the effect of Largactil, " dummy " Potassium Antimony Tartrate injections in the form of Aqua distillata were given, 2 c.c. intravenously every day for six days along with Largactil tablets. In some instances when Largactil alone failed to relieve the distressing symptoms after a reasonable period of time, Potassium Antimony Tartrate injections were given in addition to Largactil therapy.

In other words, the total number of 31 cases can be put in three categories:

(1) A group of 18 cases who were treated with Largactil tablets alone.

(2) A second group of 9 cases who were treated with Largactil tablets plus " dummy " Potassium Antimony Tartrate injections.

(3) A group of 13 cases treated with Largactil and intravenous injections of Potassium Antimony Tartrate (including 5 cases transferred from group (1) and 4 transferred from group (2)).

The Results

Group (1): In the first group comprising of 18 cases treated with Largactil alone, 10 were suffering from neuritis, 2 from neuritis and joint pains, 3 from generalised aches and 3 from joint

pains alone. One out of the 10 cases with neuritis and one of the 3 cases with joint pains were earlier treated with intravenous injections of Potassium Antimony Tartrate, but the painful symptoms persisted unabated.

Under Largactil therapy which was administered orally in doses of 50 to 75 mgm. per day with Phenergan 25 mgm. at bed-time, 7 cases of neuritis (including the one that did not benefit with Potassium Antimony Tartrate), 2 cases of neuritis and joint pains, 3 cases of generalised body ache and one case of joint pains (which was earlier treated with Potassium Antimony Tartrate) obtained complete relief in periods varying from 4 to 16 days. The three cases of neuritis and two cases with joint pains which failed to respond to Largactil were transferred to Group (3).

Group (2): In this second group comprising of 9 cases, 8 suffering from neuritis of a mild to moderate degree and one case of generalised pains and aches, Largactil was administered orally in doses of 50 to 75 mgm. per day. Phenergan 25 mgm. at bed-time along with "dummy" Potassium Antimony Tartrate (viz. 2 c.c. of Pyrogen-free distilled water) intravenously. Out of these 9, 5 cases of neuritis obtained complete relief after a period of 5 to 9 days' treatment. The 3 cases of neuritis and the solitary case of body pains and aches which did not respond favourably but showed exacerbation of symptoms were transferred to Group (3).

Group (3): The third group of 13 cases comprised of 3 cases of neuritis and 2 cases of joint pains transferred from Group (1), 3 cases of neuritis and one case of generalised body pain transferred from Group (2), three fresh cases of neuritis and one new case of generalised body pains and aches. In other words, there were in all 9 cases of neuritis, 2 cases of joint pains and 2 cases of generalised body pains. The 3 fresh cases of neuritis and one new case of generalised bodily pain in this group were straightaway started on combined Potassium Antimony Tartrate and Largactil therapy, because of severe and distressing pain symptoms. All the 13 cases obtained complete relief under combined Largactil and Potassium Antimony Tartrate therapy which lasted for 6 days, the time taken for the course of Potassium Antimony Tartrate injections.

Complications

No untoward effect that could be directly attributed to Largactil therapy was encountered in any of the cases treated.

Discussions

It is obvious from the results obtained in Group (1) Largactil

is quite useful in relieving painful complications of leprosy, provided they are not of severe intensity. Another point that is brought out in Group (1) in favour of Largactil is its usefulness in cases who have had intravenous Antimony therapy, but failed to receive the expected beneficial results.

The Group (2) cases which received Largactil and " dummy " Potassium Antimony Tartrate injections, indicated in some measure the part played by the psychology of the patient with regard to the relief or otherwise of his painful symptoms. Five out of nine cases in this group improved with Largactil. In the remaining four cases, Largactil failed to relieve the symptoms, perhaps due to exacerbation of the existing symptoms. Generally speaking, experience with this group appears to confirm the results obtained in Group (1).

In Group (3), apart from the four cases which were straightaway started on combined Largactil and Potassium Antimony Tartrate therapy (on account of the distressing pain symptoms), the nine cases which had proved resistant to Largactil therapy ultimately received the beneficial result under the combined therapy. It appears likely, the cases which present themselves with agonising painful symptoms, or those who show an exacerbation of mild painful symptoms, are the ones where the combined Largactil and Potassium Antimony Tartrate therapy is strongly indicated.

In the writer's experience, Potassium Antimony Tartrate has proved to be one of the most effective and useful agents that could be employed for the relief of neuritis, joint pains, etc., occurring as the presenting symptoms or as component of the lepra reaction syndrome. Experience in the treatment of painful complications with the combined therapy (Largactil and Potassium Antimony Tartrate) on the one hand and Potassium Antimony Tartrate injections alone on the other, seems to indicate that the former brings about an " easing " of the acute painful state much earlier. Lastly, cases which prove resistant to Largactil therapy alone, obviously due to exacerbation of symptoms, obtained relief with the combined therapy.

Conclusions

1. The pain relieving properties of Largactil in the painful complications of leprosy are confirmed.

2. Largactil, administered alone, seems to obtain the desired results in those cases where the pain is of a mild or moderate severity.

3. Largactil appears to be of value especially in those cases where the usual measures employed for the relief of pain, namely Potassium Antimony Tartrate injections, have failed.

4. Largactil could be used with advantage in outstation clinics, where intravenous injections of Potassium Antimony Tartrate or any other form of therapy necessitating daily attention could not be given.

5. Largactil, given in doses indicated above, appears to be free from toxicity.

6. Combined Largactil and Potassium Tartrate therapy appears to give better and quicker results in cases with agonising pain symptoms, than when either of them is given alone.

Summary

The treatment of 31 cases suffering from one or more of the painful complications of leprosy with Largactil administered orally under various regimen are presented. The results obtained are analysed, discussed and the conclusions drawn from the investigation recorded.

Acknowledgement

Thanks are due to Messrs. May & Baker (India) Private Ltd., for stimulating the interest to undertake this study and for the generous supply of the drug. I wish to place on record my grateful thanks to the patients, without whose co-operation this investigation would not have been possible. Thanks are also due to the Officer-in-Charge, Central Leprosy Teaching and Research Institute, Chingleput, for permitting the publication of this article.

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FAMILIAL LEPROSY

HAMISH MACGREGOR, M.B.E.
Superintendent of the Rajah Sir Charles Brooke Memorial Settlement, Kuching, Sarawak

In 1936, Brakon, a male Land Dayak from Kg. Sudoh, Upper Sarawak, Bau, aged 36 years, was admitted to this Settlement complaining of " numbness in the shoulders and back "; after a year's treatment he was sent back to his home. During the Japanese occupation of Sarawak he noticed nodules on his left upper arm, this was about 1943, and these gradually extended until he was sent to the Settlement in 1950, where he has remained ever since.

