# LEPROSY REVIEW

The Quarterly Publication of THE BRITISH LEPROSY RELIEF ASSOCIATION

VOL. XXV. No. 2

April, 1954.

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Treatment of Leprosy with Thiosemicarbazone

Diaminodiphenylsulphone in Leprosy

A case of Leprosy in a seven months old Child

Improved histological method for Examination of Cutaneous Nerves in Leprosy

Plastic Surgery in the Rehabilitation of the Leprosy Patient

Reviews

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## LEPROSY REVIEW.

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\* From May 1st, 1954, Dr. J. LOWE, has been appointed Medical Secretary of the British Empire Leprosy Association, and will edit the Leprosy Review.

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#### EDITORIAL

We publish in this number of the Review two articles, one reporting favourable results with thiosemicarbazone and the other with isonicotinic acid hydrazide (isoniazid). In both instances the writers claim that these drugs have a favourable effect in leprosy. At the relatively recent international leprosy meetings-the International Leprosy Congress held in Madrid and the Leprosy Missions Conference in Lucknow-thiosemicarbazone received favourable comment, but isoniazid was not recommended. These two contributions indicate that we have not yet discovered the ideal antileprosy remedy, and therefore we must not rest content with the fact that because the sulphones are definitely superior to the older remedies, and because there are alternative remedies for use where there is sulphone intolerance, we now can be satisfied with the therapeutic position in leprosy. While the percentages of negatives under sulphone and certain other treatments are encouragingly high, there are a sufficient number of cases who remain positive over a period of five years and more, and others who seem quite intolerant to sulphones, to make us concerned lest the excessive enthusiasm engendered by the new treatments causes public health workers to feel that this treatment, if only widespread enough to reach the majority of leprosy patients, will ultimately-and some appear to believe in a relatively short time-eliminate leprosy from the world. It must be remembered that the primary principles of prevention-the separation in some form or another of the infective case from the healthy child—is neglected at our peril. It also must be borne in mind that no definite conclusions with regard to the effectiveness of a drug in leprosy can be drawn under a period of three years. We welcome the reports of careful workers, and are confident that the new successes in therapy of leprosy will stimulate these and others to search for more effective remedies, so that the final control of this baffling disease will be hastened. There is a growing body of opinion which is inclined to favour the parenteral use of sulphones. In view of the general acceptance of oral dapsone, this opinion must be taken into account, lest we put aside as impractical or inconvenient a method of administration which in the long run may show more satisfactory results.

The article discussing a case of leprosy in a seven months old child serves as a salutary reminder of the danger of exposing children to infection, and emphasises that the greatest care must be taken to separate the healthy child from contact with the infective case.

This number of the Review again stresses the need for reparative surgery in the rehabilitation of the leprosy patient, and challenges us to endeavour to see that when a patient is discharged the physical stigmata of the disease shall as far as possible be neutralised so that our friends can return to society with a healthy outlook, and not with warped minds due to the ravages of leprosy on their bodies. The importance of this cannot be stressed too often.

We are glad to publish an article from the Christian Medical College, Vellore, on the technique for staining M. leprae in nerve preparations. The staff of this college have contributed greatly to the better understanding of leprosy, and they, along with the Bombay and other workers in India, have maintained the high excellence of the work which has been done in India ever since the pioneer days of Rogers and Muir.

It is with regret that the Editor has to take farewell of his readers, but would like cordially to welcome the new Medical Secretary of BELRA, and the Editor of *Leprosy Review*—Dr. John Lowe. Dr. Lowe needs no introduction to the Review, and his outstanding achievements in leprosy, particularly his contributions to the therapy of the disease, guarantee the future usefulness of the Review, and ensure that workers in leprosy, especially those who have no access to the more scientific journals, will not only be able through the medium of this quarterly to keep abreast of modern knowledge, but will be encouraged and stimulated to continue their efforts with increased zeal, hastening the coming of that day when leprosy is no longer a scourge which mutilates the body, and what is more tragic, the mind, of so many in this world of men.

## ISONIAZID ALONE AND IN COMBINATION WITH OTHER DRUGS IN THE TREATMENT OF LEPROSY

#### W. S. DAVIDSON, M.B., CH.B., D.P.H.

The known efficacy of modern drugs with prolonged treatment in leprosy limits the opportunity for experiment with new drugs which also require considerable time to give a true indication of their usefulness. Experiments are generally limited to a few individual cases. Unfortunately, in a disease of remission and relapses, a true picture cannot be obtained from a few cases. This report does not therefore presume to present the whole picture regarding the effects of isoniazid but merely to give an indication of its effect on two small series of cases so that the results may be added to those of other workers and thereby contribute in some small measure to the final judgment.

Series I consists of 10 cases (6 new cases and 4 cases previously given sulphetrone, etc.) under trial with isoniazid for 17 months. Intramuscular sulphetrone was introduced during the course of this treatment.

Series II consists of 6 cases, all old cases previously treated unsuccessfully with sulphetrone.

Isoniazid was under trial in this series for 12 months and neustab was introduced for the last three months.

Progress was recorded by the group marking system for clinical appearance and smear count explained in a previous report in this Journal<sup>(1)</sup>.

SERIES	I:	

Treatment:	reatment: INH 200 mg. daily.				
Progress:	No improvement was evident until				
	after 3 months, whereupon pro-				
	gress was rapid.				
Progress ind	dex at end of 6 months: 1.425.				
Treatment:	INH 250 mg. daily.				
Progress:	Slower but maintained.				
Index:	.4				
Treatment:	INH 350 mg. daily plus intra-				
	muscular sulphetrone increasing to				
	4 ccs. 50% sol. twice weekly.				
Progress:	Little improvement noted in any				
	case and several cases deteriorated				
Index.	—.075.				
	Treatment: Progress: Progress ind Treatment: Progress: Index: Treatment: Progress: Index.				

The general deterioration of progress was so marked throughout this five month period that the possibility of interference or biological incompatability of the drugs had to be considered. To test this possibility, the ten cases were divided into two groups of five as nearly similar as possible. To Group A for the next three months only isoniazid was given, and to Group B only intramuscular sulphetrone.

	Group A	of Series I
15th—17th month:	Treatment:	INH 350 mg. daily.
	· Progress:	Good.
	Index:	.6
	Group B	of Series I
15th—17th month:	Treatment:	4 ccs. 50% sol. Sulphetrone intra- muscularly twice weekly.
	Progress:	Good.
	Index:	•5

To illustrate better the meaning of these indices against the background of time involved in their production, reference may



be made to the graph which clearly indicates the steady progress under INH or sulphetrone alone and the marked decline in progress when the drugs were exhibited concurrently. Though statistically insignificant, it is interesting to note that Group A (the INH group) made a slightly better recovery than Group B (the sulphetrone group).

In general, it can be said that in spite of the setback during the combined treatment, the index of progress in INH treatment was 2.3 over a 17-months period. This compares favourably with the index of 2.16 for 12-months' treatment with intramuscular sulphetrone, and the index of 2.58 for 24-months' treatment with oral sulphetrone previously reported by me<sup>(1)</sup>.

How much of the decline in progress during the combined treatment was actually due to the treatment and how much was a normal vagary of the disease, is difficult to determine, but the following observations must be borne in mind.

The decline in progress was general throughout the series, and the low index is not the result of severe relapse in one or two cases. The decline was noted at an examination after 3 months of the combined treatment, and is not solely dependent on the one examination at the end of 5 months. When the treatments were separated (Groups A and B) the normal progress was again immediately resumed. There are therefore indications that the combined treatment may be the cause of the decline, and it is interesting in this connection to note the work of Grunberg and Schnitzer<sup>(2)</sup> in experimental tuberculosis of mice and Szybalski and Bryson<sup>(3)</sup> with various saprophytic organisms in vitro.

These workers report the apparent inhibitory effect that streptomycin and isoniazid have on one another when exhibited in subtherapeutic dosage.

#### SERIES II:

There were 6 old cases resistant to sulphetrone and other drugs.

They were treated for the first 9 months on INH 350 mg. daily. One case showed improvement and two deteriorated.

For the following three months the INH treatment was combined with neustab (TB1) commencing with 50 mg. daily and increasing gradually to 20 mg. daily. During this period, two further cases showed improvement. The total result of the 12 months' treatment was therefore improvement in three cases, deterioration in two, and no change in one. This experiment in treatment continues and is not therefore reported in greater detail. The point of interest is that the combination INH with neustab appears to be beneficial and not detrimental as in the combination INH and sulphetrone. This will require further trial but, again, it is of interest to refer to Szybalski and Bryson who, in their experiments, found no antagonism between isoniazid and nicotinaldehyde thiosemicarbazone.

#### **TOXIC EFFECTS** :

In the 16 patients under treatment there were only two instances of toxic manifestations, one case of headache and cramps and one case of rash. Both recovered quickly with a period of reduced dosage

Haemoglobin levels increased and remained high, and only fell on the introduction of sulphetrone or neustab as an addition to the treatment.

#### GENERAL CONDITION :

An improvement in general condition was noticeable, and weights markedly increased. Weight increase was not only apparent in new cases where improved diet and institutional care induce such results; it was also noted in the old cases after years in the leprosarium. The average weight increase in new cases was 16 lbs. and in old cases II lbs.

