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LEPROSY REVIEW

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PRINCIPAL CONTENTS

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LEPROSY REVIEW

VOLUME XXXIX NO. 1 JANUARY 1968

Contents

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We have received the Medical Bulletin, MB-10, dated May 25, 1965, of the Department of Medicine & Surgery, Veterans Administration, Washington, D.C. 20420, U.S.A. The Editor of the Bulletin writes as follows: -

'It is a testimonial to Dr. James A. Doull, the author of the first edition of the Bulletin on Leprosy, dated March 15, 1954, that that bulletin has sustained a high demand for copies in the intervening 11 years since its publication. After a distinguished career, at Brompton Hospital in London, John Hopkins University, Western Reserve University, and with the U.S. Public Health Service, in 1948 Dr. Doull assumed the position of Medical Director of the Leonard Wood Memorial (American Leprosy Foundation). Under his guidance the first scientific method for evaluating the chemotherapy of leprosy in man was evolved, to which reference is made in this revision. The authors of the revision of Dr. Doull's original article, Drs. Guinto and Binford, were long time associates of Dr. Doull's, and it is believed that this revision will be as authoritative, and in as much demand as was the original bulletin. This second bulletin on Leprosy, therefore, may serve as an additional fitting tribute to the memory of Dr. Doull who died on April 6, 1963.'

We are pleased to see this tribute to Dr. Doull who always was a faithful friend of leprosy workers throughout the world and himself did many things to help them. His like has not been seen since. The papers in this issue of 9-*%!=+ÎB-5 -?Îare such as would have delighted Dr. Doull who had a heart with a big room in it for all who worked away at the problems of the leprosy patient. Also, he especially liked all who made experimental trials.

We have received the following message from Dr. S. G. Browne, Medical Secretary of LEPRA: -

As from 27 November, 1967, the Headquarters of LEPRA (The British Leprosy Relief Association) will be transferred from the present offices at 8 Portman Street, London, W.1, to

50 Fitzroy Street, London, W.1.

The new Headquarters, in which the office of the Medical Secretary of LEPRA will be situated, are conveniently near the main railway terminals for trains going north from London, and are also within a short distance of Great Portland Street and Warren Street Underground stations.

The Editorial Office for *Leprosy Review* will continue to be located for the time being at

6 Hillcrest Avenue, Pinner, Middlesex.

We send our greetings to the General Secretary of LEPRA and his Staff and our best wishes for the campaign against leprosy waged by the Association.

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LONDON — 16th-21st SEPTEMBER

Plans are going ahead for the Congress.

The definitive programme of the Congress is in course of preparation. A copy will be sent in due course to all members of the International Leprosy Association and to non-members who have indicated their interest.

Despite initial uncertainty, it has been found possible to provide simultaneous translation for the main scientifc sessions at the Congress in the following languages: English, French, Portuguese and Spanish.

Plans are far advanced for a Ladies' Social Programme and for Receptions, etc., for the participants and their wives.

Since devaluation of the £ may make a stay in Britain even more attractive to overseas visitors, it is hoped that the attendance at the Congress will break new records.

Lep. Rev. (1968) **39**, 1, 3-7

B663 in Lepromatous Leprosy. Effect in Erythema Nodosum Leprosum*

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B663 is a riminophenazine derivative. The antimycobacterial activity of this class of drugs was reported in 1948[1]. In 1952 a derivative of these compounds, B283, was used in the treatment of leprosy[2]. More recently B663 has been used in the treatment of murine leprosy[3 4], mouse footpad infections with *Mycobacterium leprae*[5], and in several clinical trials in human leprosy[6 7 8 9 10 11 12 13 14 15 16].