Remarks recorded on his admission show " nodules all over his body, right hand deformed, some anaesthesia, smear positive." According to staff and patients he was " one of the worst in the settlement " and was quite obviously a grossly lepromatous case. Since then the other hand has become involved with some absorption of the fingers. His smears remained positive until 1954, when they became negative and have remained so to date. He has attended treatment very faithfully and there are now no signs of active disease, although the stigmata remain. He has stated that he cannot recall any other person suffering from leprosy in his immediate vicinity but adds that it is very difficult to recall this with any certainty after these years.

On the 5th November, 1956, a member of our staff met a young boy wandering along the road which leads to the Settlement. Noting that he appeared to be lost he stopped and spoke to him, observed the crippling of the hands, and found from the boy that he was looking for his father—Brakon. He then brought the lad to the Settlement where his spot diagnosis was only too easily confirmed, the boy was admitted and he and his father re-united. The boy stated that he had been living with his grandfather on his farm but wanted to see his father, so left to find him—it is more than likely that the grandfather became anxious about the crippling, etc., and sent him here, knowing that his father was already a patient under treatment. (See appendix for details.)

Knowing that there was a large family left at home we asked the Divisional Medical Officer to arrange for an examination and this was done. The Hospital Assistant, Bau, collected the family and sent them to the General Hospital, Kuching, where five of the remaining eight members of the family were found to be suffering from leprosy. Thus, out of a family of ten, seven are suffering from the disease.

Of the six members of the family admitted in November, 1956, only one is smear positive. It would appear that the other five are of the Indeterminate type and it may be that the other has evolved through Indeterminate to Lepromatous. Whatever his condition in 1936/7 the father was, in 1950, a grossly lepromatous case and, it would seem, has infected most of his family. The remaining three members of the family have returned to their home and farm and will be kept under regular observation.

The kampong from which this family comes has not been living together in the usual way but split up some years ago—each family living on its own farm. Brakon himself states that he and his family lived on their own farm for many years before he came here in 1950.

This family is a proof, if it were required, of the value of the checking of the contacts of known cases—a policy which we have recently stressed and which is being put into effect not only as each new case is admitted but also throughout the various divisions.

Appended herewith please find details of each member of the family concerned.

Examination of patients admitted November, 1956, being members of family of Brakon

No. 1. Son, aged 18 years; admitted 5th November, 1956. Smears negative; extensive hypopigmented skin lesions with slightly active edges on shoulders, back and chest; hypopigmented flat lesion on face; glove anaesthesia both hands; main-en-griffe both hands; trophic ulcer on each foot. First observed lesions about four years ago.

No. 2. Wife of Brakon, aged 45 years; admitted 19th November, 1956. Smears negative; small hypopigmented skin lesion on right elbow; glove anaesthesia right hand; crippling with absorption of fingers of right hand. First observed lesion about two years ago.

No. 3. Daughter, aged 20 years; admitted 19h November, 1956. Smears negative; lesions on face active in appearance; extensive hypopigmented flat skin lesions on back, shoulders, chest, abdomen and right thigh; glove anaesthesia both hands; slight crippling in fingers of both hands. First observed lesions on back about three years ago.

No. 4. Daughter, aged 14 years; admitted 19th November, 1956. Smears negative; lesions on forearms and legs with active appearance; no anaesthesia or crippling. First observed during the past few months.

No. 5. Son, aged 13; admitted 19th November, 1956. Smears positive; faintly diffused lesions throughout chest, arms, back and legs; lesions on face with active appearance, and ears slightly nodular and swollen; no anaesthesia or crippling. First observed lesion on right cheek about two years ago.

No. 6. Son, aged 11; admitted 19th November, 1956. Smears negative; lesions on face with active appearance; on back faintly diffused; on legs extensive flat and hypopigmented; trophic changes in legs; anaesthesia very slight; signs of slight absorption of toes on right foot. First observed lesions about one year ago.

REVIEWS

Leprosy in India. Vol. 27, No. 3, 180-85, July, 1955. 16 figs. on 6 plates.

Dharmendra, S. N. Chatterji and N. R. Sen write on *A By-Product of DDS for Treatment of Trophic Ulcers in Leprosy.* The by-product used is obtained in the manufacture of DDS, and is the substance from which DDS has been extracted with the use of alcohol. It is a dark coloured sticky substance, containing a quantity of 2:4-diaminodiphenyl sulphone, in contrast to DDS which is 4:4 diaminodiphenyl sulphone. The former is much more soluble in alcohol than the latter. The sticky substance also contains a certain amount of DDS. It is applied to trophic ulcers of the soles of feet as a dressing and the patients are allowed to walk about. The treatment was used in 22 patients chiefly of the tuberculoid type, 18 of which had had previous treatment without results. In 15 the ulcers healed completely and had remained without relapse for a period of a year. In the others, though the ulcers became cleaner and smaller, there was not complete healing. X-ray examination showed that in those that did not heal there was diseased or dead bone. Trials with DDS dissolved in alcohol showed that the healing effects could not be due entirely to the DDS present in the by-product.

A. T. Roy gives his experience with *Thiosemicarbazone in the Treatment of Leprosy,* in DDS Intolerant Cases and in Combination with DDS. Nine patients intolerant of DDS because of lepra reaction were treated with thiosemicarbazone with a daily dosage of 25 rising to 150 mgm. The reactions were less severe and frequent than they had been with DDS, and there was clinical and bacteriological improvement. A combination of DDS and thiosemicarbazone did not give better results than with either drug separately.

International Journal of Leprosy, Vol. 24, No. 2, Apr.-June, 1956.

J. S. Shuttleworth writes on *Clinical Studies in the Use of Cortisone and Corticotropin in the Reactive Episodes of Leprosy.* In the National Leprosarium, Carville, 63 per cent of lepromatous cases have erythema nodosum reactions, and of these about 93 per cent occur after receiving sulphone treatment. Cortisone and corticotropin were found particularly useful in controlling the more acute reactions, but in the more chronic forms the results were more doubtful. In neuritis caused by leprosy the value of hormones is very definite, and it may be possible to prevent severe nerve damage if their use is begun in time. Ten cases are detailed showing

the effects obtained with these hormones often after other remedies had failed. The oral dosage of cortisone was 50 mgm. every 6 hours, diminishing to 12.5 mgm. twice daily in one case. In another it was 100 mgm. twice daily, diminishing to 50 mgm. twice daily continued for a month. One patient was kept on 50 mgm. of cortisone 4 times daily along with diasone for 7 months, during which the erythema nodosum reaction was successfully suppressed. further work on the effects of hormones in controlling leprous neuritis is being undertaken.