#### CONCLUSION :

As far as it is permissible to draw conclusions from such a short exhibition of the drug in a small series, there is an indication that isoniazid has a position in the treatment of leprosy not necessarily inferior to sulphetrone and further work is necessary to establish its true position.

There is little evidence of improvement before the fourth month of treatment.

There are indications that its concurrent exhibition with sulphetrone is detrimental to cure, possibly as a result of a biological incompatability. This incompatability has not been evident when INH has been combined with neustab in the treatment.

Hæmoglobin remains high and toxic effects are few, and the general condition of patients under treatment markedly improves; this drug would be invaluable in the treatment of leprosy if the results in the above series were sustained in extensive trial.

#### SUMMARY :

Ten cases for 17 months and 6 cases for 12 months were treated with INH. The results compare favourably with results obtained with sulphetrone.

There are indications against its use in conjunction with sulphetrone, but in conjunction with neustab results improved. ISONIAZID AND OTHER DRUGS

The above is published with the permission of Dr. L. Henzell, Commissioner of Public Health, Western Australia, and my acknowledgments are due to Dr. Grigoroff and Mother Alphonsus of Derby Leprosarium, who carried out the care, treatment and examination of the patients.

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## THE TREATMENT OF LEPROSY WITH THIOSEMICARBAZONE

#### C. W. J. MORRIS, M.D.

The thiosemicarbazones (e.g.  $TB_1$ , conteben, thiacetazone, neustab, berculon A., etc.) have now been used fairly extensively in the treatment of various forms of tuberculosis and leprosy.

A number of workers have reported the results obtained in the treatment of leprosy. Keil<sup>(1)</sup> reported the work of several groups who have used conteben  $(TB_1)$  with satisfactory results in patients with lepromatous leprosy. Ryrie<sup>(2)</sup> used the drug in patients with advanced lepromatous disease and lepromatous disease of long standing and found it effective. Schujman<sup>(3)</sup> described favourable results obtained by Schneider in fourteen lepromatous cases treated for nine months. In his own personal experience he described trials with the drug in fourteen patients, twelve of whom were suffering from the lepromatous type of disease. He reported that the drug was well tolerated, few patients had lepra reactions and the results obtained were very satisfactory as judged by the clinical improvement.

Cochrane<sup>(4)</sup> does not believe the thiosemicarbazones are as

effective as the sulphones but should be used as a second line of attack. Lowe<sup>(5)</sup> treated several large groups with the drug, with satisfactory results. However, in one group of one hundred and forty-six patients treated for a period up to twenty-one months, he reported three cases of acute agranulocytosis. These, however, occurred during the first few weeks of treatment, all between the third and sixth week, and all recovered. A fourth patient with mild agranulocytosis, after recovery, continued with the same treatment, and with no sign of a recurrence of the agranulocytosis. He believes that agranulocytosis appears early or not at all and that his findings support the idea that this agranulocytosis is an allergic rather than a toxic action of the drug.

At the Oyi River Leprosarium in West Kabba Province, Nigeria, patients have been treated with sulphones since 1949. Some were first treated with diasone, then sulphetrone, and finally all were put on diamino-diphenylsulphone. During 1951 quite a number of the patients were found to be unable to tolerate DDS in the higher doses. A few were found who developed severe allergic reaction to the drug. A small number developed psychotic symptoms which usually cleared up in time on cessation of the drug.

In 1952 there were about twenty-two patients of the one thousand under treatment in the Oyi River Leprosarium (West Kabba Provincial) who were unable to tolerate DDS. It was decided to try them on thiosemicarbazone. In addition to most of these, twenty new admissions—unselected consecutive cases—were added to this group in order to determine if the drug could be used generally without elaborate controls. These new patients were taken as they came, regardless of sex, type, or stage of the disease. They were added to the general group if their haemoglobin was 70% or over and their general condition was satisfactory.

The thirty-eight patients who were then put on thiosemicarbazone consisted of two groups; one group A, composed of eighteen patients who had previously received treatment with hydnocarpus oil and DDS, while the other group B of twenty included those who had received no previous treatment under medical supervision. (Some and perhaps all may have had some form of native remedy prior to admission.) Others were put on neustab later but these are not included in the group of thirty-eight.

Before starting the drug, all the patients were examined clinically and bacteriologically, the haemoglobin was estimated, and the usual laboratory examinations of stool and urine were carried out.

The drug used was " Neustab " brand of thiacetazone, which is

para-acetylaminobenzaldehyde thiosemicarbazone. It is packaged in tablets of 25 mg. for oral administration. For use in this group of patients, it was supplied without charge by Boots Pure Drug Co., Ltd.

In spite of the probable truth that "agranulocytosis is an allergic rather than a toxic action of the drug," it was felt advisable to proceed with caution. Patients were started on 12.5 mg. or 25 mg. and increased slowly up to a total daily dose of 150 mg. In most cases the dose of the drug was increased by 25 mg. at intervals of roughly three weeks. The patients were given the total dose at one time (the evening) on six days of the week.

Treatment was commenced in June, 1952, but doses were reduced in amount in August due to short supply and during October treatment with neustab had to be suspended, due to lack of tablets. During this period patients received only ferrous sulphate tablets grs. iii, thrice daily. From November 1, 1952, neustab was given regularly up to July 31, 1953. The thirty-eight patients were thus on continuous treatment with neustab for a period of nine months with the exception of one female patient (No. 471). who left the leprosarium in January.

Of the total of thirty-eight patients, twenty had lepromatous leprosy, ten of these being in group A and ten in Group B. The remainder included tuberculoid, simple macular, and indeterminate cases.

Four of the patients in Group A had developed psychotic symptoms while on DDS, at least one of them having had a preexisting psychotic background. Three in the same group had developed severe repeated lepra reactions on DDS and most of the remainder were allergic to the drug.

#### Effectiveness of Treatment with "Neustab"

Clinically, all the patients have shown various degrees of improvement, nineteen being markedly improved, thirteen moderately improved and five slightly improved.

All the patients with lepromatous disease and positive bacteriological findings have shown both clinical and bacteriological improvement.

While only one patient with lepromatous disease, (No. 1284), strongly positive at the beginning, has become bacteriologically negative, routine examination of skin and nasal smears showed evidence of a diminution in the numbers of bacilli in the other positive cases. No bacteriological index was done since it was desired to keep the laboratory work at a minimum. Patients who developed psychotic symptoms on DDS have shown no evidence of a recurrence on full doses of neustab over a period of six months.

One patient, (No. 1194), who had pulmonary tuberculosis with associated chronic productive cough and sputum positive on direct smear, did exceptionally well. During treatment he frequently had an elevation of temperature, between 99° and 100°, but treatment was continued. Most of his signs and symptoms of leprosy have disappeared, his cough has greatly diminished, and the sputum is now negative for mycobacterium tuberculosis.

#### COMPLICATIONS

Relatively few severe complications arose, and the drug was, in most instances, well tolerated.

Fourteen patients had mild lepra reactions while under treatment but in every case showed considerable improvement following the reaction. In some of these the drug was continued throughout the reaction.

One patient, (No. 1706), had two mild lepra reactions and one patient, (No. 1705), an adult male with far advanced lepromatous disease, had an acute lepra reaction and was unable to resume treatment for three months.

One elderly female patient, (No. 1284), with the marked tubero-nodular form of the lepromatous type and strongly positive bacteriologically, had two moderately severe lepra reactions. She is now much improved clinically and is bacteriologically negative.

As with diaminodiphenylsulphone and other drugs, during treatment there was a fairly uniform fall in the haemoglobin level. By giving two tablets (grs. vi) of ferrous sulphate daily, the haemoglobin could be maintained at a suitable level and the patient's condition improved.

#### DISCUSSION

These trials were in no sense a "controlled" experiment. A minimum of laboratory work was done. While the number of patients is very small, all showed improvement clinically and no serious complications occurred. In the group of patients who previously had treatment with DDS but were unable to tolerate the drug, neustab gave satisfactory results. A second arrow for the pharmaceutical bow in the battle against leprosy is indeed acceptable and welcome.

#### Summary

Thirty-eight patients, twenty having lepromatous leprosy, were

treated for nine months to one year with neustab. Of the thirtyeight patients, eighteen had had previous treatment with hydnocarpus oil and DDS.

Very few complications occurred during treatment.

All patients showed evidence of clinical improvement and one lepromatous case previously bacteriologically positive became bacteriologically negative.

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#### ACKNOWLEDGMENT

We wish to express our thanks to Boots Pure Drug Company and their local representatives for the supply of "Neustab" to carry out these trials.

## DIAMINODIPHENYLSULPHONE IN LEPROSY ITS ORAL AND PARENTERAL USE

#### (A Comparison)

#### A. T. Roy

The compound diaminodiphenylsulphone was first synthesised in 1908 by Fromm and Wittmann. It was first used in 1937 in experimental streptococcal infection. In 1940 Feldman *et al* first used its proprietary preparation "Promin" in experimental tuberculosis with success. Other proprietary preparations such as diasone, sulphetrone, etc. by Abbott Laboratories and Burroughs Wellcome & Co., were promptly made to overcome the reported toxicity of the parent compound. Later in 1949 in spite of these preparations having been found effective in leprosy, their method of administration and high cost stood in the way to their use in a large number of persons suffering from leprosy in India, China and Africa. The parent compound diaminodiphenylsulphone, or DDS as it is generally termed, in spite of its greater toxicity was suggested for an extensive trial to find out its effect and minimum subtoxic effective dose.