Conclusions reached concerning the riminophenazines and B663 in particular include the following: (1) the drug is effective against a number of mycobacteria[1 17], including *Mycobacterium lepraemurium*[3 4] and *Mycobacterium leprae*[5 6 7 8 9 10 11 12 13 14 15 16], (2) the drug is apparently free of serious toxic side effects in both animals[3 18] and in humans[11 13 16]. In man and animals these compounds produce reddish skin pigmentation[2 3 6 11 13 16]. The effect of B663 on erythema nodosum leprosum (ENL) reactions in lepromatous leprosy has recently been a subject of controversy. Several studies have indicated that B663 is beneficial in ENL[9 12 13]. On the other hand, Pettitt[15] has recently claimed that B663 has no effect on ENL. The present communication deals with the effect of B663 on patients with ENL reactions at the U.S. Public Health Service Hospital, Carville, La.

METHODS

Six patients with active lepromatous leprosy associated with established erythema nodosum leprosum reactions, all requiring regular corticosteroid therapy, were selected for a trial of treatment with B663. Another group of 6 patients was selected by matching with the B663 group as nearly as possible for the factors of age, sex, race, classification of leprosy, bacteriological status, duration of leprosy, current anti-leprosy treatment, duration of ENL, and severity of ENL as measured by current steroid requirements. The second group was given regular anit-leprosy treatment with intramuscular Solapsone B.P. (Sulphetrone). The clinical data are summarized in Table 1.

The dosage of B663 employed was usually 100 mg. 3 times daily by mouth, although this varied somewhat, particularly early in the study. The dosage of Solapsone was usually 0.1 ml. of the 50% aqueous solution intramuscularly per week initially, and with the dose being raised at 2-week intervals by 0.1 to 0.2 ml. per week, when feasible, until a maximum dosage of 2.0 ml. per week was achieved. The average dosages of B663 and Solphetrone for each calendar month of the study are given in Table 2.

Each patient was seen from once daily to once weekly as long as ENL reactions were present, and corticosteroids were prescribed by one of the authors (R.C.H.) in the least dosage which would prevent (1) debilitating fever, (2) ulceration of ENL, (3) reactive neuritis producing anaesthesia of the palms, soles or cornea, and (4) reactive neuritis producing any motor weakness. The corticosteroid preparations used were oral prednisone U.S.P., injectable prednisolone sodium phosphate U.S.P. (Hydeltra-

* Presented before The USPHS Clinical Society and Commissioned Officers' Association Meeting, Atlanta, Ga., May 11, 1967.

TABLE 1

CLINICAL DATA AT THE BEGINNING OF TREATMENT

SOLAPSONE GROUP Patient	Age	Sex	Race	Class	Skin Scrapings BI*	Skin Scrapings MI	Dur. of Leprosy	Anti-leprosy** Rx in 3 mo. pre. Rx	Dur. of ENL	Dur. of Cont. Steroids	Av. daily Ster. req.for 3 mo. a Rx Pred.	Av. daily Ster. req.for 3 mo. a Rx ACTH
						%	yrs.		yrs.	mo.	mg.	u
S-1	46	M	N	BL/LL	4	1	23	None	1	14	16.6	50
S-2	27	M	W	LL	4	1	1	DDS 100 mg/wk	0.25	0	0	0
S-3	47	M	W	LL	4	1	6	None	6	3	3.8	0.9
S-4	37	M	As	BL/LL	4	1	5	DDS 5 mg/wk	1	3	9.4	1.7
S-5	37	F	W	LL	4	1	11	DDS 125 mg/wk	0.17	1	4.3	1.3
S-6	25	F	As	LL	3	1	12	DDS 50 mg/wk	2	18	19.0	2.2
Mean	36.5	2 F 4 M	2 As 3 W 1 N	2 BL/LL 4 LL	3.8	1%	9.7 yrs.		1.7 yrs.	6.5 mo.	8.9 mg.	9.4 u.
B663 GROUP Patient												
						%	yrs.		yrs.	mo.	mg.	u.
B-1	23	M	N	LL	3.3	10	6	DDS 2 mg/wk	4	13	57.8	15.0
B-2	36	F	W	BL/LL	4	1	12	DDS 8 mg/wk	2	39	5.0	22.8
B-3	53	M	W	LL	4	5	11	None	1	7	15.4	4.4
B-4	32	M	W	LL	3	2	1	Su 0.25 gm/wk So 0.008 ml/wk	1	2	3.7	1.3
B-5	51	M	W	BL/LL	4	10	30	Sm 1.0 gm/wk	26	88	11.3	9.7
B-6	29	M	As	LL	3.3	1	1	Su 0.008 gm/wk	1	11	12.2	1.1
Mean	35.7	1 F 5 M	1 As 4 W 1 N	2 BL/LL 4 LL	3.6	4.8%	10.2 yrs.		5.8 yrs.	26.7 mo.	17.6 mg.	9.1 u.