A review of *The Value of Slow-acting Chemotherapeutic Agents in the Campaign against Leprosy* is given by L. Lauret, P. Laviron, P. Kerbastard and C. Jardin. In French West Africa it is calculated that there are about 250,000 persons with leprosy. To control the disease it is necessary to take the treatment to the patient by means of mobile units, which at the same time deal with malaria, trypanosomiasis, ophthalmic conditions, etc., visits being made once or twice a month. The question of the most effectve method of administering sulphones to these wide-spread leprosy patients has been studied for the last 5 years, especially whether it was better to give DDS tablets daily or twice-monthly injections of a suspension of DDS. At present the treatment for those in the field is 1.25 gm. of DDS suspended in 5 or 6 cc. of ethyl esters of chaulmoogra oil, and injected intramuscularly twice a month. In 1955 as many as 36,000 patients received this form of treatment. It is considered that the chaulmoogra adds to the effectiveness of the treatment, and that better results are obtained with these injections than with oral DDS. The latter treatment, however, is reserved for those in towns who can attend more regularly. It may be found possible to extend the interval between injections to once a month, as the drug is very slowly absorbed.

H. Floch gives his experience of *Slowly Absorbed Injections of Coarse-Grained DDS.* He finds that by injecting DDS suspension he has fewer leprosy reactions than with oral administration. As suspending agents he has tried pea-nut, olive and chaulmoogra oils and also chaulmoogra esters. With these he has got good results, but he prefers an agar-saline menstruum (0.2 per cent)using DDS grains of 90-120 micromillimeters, and giving 1.5 gm. of DDS every 3 weeks, or 1.8 gm. once a month. He does not consider that the chaulmoogra menstruum adds to the effectiveness of DDS.

H. Hibi describes his *Findings in the Leprous Cornea with the Slit-Lamp Microscope* from a study made at the Nagashima Aiseien National Leprosarium in Japan. The 103 patients were divided into 4 groups, A, B, C and D, according to their age group. A

group being those under 15. The anterior part of the eye was examined with the Hartnack loupe, and the results compared with the findings with the biomicroscope. The principal changes found were: (1) thickening of the corneal nerve with a beaded effect in 47 per cent, found in all types of the disease, but chiefly in lepromatous; (2) new vascularization of the limbus in 60 per cent, only found in the lepromatous type; (3) pannus in 49 per cent, but only in the lepromatous type. It is considered that such examinations may be useful in classifying cases and even in making a diagnosis of leprosy. " In 8 of 25 lepromatous cases in Group A, infiltration in the face and limbus was almost indiscernible and the clinical appearance was of neural leprosy; but with the biomicroscope leprous changes in the limbus corneae were observed in 6 of them, and pannus corneae in 4."

A. Nègre and R. Fontan write on their experience of *Physiotherapy in the Sequelae and Complications of Leprosy.* Various forms of electro-therapy were used at the Orafara Sanatorium in Tahiti. The principal conditions treated with benefit were neuritis, perforating ulcer, claw-hand and paralysis. If any one form of treatment is not successful in a patient, another form is substituted. " Morphine, previously used in large doses, in the treatment of neuritis is no longer in use; ' neuromas ' subside after a few treatments; plantar ulcers, even old ones, can be healed in 20 days at most. If there are relapses, the same treatment can be repeated with success." The various forms of electrotherapy used are: faradic current, short wave, exponential, infra-red, diathermy, radio-therapy, ultrasonic, ionization with potassium iodide or calcium chloride. It is claimed that in 88 per cent of neuritis cases they were cured, often at one sitting, without any later relapse of pain.

The same writers also make a *Contribution to the Study of the Pathogenesis of Bony Lesions in Leprosy.* They consider that lesions of the small bones of the hands and feet are due partly to small injuries following anaesthesia of the hands and feet, and partly to vascular disturbance following neuritis of the supplying nerves. Periodically radiograms were made of 110 patients, and it was found that between February and June of 1954 considerable degenerative changes had taken place in the bones. It is difficult to remedy this, as it continues even after active disease has been checked by sulphone treatment.

A third contribution by the same two authors deals with the *Radiological Appearances of the Lungs in Leprosy.* Out of 110 leprosy patients who were subjected to radiography of the lungs, the

examination being repeated after a year, 3 showed shadows on the second occasion, shadows being absent on the first. These occurred during lepra reaction, but disappeared after the reaction had subsided. It is considered possible that these shadows were due to a temporary allergic infiltration similar to reactionary infiltration in the skin. It is suggested that where possible the lungs of patients should be radiographed, and that this should be repeated whenever they suffer from lepra reaction.

R. Kooji and T. Gerritzen write on *Positive "Lepromin" Reactions with Suspensions of Normal Tissue Particles.* By using suspensions of normal skin as antigen in the lepromin test in place of the ordinary Mitsuda-Wade suspension, they obtained positive early and late reactions, though they were not quite as strong as with the ordinary antigen. The results are shown in tabular form, the strengths of reactions being measured in millimeters. Suspensions of normal liver as well as suspensions of lepromatous liver and spleen were also used as antigens. Although the strength of the reactions varied, all the preparations reacted in the same way. From their results the authors propound a hypothesis that the Mitsuda phenomenon is a foreign-body reaction, and, if that is correct, that "attempts to find a correlation between the results of the lepromin and tuberculin tests, to prove an immunological relationship between leprosy and tuberculosis, are incorrect". The authors make a plea for the Madrid Congress criteria to be used in reports of lepromin readings, and in any case that the readings be given in millimeters so that comparisons will be possible.

In two editorials Dr. Wade discusses *The Manner of Use of DDS in Treatment.* and gives a timely history of *The Beginnings with BCG in Leprosy Work.*

REPORTS

Report of the Japanese Leprosy Foundation for 1954

The leprosy relief programme in modern Japan was initially carried out by religious workers of Japanese and foreign nationalities. In 22nd year of Meiji (1889), the French missionary Father Testevide established the Koyama Fukusei Hospital at Gotemba, Shizuoka Prefecture, and Miss Hannah Riddel started the Kaishun Hospital at Kumamoto City; in 39th year of Meiji (1906), Japanese bonze Rev. Ryumyo Tsunawaki established the Minobu Jingyo-en.

In accordance with the first Leprosy Prevention Law, which was enforced in 40th year of Meiji (1907), five public leprosy institutions were established by joint administration of several prefectures and institutionalized the leprosy patients. In 5th year of Showa (1930) for the first time, a national leprosarium was constructed, and in 16th year of Showa (1941), the aforementioned leprosy institutions by prefectures were transferred to the national government, and the programme for leprosy was put on the proper track.

In addition to these, the programme for leprosy was greatly promoted by the patronage of the Imperial Household. Especially Her Late Majesty The Empress Teimei gave countless contributions for the leprosy patients and concerned Herself about their welfare. After Her decease on 17th May of the 26th year of Showa (1951), the entire property was donated to the Leprosy Prevention Foundation for the welfare of the leprosy patients, and Her belongings were given to all leprosaria.