#### ITS ORAL USE

With the idea stated above, Dr. Muir in Purulia selected 119 lepromatous cases of leprosy at different periods. At this stage, April 1949, the tablets were not manufactured; the DDS powder was given in the form of a 2.5% suspension (0.1 grm. in 4 c.c. or 10 mgs. in 4 c.c.) in sweetened acacia mucilage, and was squirted into the patients mouth from a syringe, but after a year, when the tablets were made by I.C.I., this method of administration was replaced by tablets. The dose was administered according to the tolerance of each individual. Little importance was attached to age and sex. Particular importance was attached to the estimation of hæmoglobin. While assessing the result after 2 years, it was found that the period of treatment in the 98 cases treated orally varied as follows.

Period of	treatment		No. of cases
24 I	nonths	 	 25
22	,,	 	 14
20	,,	 	 20
18	,,	 	 2
16	,,	 	 19
14		 	 7
I <b>2</b>	,,	 	 4
10	,,	 	 I
8	,,	 	 4
6	.,	 	 2

Dosage.—The usual dose of the suspension by oral route was 2 c.c. to 8 c.c. (50 mgs. to 200 mgs.) daily, 6 days in a week, and of the tablets  $\frac{1}{2}$  to 3 tablets (50 to 300 mgs.) daily, 6 days in a week. The dose was regulated by the reaction and percentage of hæmoglobin. Sulphone was discontinued when the Hb. was below 50%. Tests were done by Sahli's hæmoglobinometer.

The assessment of the results of treatment was made by examining 5 skin smears from the most infected part of the body and finding out the average points for 5 smears; giving 4 points to the smears of highest bacillary concentration, I to the lowest concen-

#### DIAMINODIPHENYLSULPHONE IN LEPROSY

tration and 3 or 2 to the findings between these extremes. Almost negative has been used for those smears which had only a few bacilli in all the 5 smears.

#### TABLE NO. 1 ORAL TREATMENT

The following result was observed in 98 cases after expiry of 2 years.

Result	No	of cases	Te	Total DDS given in grms. Average	Period of treatment in months Average
Negative		2	2	45.8	21.5
Almost negative		5	5. I	63.5	18.5
75% less bacilli		10	10.2	79.6	17.8
50% less bacilli		14	14.2	66. I	10.0
Slightly improve	d (les	s			
bacilli, below	50%)	43	43.8	45.9	17.8
Stationary		14	14.2	39.5	15.9
Worse		10	10.2	58.9	18.6

#### ITS PARENTERAL USE

Cochrane<sup>(1)</sup> in 1947 started injecting 15% suspension of DDS in arachis oil intradermally. Later finding the drug concentrated in the skin, he preferred the subcutaneous injections. He reported very favourable results from the subcutaneous injections of 25% suspension of DDS in groundnut oil, and used 2.5 grm. per week per patient. This experiment was taken up by Molesworth and Narayanswami in Malaya<sup>(2)</sup>. They used 20% DDS suspension in purified deodorised neutral cocoanut oil. Injecting the suspension subcutaneously I grm. per week per patient, their findings on 100 cases after I year's treatment were as follows:-Clinically, improved 96 and Stationary 4. Bacteriologically, improved 27, Stationary 64 and Worse 9.

On injecting 2 c.c. of 20% suspension of DDS (400 mgm.) first in hydnocarpus oil and then in cocoanut oil, the following results were found by us, in 140 lepromatous cases, after 1 year's treatment.

#### TABLE NO. 2 PARENTERAL TREATMENT

#### Showing the status after 1 years' treatment with DDS of 140 lepromatous cases.

Result	N	n. of cases	90	Total DDS given (in grms)	Period of treatment in months
Negative		Nil			
Almost negative		12	8.5	18.42	12
75% less bacilli		27	13.2	19.90	12

50% less bacilli Slightly improved (1	. 18 ess	12.8	19.40	12
bacilli below 50%)	47	33.5	18.50	12
Stationary	<b>2</b> 0	14.3	19.40	12
Worse	16	11.4	20.75	12

#### TABLE NO. 3

TABLE N	NO.	1 AND	TABLE	No.	2	COMPARED
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	Oral DDS.	Parenteral DDS.
	98 cases	140 cases
Improved average	74 or 75%	104 or 74.2%
Average time per case	17.1 months	12 months
Average grm. per case	57 grms.	19.38 grms.
Stationary	14.2%	14.3%
Worse	10.2%	11.4%

Comparing results in Table No. 1 and Table No. 2, it will be found that the negative cases mentioned in Table 1 were very early cases of low bacteriological index, so much stress cannot be put on this finding. The main difference is in the period of treatment and in the quantity of DDS used. With the suspension, the same result has been achieved as that with the sulphone tablets but in half the time. Very little difference can be noticed in the numbers classed '' stationary '' and '' worse ''.

Conclusion.—If the trouble of injecting the suspension is not taken into consideration, there is a real advantage in using the suspension of DDS parenterally. Here both the amount of the drug and the period of treatment are lessened. Expense too is thus reduced.

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## A CASE OF LEPROSY IN A SEVEN MONTHS OLD CHILD John A. Dreisbach, m.d.

The incubation period of leprosy is usually stated as being from 3-5 years up to 10-15 years, or at times even longer. Workers with experience in highly endemic areas, however, occasionally see cases under three years of age with clinical leprosy. The youngest case I have noted in the literature is that of an eighteen months old child.

In January, 1951, a Hausa family of five presented themselves for examination and admission at the Kano Leprosy Settlement of the Sudan Interior Mission. Careful clinical and laboratory examinations were carried out. The mother showed no clinical or laboratory evidence of leprosy. The father was a very far advanced case of lepromatous leprosy, showing heavy nodulations and infiltrative lesions. There was marked mucous membrane involvement with labial, buccal, lingual, pharyngeal, and laryngeal nodules and infiltrations. There was nasal septal ulceration and perforation. There were three sons, of ages five years, three years, and seven months. All three had early incipient lesions manifested as flat, hypopigmented macules.

We shall confine this report to the youngest child. This baby was quite young and according to the parents was seven months old. The infant did not appear to be any older than this. The history was that, due to his condition, the father was unable to work the family farm and do the other tasks ordinarily performed by the man. As a result, the wife had to assume the responsibility of these tasks, and turned the care of the children almost completely over to the husband. He had had almost constant contact with this child from birth.

The parents state that they first noted the skin lesions, which are described later, two months previously, when the child was five months old. They stated that the lesions were larger and more noticeable at the time of admission.

#### PHYSICAL EXAMINATION

The patient was a well developed, well nourished male infant of seven months. The physical examination by systems was essentially negative, with the exception of the spleen, which was palpable two fingers' breadth below the left costal margin, and the skin lesions to be described.

There were three lesions noted upon admission. There was

a large, flat, hypopigmented macular lesion of the mask area of the face. This was rather vague. A second lesion was noted on the posterior aspect of the left thigh, extending up on to the left buttock. This, likewise, was a flat, hypopigmented, macular lesion with vague margins. The third lesion was on the anterior aspect of the right thigh. It was a discreet, moderately hypopigmented, macular lesion with more definite margins and tending to slight central infiltrations.

The infant was too young to co-operate for a neurological examination. The lesion on the right thigh was subjected to the mecholyl test. There was a failure of response of the sweating mechanism in the lesion, whereas there was a normal active response in a control area of healthy skin.

The routine laboratory examinations were all within normal limits with the exception of the skin smears. A smear taken from the lesion on the right thigh revealed a few single Mycobacteria leprae. Smears taken from the other lesions and areas were all negative. The child was diagnosed as having macular leprosy incipient lesions of childhood. The child was admitted and treatment instituted.

The child was placed on sulphetrone, which was administered as a sterile 50% aqueous solution and given by subcutaneous injection. These injections were given twice weekly with a maximum weekly dose of one gram. The child has tolerated this treatment very well. There has been a mild anaemia throughout the period of treatment, but never marked enough to warrant discontinuing treatment.

At the end of the first year the child had an episode that probably was evidence of mild drug toxicity. It was manifested as objective pruritus. There were no other manifestitations. The child was given a rest of one month, after which treatment was started again and has continued uninterruptedly to the present.

By the end of the fifth month of treatment the lesions on the face and right thigh were completely repigmented. The lesion on the left thigh persisted for over a year. At this time, after 28 months of treatment, there are no clinical manifestations of activity of the disease. We plan to discharge the patient after 36 months of treatment if the disease is still clinically arrested.

With the exception of the admission skin smears, all of the smears have been negative for Mycobacteria leprae.

#### SUMMARY

A case is reported of a seven months old child with clinical leprosy. The clinical findings and response to sulphetrone treatment are discussed.