*4 = numerous = hundreds of acid-fast bacilli/oil immersion field
3 = moderate = 10 to 100 AFB/o.i.f.
2 = few = fewer than 10 AFB/o.i.f.
1 = rare = fewer than 10 AFB/entire smear
0 = none found = no AFB in 50 oil immersion fields

Su = Sulfadimethoxine (Madribon(R)—Roche)
So = Solapsone B.P. (Sulphetrone)
Sm = Streptomycin
DDS = diaminodiphenyl sulfone (Dapsone)

** None of anti-leprosy treatment regularly taken. Amounts shown are average.

TABLE 2

MEAN DOSAGES OF SOLAPSONE IN ML. OF 50% AQUEOUS SOLUTION PER WEEK AND B663 IN MG. PER DAY

SOLAPSONE GROUP Patient	MONTH* 0	+1	+2	+3	+4	+5	+6	+7	+8	+9
S-1	0.15	0.25	0.5	0.9	1.3	1.5	0.9	0.8	1.0	1.0
S-2	0.05	0.1	0.3	0.5	1.1	1.6	2.0	2.0	2.0	2.0
S-3	0.05	0.2	0.35	0.8	1.1	1.45	1.6	1.6	1.9	2.0
S-4	0.05	0.1	0.1	0.03	0.1	0.1	0.2	0.2	0.2	0.2
S-5	0.07	0.5	0.4	0.6	0.6	0.8	0.8	0.4	0.4	0.25
S-6	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.35	0.4	0.6
Mean	0.08	0.23	0.31	0.51	0.73	0.94	0.95	0.89	0.98	1.01
B663 GROUP Patient										
B-1	150	167	300	300	100	200	200	—	—	—
B-2	30	300	200	250	300	300	300	300	300	300
B-3	300	300	300	300	300	300	300	300	300	300
B-4	100	200	267	300	300	300	300	300	300	300
B-5	13	250	300	300	300	300	300	300	300	300
B-6	100	200	267	150	35	100	100	100	120	200
Mean	115	236	272	267	223	250	250	260	264	280

*Note: The 0 month indicates the calendar month in which the medication was begun; +1 indicates the first full calendar month of treatment, etc.

sol(R) Merck, Sharp & Dohme), aqueous corticotropin injection (Acthar(R) Armour), and repository corticotropin injection (H. P. Acthar Gel(R) Armour). Each dose of anti-leprosy medication, i.e., B663 and Solapsone, and each dose of the corticosteroids was dispensed by hospital nursing personnel and the medication taken either orally or by injection in the presence of the nurse on duty.

From the total amount given in each calendar month, a mean daily dose of each type corticosteroid preparation was calculated for each patient, for each calendar month, from 3 months before treatment, through 9 months