The estimated number of leprosy patients in Japan in 1953 was 15,000, out of which 10,129 are institutionalized in leprosaria. There are 1,077 leprosy patients registered but not institutionalized. The estimated number of non-registered leprosy patients is, consequently, 3,378.

As for the number of beds in leprosaria, eleven national leprosaria have 12,800 beds, three private institutions have 291, making the total beds for leprosy patients as 13,091.

The gradual decrease of the number of leprosy patients in Japan is shown by the fact that, whereas in the census of 1904 30,393 leprosy patients were identified, the present number of leprosy patients has decreased to about half, or, allowing for the increase of population and the ratio of occurrence to population, to about one-third. However, there are still many leprosy patients non-institutionalized who are a source of infection. It is urgently desired, therefore, to institutionalize them all as soon as possible.

As for the treatment of leprosy, Chaulmoogra oil has been substituted by DDS derivatives, and at present, Promin, Promizol, Diason are commonly used.

The whole of the leprosy patients in leprosaria are taken care of free of charge by the government. Non-infectious children, who have no relations, are taken into the eight children's institutions (capacity: 355) attached to the national leprosaria. In are in need, assistance is given in accordance with the Leprosy Prevention Law. For the aged persons in leprosy patients' families who have no relations, a special institution (capacity: 74) is provided at Kumamoto City.

Fiji Leprosy Hospital, Makogai

In the Report for 1954, the Medical Superintendent, Dr. W. H. McDonald, gives the number of patients at the end of the year as 647. Of the 13 different racial components of this number, the largest is Indian, being 203. There were 57 admissions during the year, 7 were readmissions. It is mentioned that 99 of the patients had received treatment with sulphone derivatives during the year; " at the end of the year nearly all the patients were receiving DDS ".

Many of the patients from American Samoa who were formerly in Makogai have been returned to their native land, where there is now a leprosarium with 23 patients.

Leprosy Regulations in England (from Report of the Ministry of Health, presented April, 1953).

The Public Health (Leprosy) Regulations, 1951, came into operation on 22nd June, 1951. Under these Regulations leprosy is directly notifiable to the Chief Medical Officer of the Ministry of Health. This is to enable the patient to receive such specialized examination and treatment as his illness requires, and for this the notifying practitioner is approached by the Minister's consultant adviser in leprosy with an offer to see the patient in consultation with him and discuss the arrangements necessary for his treatment and care.

The Regulations came into operation simultaneously with the opening of the Jordan Hospital, near Reigate, for the reception of lepers resident in this country. This hospital, with beds for 18 patients (8 females, 10 males) is administered by the University College Hospital group of hospitals for the Ministry of Health.

Not every sufferer from leprosy requires hospital care, nor is every patient infectious. The problem presented by the infectious patient is rather that of caring for and treating him and of pro-

tecting his immediate family contacts, than of taking widespread measures to protect the healthy community. Whenever the particular circumstances necessitate, the Minister's consultant adviser discusses the case with the medical officer of health. At the time of the preparation of this report (spring 1952) there are just over one hundred known cases of leprosy in England and Wales.

Annual Report of Calcutta School of Tropical Medicine, 1954

[The following extracts will be of interest to our readers.]

Effect of BCG Vaccination on the Lepromin Test.—More than two years ago 64 healthy persons, negative to both the lepromin and the tuberculin tests, were vaccinated with BCG by the intradermal route. They were re-tested 3 months after vaccination and again at 1-2 years intervals. The results of this study are shown in the following table:—

Nature of the Test	Number of persons tested	Initial results		Post-vaccination results			
				After three months		After 1-2 years	
		−	+	−	+	−	+
Lepromin ...	64	64	0	36	28	2	62
Tuberculin ...	64	64	0	4*	60	16†	48‡

* Were re-vaccinated with BCG and later became tuberculin +.
† All out of the 60 cases which were found to be positive on testing 3 months after BCG vaccination. Some of these again became positive when they were re-vaccinated.
‡ Includes four cases which remained negative after first BCG inoculation but which became positive after re-vaccination; the remaining 44 are out of the first 60 cases which had become positive after first BCG vaccination, the other 16 having again become negative (*vide* note † above).

It will be noted that in case of the lepromin reaction the number of positive reactions is much higher 1 to 2 years after the vaccination than 3 months after vaccination, and that there has been no reversal in a positive lepromin reaction induced by BCG. In case of the tuberculin test on the other hand the number of positive reactions 3 months after the vaccination was considerably higher than that 1 to 2 years after the vaccination, and that in 16 of the 60 persons the BCG induced tuberculin positivity disappeared during the following two years.

It would appear that the BCG induced positive lepromin reaction persists quite long, at least for 2 years, and possibly much longer. If this change from a negative to a positive lepromin reaction has a protective value against leprosy, it is not likely to be of a transient nature but is likely to be of real value as it lasts for a considerable time. However, it is yet to be proved whether this induced sensitivity to lepromin confers any protection against the disease; and this can be done only by well-planned and long term field experiments.

Intra-cellular lipoids in the various types of Leprosy.—Last year a study was reported on the significance of the presence of intra-cellular lipoids in the various types leprosy. The study was continued during the period under report and the following conclusions have been arrived at. In sections stained with Sudan III, coarse orange coloured granules (lipoid granules) are found in a majority of the lepromatous cases and are confined to such cases. They are absent from quiescent or reacting tuberculoid cases. It is concluded that presence of such granules offers an additional evidence to the lepromatous nature of the lesion.

Leprous lesions of the fundus of the Eye.—This study has been carried out in collaboration with Major E. J. Somerset, ex-Professor of Opthalmology, Calcutta Medical College. In addition to looking for lesions on the fundus, a note was made on the presence of leprous lesions on the cornea or iris.

Two hundred and forty-six lepromatous cases have been included in the investigation, and examinations were made after dilating the pupil with homatropine drops. In all the cases the disease was moderately to markedly advanced (L_2 or L_3 cases), and the duration of the disease varied from 2 to over 10 years. The cases were not specially selected and represent a fair cross section of the lepromatous cases as seen in Calcutta.

Only in two of the 246 cases were nodules found in the fundus, the condition being thus very rare. The small nodules seen in the fundus in these 2 cases, were very much like the nodules seen on the iris. They were about 0.25 mm. in diameter, yellow in colour, with smooth rounded outline, homogeneous surface, and appeared to protrude forward in the vitreous.

Lesions of the cornea or iris, or both, were seen in one or both eyes in 65 cases (26.4 per cent). Signs of iritis (with or without corneal lesions) were seen in 15 per cent of the cases in one or both eyes. Iritis is a potent cause or more or less preventable blindness, and the fact that it was found in 15 per cent of the cases brings out the importance of routine eye examination in lepromatous leprosy, especially because early symptoms of iris involvement are very slight.