## AN IMPROVED HISTOLOGICAL METHOD FOR EXAMINATION OF CUTANEOUS NERVES IN LEPROSY\*

M. BALASUBRAHMANYAN, A. PAUL JAYARAJ, and H. H. GASS.

The study of the changes in cutaneous nerves in leprosy was undertaken by us during the course of the last two years at this hospital. It was necessary to devise and perfect the histological methods, so that consistent results could be obtained and conclusions drawn. Davonport's method, Bodian's protargol method and the Bielchowsky's technique were tried for the demonstration of axons. None of these original methods gave entirely satisfactory results in our hands. The following silver impregnation technique is a modification of the previously well known techniques and has given uniformly consistent results. The study of the myelin sheath of the nerves was also undertaken and a method for the simultaneous demonstration of acid fast bacilli and myelin on the same section has been devised. This has proved to be a valuable technique to study the exact location of the bacılli. The object of our recording these techniques below is to enable, if possible, other workers in this field to undertake the study of the nerves in leprosy

#### TECHNIQUE

- Pieces of skin are taken and fixed immediately in 10% neutral formalin (neutralised with excess of calcium carbonate) for not less than 24 hours. It is important that the tissue is not crushed and the infiltration with the local anaesthetic does not distort the tissues.
- 2. Wash in several changes of water and cut frozen sections of 15-20 microns thickness.
- 3. Wash sections in three changes of distilled water.
- 4. Place in 60% alcohol containing a few drops of concentrated hydrochloric acid for half an hour. This step is important to produce a good contrast between collagen fibres and the axons.
- 5. Wash in 3 changes of distilled water.
- 6. Transfer to 20% silver nitrate in an amber coloured bottle for 20 to 30 minutes.



Fig. 1. Normal palmar skin showing Meiss- Fig. 2. Normal hair follicle showing network of fibres around.  $\times$  100.



Fig. 3. Fine nerve endings inside the epithe- Fig. 4. lium.  $\times_*$  100.

4. Lepromatous leprosy showing ballooning and swelling of axons inside inflammatory infiltrate.  $\times$  470.



- Fig. 5. Lepromatous leprosy myelin stain Fig. 6. showing ballooned up myelin sheath inside inflammatory infiltrate. × 470.
  - ig. 6. Same as above showing acid fast rods and granules inside the myelin sheath.  $\times$  900.

- Transfer sections without washing to ammoniacal silver solution for two minutes and keep moving the section in it to avoid precipitate.
- 8. Pass the section through three changes of developer with constant agitation. The time in the third change of developer is controlled by the desired intensity of brown colour imparted to the section.
- 9. Wash well in distilled water and place in 5% liquor ammonæ till the section becomes translucent.
- 10. Wash, dehydrate in alcohol, clear in xylol and mount in canada balsam.

#### **AMMONIACAL SILVER SOLUTION**

To 5 cc. of 20% silver nitrate add 5 drops of 40% sodium hydroxide. Dissolve the precipitate that is formed by adding liquor ammoniæ drop by drop. Make up to 50 c.c. with distilled water. For staining purposes take 2 cc. of this solution and add 5 drops of liquor ammoniæ. The amount of liquor ammoniæ added should be determined by trials till the desired depth of impregnation of the axons is obtained.

#### DEVELOPER

Prepare 10% formalin using tap water. The pH of this solution is adjusted to 7.6 to 7.8 with tenth molar citric acid and fifth molar disodium phosphate buffer. A precipitate will form and it does not interfere with the staining process. We have tried other buffers but failed to get the same results. Different pH levels were tried to develop the sections. It is possible to vary the intensity of the background stain and of the axons by altering the pH level. At pH 7.6 to 7.8 it is possible to produce an even impregnation of axons and the inflammatory infiltrate and Schwann's cells. Thus a detailed histological examination is possible.

Since the developer is made with tap water, the results of analysis of the water used in this laboratory is given below.

Total solids 90, total hardness 30, permanent hardness 10, temporary hardness 20, chlorine 20.8, parts per 100,000. Free ammonia trace, albuminoid ammonia 0.002, oxygen absorbed 0.022, nitrate 1.75 parts per 100,000. Nitrate, phosphate and iron nil. Sulphates marked. pH 7.2.

#### RESULTS

The axons are stained in different shades of brownish black. The background is stained yellow with the nuclei of cells light brown. (Fig. I to 4.)

#### Demonstration of Acid Fast bacilli and myelin

- Frozen sections prepared in the same way as for the demonstration of axons are washed in several changes of distilled water.
- 2. Stain sections in cold Ziehl Neelson's carbol fuchsin for 15 minutes.
- Treat section with 50% alcohol slightly acidified with I or 2 drops of concentrated hydrochloric acid for 2 minutes. This step is not meant to decolourise the section.
- 4. Mordant sections in 4% ferric alum for 5 minutes.
- 5. Transfer without washing to 1% alcoholic haematoxylin solution diluted 50 times with distilled water. Stain for 4 hours.
- 6. Wash in distilled water and decolourise in 4% ferric alum solution, controlling under the microscope till the desired contrast between bacilli and the myelin sheath is obtained.
- 7. Place in 50% alcohol containing 1% liquor ammoniæ for 2 minutes.
- 8. Wash in distilled water, dehydrate, clear and mount in canada balsam.

#### RESULTS

The bacilli stained red while the myelin sheath takes a black colour. (Fig. 5 and 6.)

#### Summary

- 1. An improved method of silver impregnation for demonstration of axons in the skin in leprosy is described.
- 2. A new method of staining for demonstating lepra bacilli inside the myelin sheath of nerves is described.

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### \*PLASTIC SURGERY IN THE REHABILITATION OF THE LEPROSY PATIENT

#### J. D. KANAKARAJ, M.B.B.S.

The principal cause of public horror towards leprosy appears to lie in its mutilations. If this fact is understood it is then easy to explain the paradoxical situation wherein one finds an early case of lepromatous leprosy with hardly discernible lesions but with a high bacteriological index and a wide range of infectivity being permitted to mingle in society freely, while another, a disease arrested and non-infective case with a certain number of residual mutilations, is harassed and hounded. The significance of this is felt when these patients are being returned to society in the final stage of their rehabilitation.

The advent of the sulphones and allied drugs has undoubtedly revolutionised the therapeutic outlook in this disease. We are now in a position to offer to the average patient a method of treatment by means of which the clinical lesions of the disease are to a certain degree abolished, his bacteriological index reduced to zero, and an opportunity afforded to him to retrieve himself from various dislocations resulting from the disease, and to return to and occupy his rightful place in society. It is in this process of recovery, physical, moral and economic that rehabilitation plays an important part.

In analysing the psychology of the leprosy patient one is confronted with the clear evidence of psychic trauma that is present in almost every case. Each individual believes that he or she has been the victim of a cruel fate, and, according to his or her own belief, a malignant disease has visited him or her: and he or she only sees in the dark future a separation from family and friends, unemployment and banishment from society as a result of these tensions. These alterations in behaviour patterns have produced the spectacle of a lonely and frustrated figure, more sinned against than sinning, and the patient loses his confidence, his faith in himself and his self-respect. To rescue the patient from this psychological abyss is yet another important function of rehabilitation.

<sup>\*</sup> A brief form of this paper without its scientific portions was read at a Conference of District Secretaries and Select Leprosy Workers under the auspices of the Hind Kusht Nivaran Sangh (Indian Leprosy Relief Association) at Madras on September 26th, 1952: and the clinical photographs were among others exhibited in the Scientific sections of the All India Surgeons' Conference, Vellore, December 30th, 31st, 1952 and January 1st, 1953 and at the All India Leprosy Confe ence at Puri, January 4th to 6th, 1953.

In my observations of the patients of the Government Lady Willingdon Leprosy Sanatorium over a period of twenty-one months, I found this factor of psychic trauma very much in evidence. In addition to this, psychic trauma appeared to be directly proportional to the degree of mutilation present in the patient. During this period, as many as three hundred patients were discharged from this sanatorium as "disease arrested" and it has been noticed that, while the relatively mutilation-free patient has been eager to go out and return to his home and to his occupation, the patient with a certain number of residual mutilations exhibits a hesitancy, sometimes amounting to reluctance, which cannot be missed. On closely questioning these patients I found them obsessed with doubts as to whether and how society would take them back. This led me to conclude that a situation was present where a final step in rehabilitation was necessary to rectify as far as possible, the disfigurements that were obstructing his return to society.

In analysing the disfigurements that exist in these patients I find they are anatomically distributed as follows. The ears are large and overgrown due to nodulation and supernodulation. The nose is deformed and distorted, and this may range from simple nodulation of the alæ nasi to frankly depressed bridges, and many intermediate types. Facial paralysis, ptosis of the eyelids, ectropion and leucomas complete the alterations in the physiognomy. Gynæ-comastia constitutes another grave disfigurement, with the additional disadvantage of the "reproach of effeminacy." Keloids may exist anywhere, and may be the result of trauma, ulceration or burns. Deformities of hand or foot complete the picture.

Work was undertaken at the Government Lady Willingdon Leprosy Sanatorium, Chingleput over a period of twenty-one months to apply various corrective procedures to some of the deformities listed above, with a view to finding out their feasibility in leprosy patients; at the same time was kept in mind the underlying motive of rehabilitation.