TABLE 3

MEAN DAILY STEROID REQUIREMENTS IN MG. OF PREDNISONE

SOLAPSONE GROUP Patient	MONTH*												
	—3	—2	—1		+1	+2	+3	+4	+5	+6	+7	+8	+9
S-1	19.9	44.0	60.5	43.0	49.5	40.0	37.5	36.0	56.7	79.3	56.9	20.5	30.5
S-2	0	0	0	6.5	17.3	9.0	7.3	9.8	11.8	12.4	9.5	9.9	11.2
S-3	0	3.8	8.8	41.2	43.9	47.6	57.8	58.7	68.7	76.0	64.6	70.0	68.6
S-4	3.9	20.1	7.0	10.3	18.5	26.9	29.2	27.2	28.0	49.2	41.4	39.0	28.6
S-5	1.6	4.7	8.7	9.9	10.0	10.0	10.0	10.0	10.0	11.8	16.2	15.0	20.0
S-6	16.2	15.0	29.1	29.5	31.3	39.7	43.5	40.3	40.1	43.3	39.5	40.4	32.7
Mean	6.9	14.6	19.0	23.4	28.4	28.9	30.9	30.3	35.9	45.3	38.0	32.5	31.9
Mean for 3 mo. interval		13.5				29.39			37.18			34.13	
B663 GROUP Patient													
B-1	56.7	62.7	76.5	60.9	43.4	18.5	14.2	5.7	0	0	—	—	—
B-2	20.2	15.1	14.0	14.1	20.4	26.8	17.7	7.9	5.0	10.0	9.3	7.8	2.8
B-3	11.2	25.8	15.8	22.4	21.4	14.1	21.6	22.4	17.9	19.6	14.6	14.7	15.9
B-4	0	4.4	8.7	21.8	28.0	29.7	2.2	0	0	0	0	0	0
B-5	18.6	18.8	11.0	10.5	11.5	13.5	14.8	17.0	20.0	20.8	21.0	21.4	20.4
B-6	3.7	6.5	28.0	44.0	16.8	1.8	0	0	0	0	0	0	0
Mean	18.4	22.2	25.6	29.0	23.5	17.5	11.8	8.8	7.2	8.4			
Mean for 3 mo. interval		22.09				17.58			8.13				

* The calendar month in relation to the month in which treatment was started; for example, 0 month refers to month in which treatment was started, H1 indicates first full calendar month after treatment was started, etc

after treatment was started. For the purpose of comparison it was arbitrarily considered that injectable prednisolone was equivalent, milligram for milligram, to prednisone tablets taken orally, and that 40 units of corticotropin, either aqueous or repository, was equivalent to 20 mg. of prednisone by mouth.

Mean daily steroid requirements in milligrams of oral prednisone were then calculated for each calendar month and vere used to indicate the severity of the ENL reaction in each patient at that particular time. Analysis of the data for statistical signifcance was done by means of the T-test for small samples".

RESULTS

The steroid requirements for each patient in relation to treatment are given in Table 3.

The severity of the ENL reactions progressivly decreased in the group treated with B663; and the ENL became progressively more severe in the Solapsone group during treatment.

In the three months before treatment was started, the Solapsone group required an average of 13.52 mg. of prednisone per day (or its equivalent), and the B663 group required an average of 22.09 mg. of prednisone. The B663 group initially, therefore, seemed to have more severe ENL than the Solapsone group. This is not statistically signifcant ($0.4 > p > 0.3$), however, and the Solapsone group can therefore be used as a control for the B663 group.

In the frst 3 full calendar months of treatment, the B663 group's steroid requirements fell to 17.58 mg. of prednisone per day while the Sola-sone group now required 29.39 mg. per day as an average.

In the second 3 months' period, i.e., from the fourth through the sixth months of treatment, the B663 group continued to improve and now required only 8.13 mg. of prednisone per day while the Solapsone group continued to have more severe ENL and now required an average of 37.18 mg. of prednisone per day. This dif erence is statistically signifcant ($0.01 > p > 0.001$).

The steroid requirements of the Solapsone group were signifcantly more by the fourth through sixth months of treatment than the >ame group's requirements before treatment .as started ($0.05 > p > 0.02$). The B663 group's average steroid requirements by the fourth

through sixth months of treatment were less than the same group's initial requirements, but this difference is not quite statistically significant ($0.10 > p > 0.05$).

DISCUSSION

It has been demonstrated that B663 is an effective drug in the treatment of human leprosy[7,12,13,14,16,23]. Although a recent report[11] in which a smaller dosage of the drug was used, concluded the contrary, B663 in the doses employed in the present study seems beneficial in established ENL reactions in lepromatous leprosy. It is definitely superior to the parenterally administered sulfone, Solapsone, in this respect. Several authors[20,21,22] feel that Solapsone is less likely to be associated with ENL reactions than the other sulfones. It therefore follows that B663 is less likely to be associated with ENL reactions than any of the sulfones, while at the same time exerting an anti-leprosy effect comparable to that of the sulfones.