The Campaign Against Leprosy in the Belgian Congo in 1955

Dr. Kivits writes a most interesting report on the efforts that are being made to control leprosy. In the total population of over 16 million in the Belgian Congo and Ruanda Urundi, it is calculated that there are about 274,000 with leprosy, of which 220,574 are under treatment. About 86 per cent of these are treated as out-

patients by general practitioners, polyclinics and temporary injection centres. There are 112 leprosaria in which there are 31,268 patients. The writer has found difficulties in establishments for the care of children of patients; the difficulty of obtaining enough suitable personnel to look after the children, and the fact that children brought up in such establishments are not adapted to normal social life outside. He believes rather that children should be given whatever benefit there is by vaccination by BCG. Whatever advantage there is in confining children to institutions, is countered by the high mortality. Experimentally partial isolation may be tried, allowing the mothers to suckle their infants, and thus avoiding artificial feeding. The tendency at the present time is to give priority to mass treatment rather than to treatment in leprosaria.

Leprosy in Malta. Report of Medical Health Department, 1955, p. 32.

There are at present 150 known cases of leprosy in Malta and Gozo. The number notified during the year was 14. Of the 150 there are 77 inpatients and 73 outpatients. Of the inpatients, 68 are classed as lepromatous. 32 patients with lepromatous disease were discharged at their own request during the year.

Leprosy and Tuberculosis in Sierra Leone

A general medical survey of Tonkolili and adjacent valleys in Sierra Leone was made by O. F. Conran and A. Conran, as arranged by an industrial development company. Their findings on Leprosy and Tuberculosis are summarized as follows in *The Journal of Trop. Med. and Hyg.* (Vol. 59, No. 12, Dec. 1956).

Seventy cases of leprosy were found. Of these, seven were frankly lepromatous, the remainder were mostly polyneuritic-tuberculoid, and several could not be classified satisfactorily.

The disease was most frequent at Kamadugu and Sokoya. In the former the village had suffered a period of overcrowding during the time of the gold mining operations some 20 years ago. In the latter standards of nutrition and cleanliness were low and housing was poor, and close contacts under these conditions are the vital factors in the spread of the disease.

The infected persons were eager to be treated, and the section chief at Kamadugu has ordered that they shall all take the treatment offered.

Thus 3.4 per cent of the population have the disease. The distance of their villages from government medical headquarters makes it impossible for many to come for treatment each week and

it is therefore necessary to take the treatment (oral sulphones) to them. To this end a leprosy register has been made and two medical orderlies detailed to visit all cases weekly and give the treatment.

Tuberculosis. Only three cases of open pulmonary tuberculosis were found, two at Kamadugu and one at Dalafe. Throughout the valley there were 12 further suspects, but the diagnosis could not be proved in the absence of X-ray facilities.

The Mission to Lepers. Report of Work in India, 1955-56.

At the Karigiri Centre (near Vellore), Mr. Fritchi reports the following subjects under investigation:

1. The study of the nature of the nodule of reactive leprosy, the nodule of erythema nodosum leprosum.

2. The action of some of the cortisone group of drugs for intractable reaction which is resistant to all the established methods of treatment.

3. The hormones in cases of gynaecomastia and the correlation between the incidence of this condition and degeneration of (a) the spermatogenic and (b) the interstitial elements in the testes.

4. The study of the effects of nerve damage on the extremities with a view to determining the nature of " trophic " changes. This work is being done in association with the Hand Research Department of the Christian Medical College under Dr. Paul Brand.

5. The treatment of the collapsed nose in leprosy and various methods of plastic reconstruction now available to us.

6. The continued new developments in the reconstructive surgery in leprosy being done in association with Dr. Brand here and in Vellore.

A note from Dr. Brand says:—

During the past year the orthopaedic work has expanded both in volume and in scope. Hand and foot reconstruction work is now engaged in at six centres.

In some of the new centres it is not easy for a newly trained surgeon to get started. It is easy to do good surgery in a fully equipped Medical College with trained anaesthetists and trained assistants and a good operating theatre. It seems quite different when there is no anaesthetist and when the surgeon himself has to train his own assistants and supervise the organization and asepsis of his operating theatre. We need to give all the help and encouragement we can to these new young surgeons in these difficult situations.

New operations have been devised and some have already become established procedures. Our present routine for hand reconstruction is quite different from what it was three years ago, and we are happy to be be able to report that the new operations are proving very definitely better than the old. We recently carried out a very extensive and thorough survey of our old cases, those who were operated three, four and five years ago. One hundred and fifty of these have been traced and re-examined and compared both with their original condition and with the immediate results of the operation. It has been very gratifying to find that seventy-five per cent of them showed a good result in spite of the difficulties and hazards through which some of these hands have had to pass. In general, it can now be stated that hands that are properly used and kept active following operation, continue not only to remain strong, but actually to improve their range of movement in the years that follow.

Greater attention has been focused on the reconstruction of the face, and we are operating on a number of deformed noses. We are hoping for the skilled advice and co-operation of experienced plastic surgeons in this field.

Leprosy patients get very distressed when they lose their eyebrows. Their distress is due partly to the fact that eyebrow baldness is widely recognised as a sign of leprosy. It is a mark that they will never lose, even when the disease is arrested. We are now happy to be able to assure patients that there is an operation which will give them a pair of healthy and vigorous eyebrows. The only disadvantage of the new eyebrow technique is that the patient needs to trim his eyebrows much as he would trim his moustache; otherwise they will grow so long that they may obstruct his vision! Fortunately this extra virility of their eyebrows seems to be source of pride rather than of sorrow to their owners.

ABSTRACTS

T. Suzuki, writing in the **Science Reports of the Research Institute, Tohoku University,** Vol. 6, No. 1, 1955, p. 89-95, reports on *The Influence of Antituberculosis Drugs upon the Oxygen Consumption of Mycobacteria.*

Three hours' observation after addition of streptomycin, PAS, TB1 and INH showed more or less inhibition of the respiration of BCG, but INH showed the strongest inhibitory power, but this was least at the most viable stage of BCG. Mycobacterial strains with relatively great respiration (tubercle bacilli of birds and cold-blooded animals and non-pathogens) showed no respiratory inhibition. The standard Warburg manometric techniques were used.

***Trop. Dis. Bulletin,** Vol. 53, No. 12, December 1956

Secondary Amyloidosis in Leprosy, by **J. S. Shuttleworth and Hilary Ross.** Ann. Intern. Med., 1956, July, Vol. 45, No. 1, 23-38.