The patients of the Government Lady Willingdon Leprosy Sanatorium fall into two broad groups: (I) a small static group which comprises those patients who are far advanced in their disease and who are blind and crippled, and in whom the question of rehabilitation does not arise, and also others who, being unsuitable for treatment with the new drugs, have been restored by hydnocarpus therapy, in whom the period of treatment is thus prolonged and the prospects of "arrest" and rehabilitation greatly reduced. (2) A large dynamic group which consists of the majority of patients who are either of the early lepromatous or moderately advanced lepromatous types. (No non-lepromatous cases are admitted in the sanatorium, as the institution is primarily meant for the segregation of infective cases). It is among these patients that rehabilitation programmes are intensively applied, as under the present day therapeutic regime with sulphones many of them are discharged. It was to this group that rehabilitative plastic surgery was applied over a period of twenty-one months, and the deformities or mutilations that received attention were only those that occur commonly among them, namely, gynæcomastia, deformed noses and unsightly ears. These are dealt with individually below. The selection of cases was always made from a rehabilitative angle, that is, the patient had to be clinically arrested or at least his clinical lesions controlled under adequate sulphone therapy: his bacteriological index had to be zero or near zero : and finally the patient had to be suitable for the particular plastic procedure contemplated.

#### Gynæcomastia

Webster recognised three distinct pathological types in this condition. In type I there is periductal connective tissue hypertrophy alone, and the gland is felt as a firm discrete nodule under the nipple. In type II there is an additional hypertrophy of adipose tissue, and the gland is less palpable. In type III the adipose tissue alone hypertrophies and the gland cannot be felt at all. The essential features of Webster's operation are (a) a semi-circular intraareolar incision, (2) a sub-areolar dissection of the breast, (3) delivery through wound in single or multiple pieces, (4) hæmostasis and (5) closure. In the second step, viz., dissection of the breast, Webster varies his technique with the type of tumour he is dealing with. In the type I group of cases where the mass of enlarged ducts and periductal tissue alone comprises the tumour, the dissection is along the surface of the gland entirely. In the intermediate type, the amount of fat within the mass is slight or considerable. When the latter condition is met with, the dissection is along the gland superficially, but as this plane cannot be maintained at the periphery and sometimes on the undersurface, a certain amount of hypertrophied fat is also excised by him. When the mass is so large that no residual fat has been left over the pectoralis fascia, there is a possibility of the nipple becoming adherent to the pectoral fascia. To prevent this, Webster performs a repair wherein he closes in a slight amount of fat under the nipple. In type III he advocates a cone-shaped resection of the breast to reduce its prominence, and performs a similar repair if necessary.

In leprosy the pathological nature of the gland appears to be a hypertrophy of breast tissue alone. To the naked eye the breasts excised by me were white, firm and well defined. Microscopic sections would have revealed their true nature but the necessary facilities were not available. There was no apparent increase in fat, and the subcutaneous fat was in direct proportion to the general adiposity of the patient.

The operative procedure adopted by me in these cases is based on a consideration of the anatomy of the part. It is similar to the procedure adopted by Webster for his Group I cases to which gynæcomastia of leprosy appears to belong, except for one or two minor details which will be mentioned later.

In considering the anatomy of the breast, it is seen as a hemispherical object with its base resting on loose areolar tissue and attached to it by means of the ligaments of Astley-Cooper. On its curved surfaces it is similarly attached to the skin by ligamentous tissue which traverse the subcutaneous fat. Taking these anatomical factors into consideration, the resection of the gland is performed along a plane close to the gland (see diagram). This " white line " constitutes a practically avascular plane, and a resection along this simplifies the procedure considerably.

The actual operation is done as follows: The assistant stretches the areola and the surrounding skin. A semi-circular incision is placed a fraction  $(\frac{1}{2})$  within the areola, and measures not more than an inch or an inch and a half at the most. It is most conveniently placed inferior to the nipple, but again can be situated anywhere on the circumference of the areola. The main difficulty is that the operative field is barely a square inch, and much of the resection is literally done through a hole, but with good vertical traction of the gland by means of tissue forceps, the plane of resection is elevated to the surface of the skin, while skin retraction widens the operative field much more than expected.

After making the incision, the plane of resection is sought for, The gland is identified and is freed a little from the skin and subcutaneous tissues. A pair of blunt scissors is then introduced along this plane and the blades opened out in all directions. By means of this procedure, the ligaments attaching the gland to the skin are torn and the gland is freed from its cutaneous attachments and its mobility as a consequence increased. The dissection is then commenced and progresses radially downwards, outwards and inwards in the first instance. Blunt dissection most often suffices except in rare instances where there has been an old peri-mastitis, or where Astley-Cooper's ligaments are dense and hypertrophic. As the gland is dissected and mobilised, it is delivered through the wound in order to keep the field clear for further resection. After the gland has been thus freed from its attachments to the skin on three sides, the

#### PLASTIC SURGERY IN LEPROSY

base is reached, which is then readily raised by blunt dissection from the underlying loose areolar tissue. The dissection is now directed upwards, where once again gland connected with skin is met with, and the dissection is proceeded with as before towards the areola till the junction of the skin with areola is reached. At the upper and outer quadrant some difficulty may be experienced, by virtue of the axillary tail. At this stage the whole gland lies outside the wound, with its apex connected to the areola and the nipple. The gland is then excised, leaving a button of gland tissue under the nipple. The object of this button is to prevent the nipple from puckering and retracting inwards. I have differed from Webster in this respect in leaving a larger amount of gland tissue, as I feel that even the slightest puckering would vitiate the cosmetic result. The wound is then primarily closed with close, interrupted cotton sutures, and a firm dressing applied. No drainage is instituted although the condition may theoretically warrant it. The wound heals by first intention, and the resultant scar is hardly visible, being camouflaged in the pigmented areola.

The important points to be observed in this operation are:

(I) to aim at removing the gland, the whole gland and nothing but the gland. As a result of this, the entire subcutaneous fat is preserved. The benefit of this is realised from the cosmetic angle. It is the subcutaneous fat that lends the normal contour of the chest, and any removal of it results in a "caving in " effect which is disastrous cosmetically to the patient, for where he had a convexity in the shape of the gland, he now would have a concavity, Also an additional advantage is this. The large area of skin involved depends for its nutrition and blood supply on the subcutaneous fat; hence its careful preservation prevents sloughing and gangrene of skin or nipple, a finding recorded in one of Webster's cases.

(2) to maintain the dissection of the gland along the "white line". By doing so, a practically avascular resection is achieved. Bleeding is reduced to a minimum. The advantage is this: the operation is by itself an irksome procedure, as separating the gland subcutaneously, mobilising it, and delivering it through the extremely small wound is a trying process, and calls for some manual dexterity and a good deal of patience. If in addition to this, one has to peer through a small hole and attempt to locate, catch and ligate bleeding points, the whole procedure becomes an unduly taxing affair. In the "white resection" there is no spurting but a mere oozing. Vigorous mopping clears the field and prevents difficulty in continuing the dissection. In no case of my series was a single ligature applied. A sucker would be most helpful in clearing the field and preserving good vision, although I had not the services of one.

The obvious disadvantage of this procedure is the possible formation of a hæmatoma, especially in view of the fact that a dead space is left behind with raw areas on all sides. Sometimes there is a fair amount of oozing, and a hæmatoma should therefore always be expected, though a firm bandage usually suffices as a preventive. Actually out of the series done by me, two developed a hæmatoma, serving to illustrate the point. The first case had to be aspirated once, and 10 cc. of bloody fluid was withdrawn; in the other case aspiration was done twice and 40 cc. of similar fluid removed. The point of interest was that the hæmatomas appeared only on the 5th day after operation. I am inclined to believe that a secondary factor operated in these cases and it is most probably this. Both the cases were on the right side in righthanded persons, and as the patients were more or less semi-ambulant after the operation, it was presumed that activity associated with their right hands encouraged some late oozing, and also disturbed the firmness of the bandage. As a result, a further precaution was added by immobilizing the corresponding arm by means of a cuff and collar. No further hæmatomas have been noted. In any case, daily opening of the dressing and looking for a hæmatoma should be done. The possibility of hæmatoma formation should not, however, deter one from employing this operation, as it is easily relieved by aspiration and can be controlled by adequate chemotherapy.

Gynæcomastia constitutes a problem in leprosy. It is seen in a small percentage of cases of lepromatous leprosy. Its exact pathology is yet unknown and attempts to treat it medically have failed. Even under sulphone therapy it has been noticed over a period of five years that there is no regression. Surgical removal constitutes the most satisfactory method of treatment. In the surgical management of this condition in the healthy, there has been a gradual evolution of a cosmetic approach with Webster's technique as a culmination of this. Webster in 1946 was the first to advocate an intra-areolar approach, and in doing this he offered a practically scar-less operation. In a series of 37 breasts done by him over a period of 12 years his results were uniformly excellent.

This technique was tried by me on patients of the Govt. Lady Willingdon Leprosy Sanatorium in the course of this work and in a series of 19 breasts over a period of 21 months I have obtained equally good results. I would strongly advocate the



Case No. 1. Before operation.

Case No. 1. After operation.



Case No. 2. Before operation.

Case No. 2. After operation.