The principal drawback of B663 at present appears to be the reddish-blue skin pigmentation it produces[11,13,16,23]. The present indications for the use of B663 at Carville are (1) sulfone-resistant leprosy patients, and (2) established ENL reactions requiring substantial doses of corticosteroids to control. In either of these indications the advantages of B663 over currently available treatment seem to outweigh any of the presently known disadvantages such as skin pigmentation.

SUMMARY

B663 was given to 6 patients with active lepromatous leprosy and established erythema nodosum leprosum reactions, and 6 similar patients received Solapsone. B663 was associated with significantly less severe ENL than Solapsone, and Solapsone resulted in more severe ENL than no regular anti-leprosy therapy at all. B663 seems to benefit established ENL reactions and is definitely superior to the sulfones in this respect.

ACKNOWLEDGEMENT

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C. L. CRAWFORD, M.B., CH.B. 7N.Z.¡, M.R.C.P., D.T.M. & H.
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In the course of a 14-month period in Northern Nigeria an opportunity was presented of examining the variety of neurological lesions in patients with leprosy.

Monrad-Krohn (1923) in a study of 63 leprosy patients concluded that the neurological lesion in leprosy was characteristic of a polyneuritis involving both sensory and motor functions. The involvement was thus distal with the sensory loss being 'glove and stocking' in distribution. Furthermore, only superfcial sensory modalities were afected; deep pressure, pressure pain and joint sense not being involved. KinnieI Wilson (1954) confrmed these fndings but found some impairment of vibration sense in 3 of his own patients. Cochrane (1964) mentions the occurrence of 'glove and stocking' anaesthesia, but only in primary neuritic leprosy, i.e., leprosy showing only neutral signs with no visible cutaneous lesions or scars of previous cutaneous lesions.

Both Monrad-Krohn and KinnieI Wilson describe the early and isolated involvement of individual nerves such as the ulnar and peroneal nerve in leprosy patients. It is this mononeuritis or mononeuritis multiplex which is regarded by Brand (1964) as causing the motor paralysis and anaesthesia in leprosy. The nerves afected are the ulnar, median, common peroneal, posterior tibial, facial and occasionally the radial. Brand also regards the sensory paralysis as following the same pattern, but in addition to the nerves already mentioned there is a paralysis of the long cutaneous nerves that run down from the upper arm to supply the forearm and hand, and those that run down from the thigh to supply the leg below the knee. The cause of the paralysis and sensory loss is due to oedema and a cellular infltration in certain sites along the nerve. This leads, frstly to ischaemia and, if prolonged, to destruction of the nerve. Why certain nerves only are afected and special sites along these nerves are involved is not clear, but Brand suggests it is primarily the nearness of the nerve to the skin where the temperature is lower.

MATERIALS AND METHODS

All types of leprosy were seen, ranging from patients with single skin lesions to those with severe deformities. Twenty patients with neurological lesions were examined in detail. These were predominantly of Hausa origin and were aU patients of the Zaria Leprosy Settleme: t.

The diagnosis of leprosy was made mainly on clinical grounds. In lepromatous patients, infltration of the ears, absence of eyebrows, depression of the nose, infltration of the skin and nodulation were all regarded as diagnostic criteria. In 5 of the 9 patients the diagnosis was confrmed bacteriologically. In one patient a skin biopsy showed lepromatous features, and the remaining 3 had been discharged, cured, and were no longer in chemotherapy.

In non-lepromatous patients the diagnosis was made by the character of the skin lesions. In those patients where there were no skin lesions, the diagnosis was made by the appearance of the extremities with loss of digits, ulceration of the feet and contractures. In one patient the diagnosis was confrmed histologically.

There was no clinical evidence of syphilis or vitamin defciency, and the general state of nutrition was good.

Sixteen patients were male and 4 were female. The age of patients was difcult to obtain but in the males varied from school children to middle age, while the 4 female patients were all young women.