In the United States the commonest cause of death in lepromatous leprosy is secondary amyloidosis. The organs of the body affected are the kidney, spleen, liver, adrenal, gastro-intestinal tract and pancreas. There is no clear correlation between the degree of leprosy and the development of amyloidosis. The first sign is progressive proteinuria leading to hypoproteinemia, followed by enlargement of the liver and spleen, nitrogen retention, anaemia and death. The Congo red absorption test is diagnostic if there is 80 to 100 per cent absorption within an hour. Persistent proteinuria is a constant finding, and must be present in order to make a diagnosis of secondary amyloidosis. When early amyloidosis is suspected it can be confirmed or otherwise by examination of biopsy material from the liver. Addison's disease due to amyloidosis of the adrenals has not been observed. The immediate prognosis depends on the development of anaemia, which, when it becomes extreme, is a sign that death is imminent. The average duration of life after the onset of proteinuria in amyloidosis was 38.33 months, with a wide range above and below that figure. Secondary amyloidosis occurs in other diseases of long standing. It is believed that the amyloid material is a protein unit with a sulphate-bearing polysaccharide, deposited intracellularly.

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Observations on Leprosy among Children born in the Culion Leper Colony during the Pre-Sulphone and the Sulphone Periods, by **C. B. Lara and J. L. Ignacio.** J. Philippine Med. Ass., 1956, Apr., Vol. 32, No. 4, 189-97.

The large number of patients at the Culion Colony, the high birth rate and the impossibility of isolating all children at birth, have provided favourable circumstances for the observation of early leprosy and its natural transmission. There have been the same workers for the last 22 years, and accurate records have been kept during that time. During the pre-sulphone period 20.9 per cent of the children showed leprous lesions, while in the sulphone period it was 19.9 per cent. In the former period 95 per cent of cases occurred in the first three years of life, while in the latter period only 57 per cent occurred in the first 3 years; there was thus a delay in the onset of the disease in the sulphone period. There is also probably a lower rate of incidence in the sulphone period. Even with the small dosage of sulphone used, lepra fever and ulcers and laryngeal complications have diminished or disappeared. However, the number of negative or apparently cured cases has not increased as rapidly as hoped for, and this is partly due to patients avoiding intensive therapy because of their reluctance to leave Culion.

The Uganda Leprosy Control Scheme, by **J. A. K. Brown.** East African Med. J., 1956, July, Vol. 33, No. 7, 259-70, 4 figs. and 1 map.

A description is given by the author of the leprosy control scheme which he first introduced in Eastern Nigeria, and has now applied in Uganda. In undeveloped countries like these with high incidence compulsory segregation is impracticable. Up to 1951 there were four settlements in Uganda, and in that year a fifth was added. In Uganda the people live widely separated, and 300 yards may separate a family from its neighbours. Surveys were carried out with the help of the District Health Staffs and the chiefs, who explained to the people the objects of the survey. In the Northern, Eastern and Western Provinces and in Buganda the estimated cases were respectively: 12,500; 39,800; 7,600 and 7,900. The proportions of lepromatous type varied in the provinces, being 7.5 per cent in the Northern, 5 per cent in the Eastern, 19 per cent in the Western, and 8.9 per cent in Buganda. It is calculated that there are 4,900 lepromatous cases in all. It was considered that opening large numbers of outpatient clinics would not be efficient, as the patients would not attend regularly. In place of this treat-

ment villages of simple construction were erected, accommodating from 20 to 400 patients. Of these there are now 40. In this way the danger of spreading infection is diminished. Under average conditions all lepromatous and all child patients within 15 miles of a medical unit should be admitted to a treatment village. Treatment is with DDS 0.1 gm. tablets, beginning with 1 tablet a week and rising by one additional tablet a week every month till a maximum of 6 tablets is reached. Between 30 and 40 per cent of the patients in the country are now able to obtain treatment regularly, as compared with 5 per cent in 1951. "The rate of progress has been due to the general anxiety of the peasants about the disease, to the influence of the surveys which have stimulated local interest, and to the attempt to keep every aspect of the scheme as simple as possible."

A Record of Fifty Years' Work with the Victims of Leprosy at the Culion Sanatorium, 1906 to 1956. Republic of the Philippines Department of Health, pp. ix and 109, 4 figs.

Leprosy is supposed to have been imported to the Philippines by Chinese immigrants long before the coming of the Spaniards. In the middle of the 19th century the San Lazaro Hospital for leprosy patients was founded in Manila. In 1905 the island of Culion, some 200 miles south of Manila, was set aside as a leprosy colony. Gradually the number of patients rose till it reached its peak of 7,000 in 1935. By the end of 1941 the number was reduced to 5,500 as the result of the founding of local leprosaria on the other islands. During the war there was great scarcity of food, and of the approximately 4,000 patients left only half survived.

Many improvements were introduced after 1915 and special treatment was introduced in 1921. During the first 4 years the death rate was 64 per cent, many of the patients being in a very bad condition when admitted, but the death rate soon fell to an average of under 10 per cent, and during the last 4 years it is only 3 per cent. Much has been done, especially on the pathological and bacteriological aspects by the Leonard Wood Memorial, and by the staff it supplied to the colony, which has been responsible for much of the recent advance in our knowledge of leprosy.

One of the great difficulties at the Culion leprosarium is the guarding from infection of the children of leprous parents. It was not found possible to remove children from mothers till some 2 years after birth, as earlier removal resulted in a high mortality. Even of those separated at 6 months some 50 per cent developed the disease by the time they were 5 years old. Of 98 children admitted

to a special nursery, only one with congenital heart disease died, and none of them had developed leprosy at 5 or 6 years of age; whereas of 219 left in the colony from 1949 to 1954, 20.4 per cent became leprous. Some 18.5 per cent of the inmates are negative and 11.4 per cent of the non-leprous children. For economic and other reasons it has been found impossible to discharge these. Patients also often refuse medicine or take it irregularly, fearing that if they recover they will be discharged to the outside world, where conditions of life are more difficult.

This brochure is a memorial of the jubilee of the colony. It is divided into 6 sections dealing respectively with general history, medical services, religious and social activities, economic and legal aspects, educational and cultural services, and such problems as those just mentioned.

[This report should be carefully studied by those interested in the control of leprosy, showing as it does the results of compulsory segregation in a distant island after a long period of years.]

The Dimorphous Macular Lesion in Leprosy, by **Khanolkar.** Indian J. Med. Sci., 1956, July, Vol. 10, pp. 499-505.

Four cases of the dimorphous form of leprosy are described and illustrated by photographs of lesions and corresponding sections of biopsy material. Histological appearances characteristic of the two main types of leprosy appear in the same lesions. Bacilli were found in all four cases, and in three of them the lepromin reaction was slightly positive. It is considered that this form of the disease may be transformed into either the lepromatous or the tuberculoid type, but more frequently into the former than into the latter.

The Testis in Leprosy, by **A. L. Furniss.** Indian J. Med. Sci., 1956, July, Vol. 10, No. 7, 506-10, 7 figs. on 2 pls.