Case No. 3. Before operation.

Case No. 3. After operation,

adoption of this technique in all leprosaria and hospitals where surgical excision in these patients is carried out.

Two specimen cases and a contrast case are presented below:-

**Case No. 1.** V. aged 20—moderately advanced leproma—duration of leprosy 3 years—gynæcomastia left side, duration 2 years—has spermatorrhea on and off—on examination the left breast enlarged to the size of a lactating breast—no swelling or tenderness of testes or cords. Under local anaesthesia the gland was excised using the above technique. There was no post-operative complication. Sutures were removed on the seventh day and the cosmetic result as seen from the clinical photograph was very good. The point of interest was that the gland was removed in one single piece.

**Case No. 2.** B. aged 30 years—moderately advanced leproma duration of leprosy 15 years, duration of gynæcomastia 2 years—had frequent attacks of spermatorrhea before onset of breast swellings. The gland was similarly excised as above. Result good. The case is mentioned as it is a small enlargement as opposed to case No. 1. In such cases the technique is easy to apply and the operating time is not longer than half an hour.

**Case No. 3.** This patient had a bilateral gynæcomastia four years ago for which he was operated on 24-8-48 and 11-9-48. Gaillard Thomas method was applied. In 1952 the patient presented himself with dense keloidal formation of his scars (see clinical photograph). In his case record there is no mention of postoperative sepsis or lepra-reactions to account for his keloids. Such a development produces a worse disfigurement than the condition itself. In June 1952 his keloids were excised and plastic repair of his chest wall performed. The result was very good. This case is mentioned to demonstrate a possible sequel when an extra-areolar route has been employed. There is no possibility of keloid formation in the intra-areolar operations.



The incision has been made, the gland identified by its white surface, and is dissected upwards through the wound from overlying skin and subcutaneous tissue.



The dissection adhering strictly to the white line proceeds radially inwards, outwards and downwards. This frees the outer and inner lower quadrants.



STAGE III The base is now reached which is separated from underlying muscle and alveolar tissue.



Here the entire gland lies outside the wound. The gland is then amputated, leaving a button. Wound closed, firm bandage.

Instruments required: Knife, dissection forceps, a pair of skin retractors, two pairs of Kocher's forceps, one pair scissors, straight with blunt points  $(5\frac{1}{2}'')$ , Mayo's needle holder, curved cutting needle, cotton sutures, swabs.

#### The Ear

In lepromatous leprosy the ear is thickened and enlarged, and this may be due to diffuse infiltration or to nodulation and super nodulation. The effect of this is to give a thick and coarse ear to the patient which is both ugly and unsightly. Under sulphone therapy the nodules regress and the infiltration clears up, but the tissues do not decrease in size though they may shrink or become loose and pendulous, particularly the lobes. When the nodules have ulcerated, marginal defects result, but this is quite rare under sulphone therapy. This constitutes a deformity not only by virtue of its physical characteristics, but also because it is a common stigma associated with the disease, known to and easily recognised by the laity.

In the past, surgical excision of the redundant tissues was practised under the name of "trimming." The procedure has been in most cases simply to apply the blades of curved scissors, and to seal the wound with Friars balsam. The cosmetic results of this were not always satisfactory. It is felt, however, that the time has come to raise this procedure to the level of the fine art of plastic surgery, particularly as under sulphone therapy many patients are being discharged to return to society. Keeping this in view, a technique contemplated to reconstruct the ear in such a manner as to restore the size and shape of the ear to normality, without revealing the evidence of surgery, was developed and practised on these patients.

The following is the technique: Two parallel incisions are made, one anteriorly and the other posteriorly on the margin of the ear including the lobe, the shape according to that which is required. The posterior incision is  $\frac{1}{8}$ " more medial than the anterior incision. This is to hide the final scar which then becomes displaced posteriorly. The tissues between these two incisions are excised in such a manner that the anterior and posterior edges slope inwards. Occasionally some cartilage may also have to be excised, everything depending on the size and shape of the ear which is desired. There is some bleeding, but usually it is not necessary to ligate any bleeding points. The two edges are then neatly opposed and sutured with fine cotton as close as possible. The " bites " should be small and as many as 40 sutures may be required for each ear. If these precautions are taken the result is very good, the ear looks quite normal and the scar-line is so thin that it is hardly seen. Two other factors must be borne in mind. One concerns symmetry of both ears. If one is not confident of judging symmetry by visual judgment alone, an outline of the ear that has been already done may be taken on a piece of tin or any other suitable sterilisable material and used for the other ear. This was not done in our series and I find that visual judgment is quite satisfactory. Another point is that it is a sound rule to do the difficult or more deformed ear first. This renders the second operation, particularly with regard to symmetry, very easy. Also a precaution to be observed is that in re-shaping the lobe, too much tissue should not be taken off, as this renders the apex of the ear prominent and gives it the appearance of " rabbit ears." A specimen case is presented.

**Case** No. 4. G. age—14 years—moderate leproma—Bacteriological index on admission 4.12 in October 1950—October 1952 Bact. Index 0.3 after continuous therapy with oral diamino-diphenylsulphone. His ears were heavily nodulated and looked unsightly. He presented himself for operation as he complained of harassment during his annual visit to his village on leave from the sanatorium. Further he alleged that he had to walk ten miles to his village from the railway station as the buses refused to take him on account of his appearance. Consequently his ears were repaired using the above technique. The result was very good and his subsequent excursions into society were uneventful. The patient awaits discharge and looks forward to return to work in the fields as he comes from an agricultural community.

#### THE NOSE

The following basic types are recognised in the alterations of the nose in lepromatous leprosy, depending on the stage and degree of the disease in which it is arrested. In type I there is a nodulation of the alæ nasi which produces changes in the shape and size of the nostrils. In type II where depression of the nose is the characteristic feature, the pathological changes have been more severe. This depression can be anatomically subdivided into (1) superior (2) intermediate, and (3) inferior sub-types. In the superior type of depression, the bridge of the nose is irretrievably lost as extensive intra-nasal ulceration ultimately leads to erosion and destruction of the nasal bone. This condition is most likely the result of secondary infection particularly with maggots causing an osteomyletis of the bone, which then sequestrates, and these are discharged along with the nasal secretions. In the intermediate type the septum of the nose has been eroded as a result of ulcerations, and the nose sinks over the corresponding area. When this occurs in the middle, the sinking in of the centre of the nose causes an approximation of the bridge and the tip of the nose, which results in the tip becoming unduly tilted. In the inferior type of depression, the lower part of the septum becomes defective with the result that the

tip collapses giving rise to a flat nose. Further the intrinsic cartilage of the alæ nasi may become eroded and replaced by fibrous tissue, which causes puckering and flattening of the nostrils.

It is necessary to recognise the above types, as each type calls for a different technique and approach in dealing with the condition. In type I it suffices to excise the nodules and pare down the tissues with due consideration for symmetry and contour of the nostrils. One case (case No. 5) is presented below.

In type II, superior depression where the bridge of the nose is lacking, bone-grafting is the operation of choice. A case in which this was done is presented below (case No. 6). The technique was to remove a graft from the tibia and transplant it to the nose. The tibia was chosen as it is easily accessible and serves the purpose well. Further, the anterior border of the tibia gives just the required shape (boat-shaped) to the graft. A median incision is then made over the nose and a bed prepared for the graft. The graft is then placed in position and sutured over. As the nose is an immobile part, it was felt that internal fixation was not necessary and this was achieved by adhesive strapping to give external support. In the one case, clinically and radiologically examined, the graft had taken.

In type II, intermediate and inferior type of depressions, cartilage grafting suffices and gives satisfactory results both early and late. The graft is taken from the ear, and the site is the posterio-superior angle of the ear where the natural shape of the cartilage is such that a boat-shaped piece of cartilage is easily secured. An incision about an inch long is placed vertically at this angle on the posterior aspect of the ear, and the required piece of cartilage excised. The wound is then closed, leaving the defect in the cartilage as it is, as no untoward effect results from this. The cartilage is then transferred to the required site according to the deformity. Where the alæ nasi are sunk and distorted, flat, oblong pieces of cartilage are required, and these have to be taken from the posterior aspect of the pinna of the ear. In general it must be remembered that postleprotic tissue is very friable and " crumbly ", and sutures often cut through. For this purpose, fine instruments and suitable suture material are required. We used cotton for all our cases, and we find it suits the purpose well.

**Case No. 5.** G.S.—aged 12 years—moderate leproma—Bacteriological index on admission on 1-11-51 was 4.51—Under sulphone therapy steady and gradual improvement, and after a year's treatment B.I. was reduced to 0.61. There was nodulation of his alæ nasi which were unsightly—had no other deformities. In view of his steady improvement, on 29-4-52 a cosmetic operation was performed as described above. The result was very good.

**Case No. 6.** P.—aged 23 years—moderate leproma—B.I. on admission on 8-3-49 was 3.12. Had been on intensive sulphone therapy from 11-5-49 and showed steady improvement. In the early period of his disease (since 1936) patient had blocking of his nose, epistaxis and a foul discharge. He showed a deformed condition of the Type II intermediate as described above. There was approximation of the bridge of the nose with the tip so that the nose was shortened and the tip tilted. Under a local anaesthesia a cartilage grafting as described above was performed. Both early and late results were very satisfactory.