All but one paIient had taken dapsone at some time, but only 6 are presently continuing

this treatment. Three patients are being treated with thiambutosine (DPT).

RESULTS

These are divided into 3 groups according to the neurological lesion.

Group 1

A'%-(+ =-#=!%+ á!(+ǫ-'% =′ 12 patients.

Eleven of the patients showed loss of sensation to light touch, pinprick, hot and cold, while sensations of deep pressure, pressure pain, vibration and joint sense were fully preserved. The twelfth patient showed preservation to pinprick as well. The distribution of the sensory loss was in a 'glove and stocking' fashion but the extent varied considerably. In some patients the sensory loss extended from the extremities to the knees and elbows, while in others it extended only to the ankles and wrists. In 3 of the patients the legs only were involved, the fngers and arms being normal. The distribution was thus predominantly distal. There was no motor loss.

Nine of the patients were classifed as lepromatous. Of the 3 non-lepromatous patients, one was a long standing patient with no skin lesions, another one had widespread macular lesions over trunk and limbs. The remaining patient, together with one of the lepromatous patients, are described in detail as they illustrate the mode of onset of sensory loss.

Patient 1—A boy of about 16 years was admitted on 7.1.67 with pain and oedema of both hands, feet and face. There were widespread, moderately well defined, macular lesions over trunk and limbs. Neurological examination was normal. Dexamethasone was started on 7.1.67 to reduce the pain and oedema, starting with 12 tablets of 0.5 mg daily and reducing the dose by 0.5 mg a day, so that the course finished on 18.1.67. This gave relief of pain and oedema, but early in February there was a recurrence of symptoms so that Dexamethasone was recommenced on 10.2.67 and stopped on 17.2.67. This again gave immediate temporary relief, but as soon as the course finished there was another recurrence. A further course of steroids was thought inadvisable and hence Camoquin was started on 13.3.67 and continued until 1.4.67. The pain and oedema finally subsided early in April. Some weeks later it was observed that there were blisters on one of the fingers, and neurological examination then showed sensory loss, involving both hands and feet, of 'glove and stocking' distribution. After 3 months' observation there has been no extension of the sensory loss. A biopsy of a macule on the back showed the following:—

'Slight cellular infiltrate is seen along a few neurovascular pathways in the deep and middle dermis. The infiltrating cells are histiocytes with a relatively large number of lymphocytes and a few plasma cells. Infiltrate is accompanying nerve tissue but there is no obvious intraneural infiltration. A few acid-fast bacilli are to be found mainly in neural tissue. This comes in the lepromatous half of spectrum but there are some slight dimorphous features.' are some slight dimorphous

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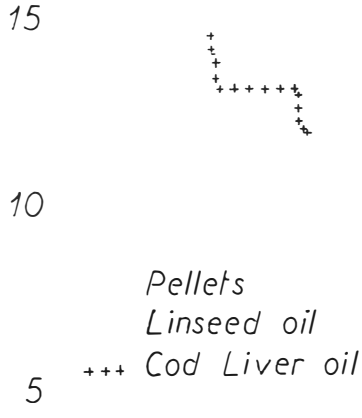

FIG. 6

Effect of the prooxidant diet on the mortality of mice inoculated with BCG Phipps after 14 days on diet.

FIG. 7

Effect of the prooxidant diet on the mortality of mice inoculated with *M. fortuitum Penso* after 21 days on diet. Ordinates indicate number of mice surving at different period of time after infection (abscissae).

FIG. 8

Effect of the prooxidant diet on the mortality of mice inoculated with *M. fortuitum Penso* after 36 days on diet. Ordinates indicate number of mice surviving at different periods of time after infection (abscissae).

4. \#!&'1" !#!H U+&!0"& % A4H!% ' '4A #$!
!4 & ? <*%!!D)"h)

In 2 different experiments groups of 20 white mice 1S-21 days old were placed on 2 diets: 7"2pellets, and 702prooxidant diet with linseed oil. In one experiment after 21 days on diet and in the other after 36 days on diet all animals were inoculated intravenously with 0.2 ml. of a 2 days old culture of U H!% ' 'X A #$!
Figs. 7 and S show the results of these 2 experiments.