For this study biopsy material was taken from 22 patients with the lepromatous or dimorphous type of leprosy and 8 with the tuberculoid type, patients being chosen who were undergoing an operation for some other condition. In none of the tuberculoid cases was the testes affected with leprosy. No affected testes appeared normal macroscopically, most of them appearing reduced in size. The normal brown tissue was replaced with strands or patches of white fibrous tissue, and with yellow areas similar to those in leprous lymph glands. Microscopically, the tubules appeared to have an internal limiting membrane, and between the tubules there was infiltration with round cells and histiocytes, between which there were acid-fast bacilli. Later there was separation of the tubules, oedema and fibrosis. Still later the

tubules became hyaline and lost their structure. The epididymis was less affected than the testis. In 190 male patients with lepromatous leprosy there was gynecomastia in 73; but in the series of 22 who underwent biopsy there were only 2 with gynecomastia, so that it is not possible to record any correlation between even gross testicular affection and gynecomastia.

It is remarked that the atrophy of the testis which is so marked in leprosy occurs " early in the disease process and unrelated to the degree of lepromatous infiltration ". In fact, the tubular degeneration may be a reaction to an injury caused by toxin or bacterium. The possible causes of gynecomastia are discussed: " It seems that leprosy provides a good opportunity for investigating the nature and cause of the hormonal imbalance concerned in the development of gynecomastia." The reason for the common affection of the testis in leprosy is discussed. It is suggested that for some unknown reason the testes may form a nidus for the leprosy bacillus as does nerve tissue, and that if this unknown reason could be found it might elucidate the problem of culturing the bacillus. The article is illustrated with 7 photomicrographs.

***Trop. Dis. Bulletin,** Vol. 54, No. 1, January 1957

The Treatment of Deformities of the Foot in Leprosy, by **W. A. A. Hodges.** East African Med. J., 1956, Aug., Vol. 33, No. 8, 301-3, 2 figs.

Deformity initially develops in neural leprosy after there is drop foot with anaesthesia. A minor trauma leads to trophic ulceration of the toes and sole. Brand is quoted as recommending extensor tenodesis in early cases, and triple arthrodesis in more advanced conditions with ulcers. [In a more recent article (see *Trop. Dis. Bulletin,* 1955, 52, 1094), Brand recommends transplantation of the tibialis posterior tendon and after re-routing insertion into the middle cuneiform bone. This operation is proving very successful (personal communication).] The author operated on 15 patients, 10 of whom had ulceration of the sole, doing a modification of the Lambrinudi operation and extending the skin incision so as to include the ulcer. A very large wedge excision is required to produce a plantigrade foot when there is equino-varus deformity. All the patients were able to walk well after 4 months. After the operation the patients had padded plaster casts for 3 weeks, followed by walking plaster casts for 9 weeks. Two of the patients observed 15 months after the operation were walking well, had no ulcers and were able to work in the fields.

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Correlation between Tuberculin and Lepromin Reactions, by **N. Souza Campos, J. Rosemberg and J. N. Aun.** Rev. Basileira Leprologia, S. Paulo, 1955, Jan.-Dec., Vol. 23-40. English Summary.

The authors first made tuberculin and lepromin tests in 3 groups of healthy people: (a) in a group of 471 children who had had no contact with leprosy; (b) in a group of 356 children who had been in contact with leprosy; (c) in a group of 860 adults who had had no known contact with leprosy. Three groups of patients were also examined: (1) 53 children with tuberculosis; (2) 73 adults with tuberculosis; (3) 105 patients with leprosy, 93 of whom had the lepromatous form of the disease.

It was found that there was agreement between the lepromin and tuberculin reactions to a considerable degree in healthy people who had been exposed to tuberculosis but not leprosy, in healthy persons who had been exposed to leprosy when they were first exposed to tuberculous infection, and in tuberculous patients. There was almost complete disagreement between the two reactions in lepromatous cases of leprosy when infected with tuberculosis. Persons vaccinated with BCG gave a high degree of agreement between the reactions, at least for a short time after vaccination. It is stated that those infected with leprosy, but with a positive lepromin reaction, will be permanently negative to tuberculin. [It is not clear on what grounds this last assertion is based.]

Isoniazid in Lepra Reaction, by **O. B. de Macedo and F. A. Berti.** Rev. Brazileira Leprologia, S. Paulo, 1955, Jan.-Dec., Vol. 23, Nos. 1/4, 41-52. 17 refs.

After recounting the history of this drug in the treatment of tuberculosis and leprosy, the authors describe the cases of 26 lepromatous patients with lepra reaction (7 acute and 19 subacute), 1 tuberculoid and 1 dimorphous. The results of treatment with oral administration of isoniazid, 100-200 mgm. daily, are given as follows: Very good 4, good 13, no improvement 4, abandoned treatment 7. The authors consider this the best oral treatment for lepra reaction in their experience. They intend to test the effects of this drug given parenterally.

The Study of the Lepromin Reaction in Rats previously inoculated with Myco. lepraemarium *and with* Myco. tuberculosis (*BCG*), by **W. A. Hadler and L. M. Ziti.** Rev. Brasileira Leprologia, 1/4, 53-75, 10 figs. and 6 graphs, 25 refs. English Summary.

Normal rats give a negative lepromin reaction. The present 3 experiments were to test the effect on the lepromin

reaction of previous inoculation with BCG or *Myco. lepraemurium*. In the first lots of rats, in addition to uninjected controls, 90 were injected 0.1 ml. of *Myco. leprae* suspension, 20 with a larger and 20 with a smaller amount of a triturated suspension of a murine leprosy lesion. The second lots of rats were first inoculated intraperitoneally with BCG and then 33 days later they were injected intradermally with mycobacteria killed by heat as follows: 30 rats with with 0.1 ml. of a suspension of *Myco. leprae*, 20 rats with a larger and 20 with a smaller quantity of titurated lesion of *Myco. lepraemurium*. The third experiment was very similar to the second, except that in place of BCG living *Myco. lepraemurium* were injected intraperitoneally 10 days before BCG giving the intradermal injections. It was found that in the rats previously inoculated intraperitoneally with BCG or with *Myco. lepraemurium*, the macroscopic lesion was larger and remained longer, while the histological lesions were more intense and showed necrosis. But the cytological appearances were not different from those in the controls.

Mitsuda's Reactions induced in the Normal Rhesus ("Macacca mulata"), by **M. J. Pereira, Jr., and F. Nery-Guimaraes.** Mem. Inst., Oswaldo Cruz., 1955, June-Sept.-Dec., Vol. 53, Nos. 2, 3, 4, 609-19, 2 figs., 10 refs.