**Case No. 7.** W.—aged 29—date of admission 24-3-50—advanced leproma—relapsed slightly as had been previously in the institution for seven years from 1942 to 1949 and was discnarged as a "quiescent case." Was placed on hydnocarpus therapy at his own request. B.I. in October 1952 was 0.69. He had a frankly depressed bridge of nose. On 1.7.52 bone grafting of his nose as described above was performed. The result was far beyond expectations. The graft "took" and the patient's appearance is very much improved. The patient's outlook has also changed considerably with this and he is now eagerly awaiting his discharge to seek employment. An additional point of interest in this case was that the operation, including the taking of the graft, was performed under local anaesthesia only. There was no means of maesthetising the bone by this method and the taking of the graft caused no pain or discomfort to the patient, the only thing complained of being an abnormal vibration sense.

#### WORK DONE

During the course of this work which extended over a period of twenty-one months as many as 39 plastic operations were performed as follows:—

Webster's	operati	on fo	r gyna	ecomastia		 19
Simple ear	repair					 8
Simple nos	e repai	r				 2
Compound	nose i	epair	Cartil	age graft	ing	 6
			Bone	grafting		 I
Keloids						 2

A greater number of operations could not be performed for various reasons, although they were very much in demand among the patients. Also, in all cases done, the criteria of selection was strictly adhered to, and this factor naturally limited the number. All cases received careful pre-operative preparation. They were all performed under local anaesthesia. A generous quantity of penicillin was expended on these patients; all cases getting 200,000 units of the drug daily for five days from the day of the operation. In only one instance did infection supervene, and this was in a cartilage grafting of the nose, where the wound was infected and the cartilage graft extruded through the wound on the second day. In all other cases the results were very good and uncomplicated by infection. Many of the rules of plastic surgery were broken in the course of the work, as the cases were done in a common theatre where many septic operations were also performed, and the cases placed in a common ward under similar conditions. In the circumstances it is surprising that infection was not present more often. I owe this largely to the protective umbrella of penicillin.

#### CONCLUSIONS

As a result of this work and the observations made on the patients of the Govt. Lady Willingdon Leprosy Sanatorium over this period, the following conclusions are put forward for consideration:

(1) that a factor of psychic trauma is present in leprosy patients and this is induced by the character and nature of the disease and the effects it has had on them, particularly in their altered relationship to society.

(2) that the intensity of this psychic trauma is in direct proportion to the degree of mutilations present.

(3) that a situation is present where the final rehabilitation of the patient is prevented by his disfigurements.

(4) that plastic surgery can to a certain extent relieve this situation by removing or reducing these disfigurements and thus facilitate his re-entry into society.

In conclusion it must be admitted that the work done in this connection has been only of a preliminary nature, and the cases on which some observations have been made are not numerous, but this paper has been written in the hope that serious consideration will be given to this aspect in the treatment and rehabilitation of leprosy patients.

#### ACKNOWLEDGEMENTS

I wish to thank Dr. H. Paul, M.B.B.S., Medical Superintendent, Govt. L.W.L. Sanatorium for having afforded me the facilities for doing this work and for his encouragement: to Sri N. Ramakrishna Iyer, Welfare and Rehabilitation Officer for his collaboration and to my wife, Dr. (Mrs.) M. Kanakaraj, B.Sc., M.B.B.S., for her assistance in the theatre and wards.

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#### REVIEWS

Leprosy in India, Vol. 25, No. 1 (Jan. 1953).

In a letter Dr. Lowe strongly criticises an article in this journal of April 1952, in which Khanolkar and Rajalakshmi claim originality for the view that infection spreads up the peripheral nerves from the skin, a view held by most leprologists for many years. He points out that dissemination through the nerves is only one of the routes by which bacilli reach the skin, and that especially in lepromatous cases bacilli spread also through the blood vessels and lymphatics. He also criticises the finding of bacilli in and on the skin of healthy contacts, and the interpretation of these findings There are many possible fallacies connected with the ubiquitousness of acid-fast bacilli, such as their presence in tap water.

"Dr. Khanolkar views all cases of leprosy as infectious and apparently equally infectious. On the latter point his findings are at variance with those of dozens of research workers of international reputation. An isolated report, such as that of Khanolkar, does not carry conviction. It must be confirmed by others."

Dharmendra, S. N. Chatterji and N. Mukherji describe A Study of the Flat Hypopigmented Patches in Leprosy with special reference to their Classification. The indeterminate form is the most difficult to classify, that is where there have been white patches from the beginning, which are not residual. The study is based on 128 out of 148 cases in Calcutta, in which there were performed bacteriological examination, the lepromin test and histological examination. In the remaining 20 a histological examination was omitted. If the lepromin test is positive and the bacteriological examination negative, a benign course may be safely forecast, and it is suggested that the case may be classified as " non-lepromatous leprosy " with the sub-title of " macular variety " alongside of tuberculoid type. If the bacteriological examination is positive and the lepromin negative the disease almost always takes a malign course, and "macular variety" may be included under the lepromatous type. Only the remaining cases left after deducting these two varieties should be retained in the indeterminate group.

E. MUIR.

#### Leprosy in India, Vol. 25, No. 2 (Apr. 1953).

This number is devoted to the Fourth All-India Leprosy Workers' Conference, which was held in Puri in the end of 1952, under the auspices of the Indian Leprosy Prevention Society and its Orissa Branch. The Governor of Orissa pointed out in his

inaugural speech that one in every seventy persons in Orissa suffers from leprosy, and that some 170,000 persons in this State suffer from the disease, of which about 67,000 may be considered as infectious. It is also calculated that more than 15,000 children are infected with leprosy every year in India. "Segregation in village isolation centres is to be preferred to institutional segregation, firstly because the cost will be very much less, secondly because the patients will be within easy reach of their families and will not be oppressed by the sense of isolation and exile, thirdly because the village will become leprosy-conscious ". The Conference was presided over by Sri Devadas Gandhi, a son of the Mahatma. He emphasised that the leprosy problem demands the closest co-operation between official and non-official agencies, and that antileprosy work should be given a high priority in the national programme. He also said that the number of persons in India now calculated to be suffering from leprosy was 2 million, and that neglect could mean that in a few years the figure might go up to 3 million. Dr. Dharmendra, speaking of a report that leprosy might be made a cause of divorce in the projected Hindu Marriage Act, asked: "Why of all infectious diseases single out leprosy? This discriminative treatment is likely to have a baneful effect on the anti-leprosy work in the country. If it is permitted to take shape, most of what we have been doing during the past several years in our attempt to reorientate and rehabilitate the opinion of the public, so that they come to adopt a rational attitude towards the disease, will be undone." Several interesting papers were read and discussed, the subjects dealing with both medical and social aspects of leprosy. There were 190 Indian delegates and some 4 or 5 from outside India. The Indian Association of Leprologists took advantage of the occasion to hold its annual meetings. E. MUIR.

International Journal of Leprosy, Vol. 21, No. 1 (Jan.-Mar. 1953). The Classification of Leprosy with a Primary division into "Benign" and "Malign" Classes, by R. Chaussinand.

The writer pleads for a simplified classification which can be understood and used by leprosy specialist and non-specialist alike. He divides the disease into two large primary groups—Benign and Malign. The former includes the tuberculoid, indeterminate and borderline forms; and the latter the lepromatous. He justifies the inclusion of the indeterminate cases in the benign group as some are stable and some change into tuberculoid. He gives a warning that if the lepromin test is negative in untreated patients a malign development is to be feared. It is more difficult to understand his inclusion of the borderline cases in this group as he says the skin lesions are 100% positive and the lepromin reactions are negative. He holds that they are an evolution stage of major tuberculoid and frequently follow a reactive state. Histological examination shows the presence of both tuberculoid and lepromatous cell groupings. The secondary classification follows the usual lines.

Treatment of Leprosy with Thiosemicarbazone and DDS; A comparative series among Australian Aborigines, by A. H. Humphry.

Ten Australian aborigines who had not responded well to sulphetrone were given thiosemicarbazone for 12 months. At first they showed some improvement but later they mostly relapsed to their previous condition.

Twenty-eight new cases were divided into two groups of 14. Half were given Neustab and half DDS. The latter showed distinctly better results than the former. No satisfactory explanation could be given for these results.

#### Clinical Trial of Thiosemicarbazone, by R. S. Buker.

The object of this experiment was to find the most suitable drug for the treatment of villagers living under primitive conditions away from the central colony. Two groups of patients of about 60 in each, one in the central colony and one in a preventive village, were taken. Half of each group were given 75 mgm daily and the other half 150 mgm. All types of cases were treated and the experiment lasted 18 months. It was found that all patients except one benefited whether they had the smaller or large doses. As with DDS, no bacteriologically negative cases were obtained but fewer had leprosy reactions. Except that the cost was four times that of DDS it was considered an excellent drug for use in underdeveloped areas with large groups of patients.

The use of Haemagglutination reactions and the conditional haemolysis test in the serological diagnosis of Leprosy, by C. Gernez-Rieux, E. Montestruc and A. Tacquet.