Living BCG vaccine was administered to 12 rhesus monkeys by various routes. Before the vaccination all the monkeys had negative tuberculin and lepromin reactions. In the monkeys which were given the vaccine into the peritoneum and the testicle the Mitsuda reaction was converted to 3 plus after 8 months, and continued so till 12 months. In those vaccinated orally, intradermally, by scarification and by multipuncture the conversion was to only 1 plus. In 5 other monkeys vaccinated orally or intradermally with killed BCG vaccine conversions were slower and less marked. The tuberculin conversions were most marked (3 plus) in the peritoneally and testicularly vaccinated monkeys; in the others the conversions were slower and more transient.

Borderline (Dimorphous) Leprosy maintaining a Polyneuritic Form for Eight Years: A Case Report, **by W. H. Jopling.** Trans. Roy. Soc. Trop. Med. & Hyg., 1956, Sept., Vol. 50, No. 5, 478-80, 2 figs.

A patient with neurological symptoms for 8 years was wrongly diagnosed as suffering from syringomyelia. When in 1954 a diagnosis of leprosy was made he was treated with DDS. After 4 months' treatment there were pains in the limbs and erysipeloid

skin lesions. Previous to this a biopsy of the auricular nerve showed foamy cells between the nerve fibres, but no epithelioid or giant cells; there were large numbers of acid-fast bacilli. Later a biopsy of the skin showed " patches of infiltration by mononuclear cells (histiocytes) and epithelioid cells," a few acid-fast bacilli, but no foam cells or giant cells. A diagnosis of dimorphous or borderline leprosy was made.

The Use of Diluted Lepromin. Results of Intradermal Injection of Carbolized Extract of Normal Skin in Patients suffering from Different Forms of Leprosy, by **H. Floch.** Arch. Inst. Pasteur de la Guyane Francaise et la l'Inini, 1956, May, 6 pp.

The antigen of Mitsuda, used in the lepromin test, is composed of 3 elements: the bacillus, leprous tissue and normal skin. Using the whole antigen, and comparing it with a suspension of normal skin as an antigen, the author found that (by the late reading) in tuberculoid cases 90 per cent were positive to the former, and 54 per cent to the latter. In lepromatous cases the early reading was positive in 25 per cent with the skin antigen, and 17 per cent with the whole antigen; but in both of these the late reading was negative.

The Campaign against Leprosy in the Belgian Congo in 1955, by **M. Kivits.** Bull. d' Information sur la Lèpre, No. 3. [Reprinted from Acad. Roy. des. Sci. Coloniales, Classe des Sci. Naturelles et Méd. Mémoires in-8, 1956, Vol. 4, 61 pp., 20 figs. on 10 pls. (55 refs.).]

Leprosy was at first neglected in the Belgian Congo because of the absence of effective methods of treatment and because there were other more pressing medical problems. But in 1926 the Congo Red Cross began work with a centre at Pawa. This was supplemented in 1936 by the formation of the *Fondation Père Damien* for the fight against leprosy. Later *Foperda* (*le Fonds du Bien-Etre Indigène*) and *Forami* made it possible to augment the number of treatment centres. The work is co-ordinated by a provincial committee under the Governor in each province. The principle is to treat all non-infectious patients at out-patient clinics, and the more infectious lepromatous patients in leprosaria. It was calculated in 1949 that there were about 215,000 leprous patients in the Congo, of whom about 90,000 were under treatment. This makes a rate of about 2 per cent, but in the equatorial forest belt the percentage goes up to as much as 4 or 5 per cent. During the year 1955 about 184,686 patients, or about 86 per cent of the whole were under

ambulatory treatment with DDS at urban polyclinics, rural dispensaries and temporary injection centres. DDS is generally given by injection of a slowly absorbed suspension (suspension-retard) once in 15 days.

A list of leprosaria is given, for which special financial provision is made: 7 are Government, 1 *Forami*, 1 Red Cross, 6 Catholic Missions, and 5 Protestant Missions, a total of 20 in all. Five of these are still in course of construction. In those in use there are about 13,820 patients. The question of BCG vaccination and its possible raising of resistance to leprosy especially among children is being examined. [This report is worthy of careful study in the original.]

***Trop. Dis. Bulletin,** Vol. 54, No. 2, February 1957

Allergy to Tuberculin and Lepromin and BCG Vaccination in those with Leprosy, by **L. Chambon and P. Destombes.** Bull. Soc. Path. Exot., 1956, May-June, Vol. 49, No. 3, 414-18.

After testing the reactions of 492 untreated leprosy patients for their reactions to tuberculin and lepromin (189 being lepromatous, 162 tuberculoid, 46 reacting tuberculoid and 95 undifferentiated), the authors come to the conclusion that leprosy does not seem to affect the incidence of allergy to tuberculin because positive reactions to the Mantoux test are practically the same in leprous subjects as in those without leprosy. Both reactions were positive in about one-third of those with leprosy, most of them being tuberculoid cases. In contrast, three-quarters of those allergic to tuberculin but not to lepromin were of the lepromatous type. It appeared therefore in the conditions of the experiment that allergy to tuberculin is not always sufficient to cause the appearance of allergy to lepromin. After vaccination with BCG, conversions to a positive lepromin reaction are always more frequent among those originally allergic to tuberculin.

An Attempt to Control Leprosy by BCG in the Loyalty Islands, by **Medecin-Capitaine Lacour.**

The following is a brief abstract of the summary and conclusions:

An attempt to control leprosy through the use of BCG vaccine has been initiated in the Loyalty Islands during 1954. These islands were selected because of the many favourable conditions

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obtaining there, namely, the stability and homogeneity of the population; an accurate knowledge of leprosy; the detailed records of annual case-finding.

Facts pertaining to population and to leprosy are shown in tabulated form and from the detailed background necessary at the beginning of the campaign. Working procedures are here briefly summarised: Mantoux test: intradermal injection of 1/40 c.c. of a 1/100 dilution of old tuberculin; Mitsuda test: classical test using an antigen diluted 1/30; BCG vaccination: dry frozen BCG vaccine given through skin scarifications.

The early results show, for the different districts and islands, and for age of inhabitants: Tuberculin and lepromin indices, the different combinations of the results and their respective values, the percentages of vaccinated persons for whom the Mitsuda test was negative; the intensity of reactions to the lepromin and tuberculin; and the nature of reaction to the lepromin tests on contagious and non-contagious lepers. It is not yet possible to formulate any opinion on the value of BCG vaccination in the control of leprosy. Only a long period of observation will provide a precise criterion for this evaluation.

During the next years an attempt will be made to control and maintain the tuberculin allergy on the persons under observation; study the variations of the Mitsuda reaction; test the persons that have not been seen in 1954, and the newly-born; study carefully all new cases of leprosy through clinical, immunological, and bacteriological procedures. Only the comparison of the results to be obtained in the future with the results reported here, will make it possible, after several years have elapsed, to formulate an opinion on the value of the BCG vaccination as a measure of control of Hansen's disease on a given collectivity.