The sera of 78 leprosy patients of various types free from active tuberculosis, were examined simultaneously by the Middlebrook-Dubos haemagglutination test and the conditioned haemolysis test, using with both tests sheep red cells sensitized with tuberculin or with polyoside St isolated from that tuberculin. The agglutination test gave a larger percentage of high dilution reactions with leprosy sera than with sera from cases of active tuberculosis, while the reverse was observed with the haemolysis test. It is held that these reactions may have some diagnostic value, for positive results were seen in 7 of the 13 cases whose diagnosis could not be confirmed bacteriologically. The Kahn Universal Serological Reaction in Leprosy, by Sister Hilary Ross and F. Gemar.

Kahn is of opinion that in lepromatous leprosy the serological pattern of the Universal reaction is distinctive and entirely different from the patterns obtained in either syphilis or yaws. The writers applied the universal serological reaction to the sera of 130 leprosy patients (20 tuberculoid and 110 lepromatous) in 1947 and repeated the test on 10 of the latter after 4 years and compared it with 20 healthy controls and 5 known cases of syphilis. They conclude that "From our results there is no indication of any distinctive serologic pattern in lepromatous leprosy. Although the test is timeconsuming, it is felt that serum reactors in leprosy are biologically significant, and that yearly checking of the universal serological test may be of some prognostic value. Our results though meagre, indicate that treatment can alter the type of the pattern in lepromatous leprosy."

La Microscopia fluorescente en leprologia, by M. A. G. Prendes, A. F. Carbonell, V. Pardo-Castello and A. C. Hernandez.

The writers describe in detail a method of staining leprosy slides by the fluorescence method with auramin O which they hold is far superior to the ordinary Ziehl-Neelson method. In a total of 100 cases they found this method gave positive results in 75% of cases compared with 30% with Z.N. stain. In 15 cases, only granules were found, but they say that these are characteristic and would not be confused with other things.

An attempt to confirm growth of Mycobacterium leprae murium on chorioallantoic membrane of live chicken embryos, by J. W. Millar.

The writer failed to confirm the report of R. Noel and Soeur Marie Suzanne that M. leprae murium multiplies on the chorioallantoic membrane of the developing chick embryo, or that following three passages on membranes the bacilli produced typical rat leprosy within 27 days after testicular inoculation. On the other hand he found that the bacilli suffered a marked loss of infectiveness during only four days on the allantoic membrane, and a continuous decline in the number of bacilli which can be recovered.

Chemotherapy of Murine Leprosy, by Y. T. Chang.

I. The Use of Mouse Leprosy as the chemotherapeutic test.

The first paper describes the method used of inoculating peritoneally young female mice with the Hawaian strain of rat leprosy. The internal organs revealed marked lepromatous growths by the 3rd and 4th months. The 3rd month was therefore chosen as the period for comparing the effect of various drugs against controls which had no treatment. The index of chemotherapeutic effectiveness (ICE) was calculated as follows:—

Total Leprosy Index of Control Group: Total Leprosy Index of the Treated Group.

The leprosy index was worked on a grading of the number and size of the lepromata in the various organs affected.

II. The effects of streptomycin, sulphones and isonicotinylhydrazines on mouse leprosy.

This second paper gives the results using the above technique. The isonicotinylhydrazines were found to be the most effective of these drugs in the suppression of the leprosy infection. Streptomycin was found to have a degree of activity similar to DDS. Diasone was the least active. Combined therapy with streptomycin and DDS showed an additive effect. The order of the antileprosy activity of these different drugs was as follows: Marsilid, Nydrazid, Streptomycin combined with DDS, DDS, Streptomycin, Diasone.

The Viability of Mycobacterium leprae murium in tissue stored with dry ice, by P. C. Eisman, S. G. Geftic and R. L. Mayer.

Lepromata aseptically removed from rats or mice were immersed in a quick freeze bath of dry ice and acetone and stored for intervals of from one to forty-two weeks (1-42) and then thawed at 5°C. and prepared as a 10% suspension and inoculated into rats or mice. All the frozen lepromatous tissues proved capable of inducing lepromata at the site of inoculation. No apparent loss of infectivity had occurred. G. O. TEICHMANN.

#### International Journal of Leprosy, Vol. 21, No. 2 (April-June 1953).

The Pan-American Classification of the Forms of Leprosy, by J. M. M. Fernandez.

In this article the writer seeks to interpret the Pan-American Classification of Leprosy and to answer criticisms especially of the use and interpretation of the word Indeterminate. He says that the fundamental feature adopted for the classification is the histological structure of the lesions, and the forms are identified and designated on that basis, although the clinical aspects of the lesions, the immunological reaction, and the bacteriological findings must be considered along with this. Leprosy starts with a simple inflammatory process, a lymphocytic infiltrate located in the skin and nerves, which is clinically manifested by macules or by areas of anaesthesia. This form of onset, undifferentiated or neutral, in which the organism has not yet defined its attitude towards the invasion of the leprosy bacillus, is the "Incaracteristica" or Indeterminate form of the Pan-American classification. The disease may remain in this condition; (hence its inclusion as a separate group) and regress temporarily or permanently, or evolve into one of the polar forms-tuberculoid or lepromatous. Histopathological examination may reveal an intermediate stage first described by Wade and called by him the Borderline ("Limitante") form which was not included in the original Pan-American classification. In it, both tuberculoid and lepromatous infiltrates are seen in the sections. He considers this a reactional phase. Once the process has reached its peak or maturity in the polar stage, it may regress spontaneously (exceptional) or under the influence of treatment (frequent). Thus is initiated a post-lepromatous or post-tuberculoid stage of regression, and this may go on until all signs of activity have disappeared; or else reactivity may start again and may take any of the previous forms. In short, experience shows that once the disease is started, no path of evolution is closed to it, although customarily it tends to follow determined courses.

In rural areas where histological examination is impossible, all macular or polyneuritic cases which cannot be definitely identified as L or T should be classified as Indeterminate. In the Pan-American classification the polyneuritic cases are placed as varieties of the three principal forms, and lepra reactions are classified according to the form in which they occur.

#### The Prevalence of Leprosy in the Cook Islands, by J. Numa.

This group of 15 small islands none of which is over 4 miles in diameter, is scattered over a large area of the South Pacific. They are divided into a northern and southern group. The total population is 15,079 of whom the majority is Polynesian. In the northern group, the people are closely related, and leprosy was introduced into the northernmost island by a returned emigré labourer in 1860. Since 1926, all known cases have been sent to the Makogai Central Hospital, Fiji. By 1951, 238 cases had been sent there, and a further 44 new cases were awaiting transport. Because of these transfers, leprosy had decreased in the northern islands, but there had been an increase in the southern group.

- In the northern group between 1926-38 there were 80 tuberculoid and 43 lepromatous cases.
- In the northern group between 1939-51 there were 50 tuberculoid and 1 lepromatous case.
- In the southern group between 1926-28 there were 10 tuberculoid and 7 lepromatous cases.
- In the southern group between 1939-51 there were 27 tuberculoid and 13 lepromatous cases.

Comparison of Diaminodiphenylsulphone and Thiosemicarbazone in the treatment of Lepromatous Leprosy, by F. Sagher and N. Brand.

In this report a comparison is made of the clinical and bacteriological results obtained in 60 cases of lepromatous leprosy treated as inpatients in a hospital in Jerusalem with DDS or thiosemicarbazone. Their conclusions are that both drugs influence leprosy favourably but that thiosemicarbazone is somewhat more efficacious than DDS. This is not very clear from the tables given, but this is probably because 18 so-called inactive cases are included, 9 of which were bacillus negative before treatment started. They remained negative during treatment and according to the writers would probably have been classed as Indeterminate by other leprologists, as they were lepromin negative.

The Pilomotor response to intradermally injected Nicotine: An aid in excluding the diagnosis of leprosy, by H. L. Arnold.

The injection of Nicotine Picrate I in IOO,000 intradermally gives a normal pilomotor (gooseflesh) reaction in the region of the macules of vitiligo, seborrhoeic dermatitis, lichen planus and other skin conditions, but fails to do so in or near a leprous lesion. On the face, however, care must be taken, as in non-leprous lesions the reaction is frequently negative. The aqueous solution of nicotine picrate is stable, and the test is easy and is of greater value than the histamine test. A positive response is strongly indicative that the lesion is not leprosy.

The effect of BCG in lepromatous cases of Leprosy, by John Lowe and F. McNulty.

This paper is a continuation of the study on BCG vaccination reported in *Lep. Rev.* 24 (1953) 104 lepromatous cases were given a single intradermal injection of 0.1gm BCG and in 12 the lepromin test was converted from negative to positive. The patients were having treatment and most of them were still bacteriologically positive. There is no proof that the lepromin reaction becomes positive more easily in those cases that have become bacillus negative. The study indicates that the change is often temporary and does not improve prognosis.

In an addendum the writers say that later retesting with lepromin showed quite a high conversion to positive and they are endeavouring to keep them positive by repeated oral administration of BCG, for repeated injections the Koch phenomenon would be serious. The possibility of reducing the danger of relapse in discharged patients and of the transformation of undeterminate cases with a previously negative lepromin reaction is considered.

G. O. TEICHMANN.