These 2 experiments show that the prooxidant diet evidently increased the death rates due to intraveous inoculation of *M.* H!% ' G4A #$!in mice. It must be remarked that the average weight of the mice at the time of inoculation was 27 g. for the control group receiving pellets, and 32.5 g. for the animals receiving linseed oil.

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!4 & ? <*%!!D)"h)

White mice 1S-21 days old were placed on the following 2 diets: 7"2pellets, and 702prooxidant diet with linseed oil. After 22 days on these diets all animals were inoculated intravenously with 0.05 ml. of an IS-hour old culture of ; "*<à1!&!&&'$"'% '$7s !%3 !2Likewise 2 other groups of animals on the same dietary regimen were inoculated intraperitoneally with 0.1 ml. of the same culture plus 5 mcg. of LPS (lipopolysaccharide) and the other group with 0.1 ml. of the Giorgio culture plus 10 mcg. of LPS. Figs. W10 and 11 show the results of these experiments.

One other experiment with 6 mICe m each group with these diets was done with an inoculation of 0.1 mI. of the Giorgio culture plus 0.1 mI. of 1/20 LPS all injected intraperitoneally. Results are shown in Fig. 12.

These experiments show that the animals on prooxidant diets are as resistant to inoculation of ; "*<+1!&!&&'$ aureus - whether LPS is added or not - as animals receiving pellets. In contrast, the results of the experiments desoribed seem to show a very small inorease in the defenoes of the group of animals on prooxidant diets.

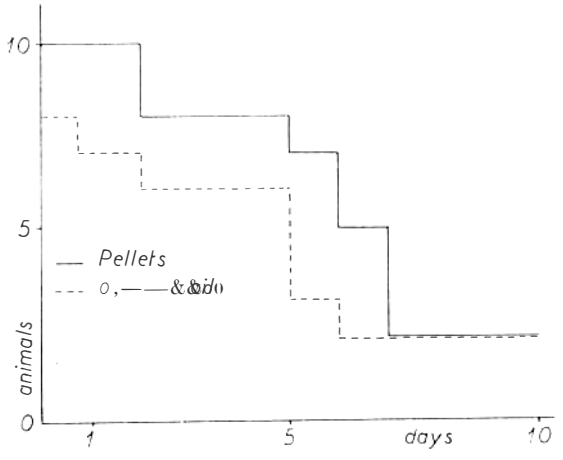


FIG. 13

Effect of the prooxidant diet on the mortality of mice inoculated with *Klebsiella pneumoniae* (Friedländer) after 42 days on diet. Ordinates indicate number of mice surviving at different period of time after infection (abscissae).

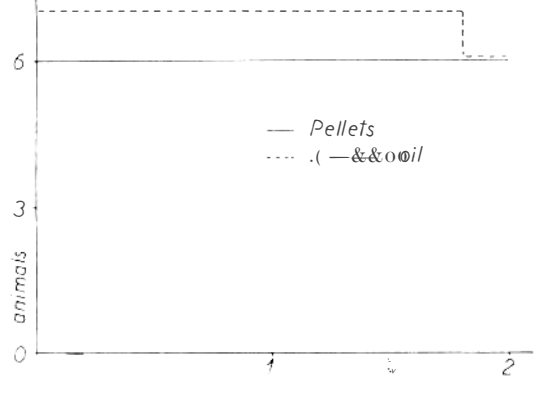


FIG. 14

Effect of the prooxidant diet on the mortality of mice inoculated with LPS (200 mcg. in 0.2 ml. intraperitoneally) after 42 days on diet. Ordinates indicate number of mice surviving at different periods of time after inoculation (abscissae).

FIG. 15

Effect of the prooxidant diet on the mortality of mice inoculated with LPS (400 mcg. in 0.2 ml. intraperitoneally) after 42 days on diet. Ordinates indicate number of mice surviving at different periods of time after inoculation (abscissae).

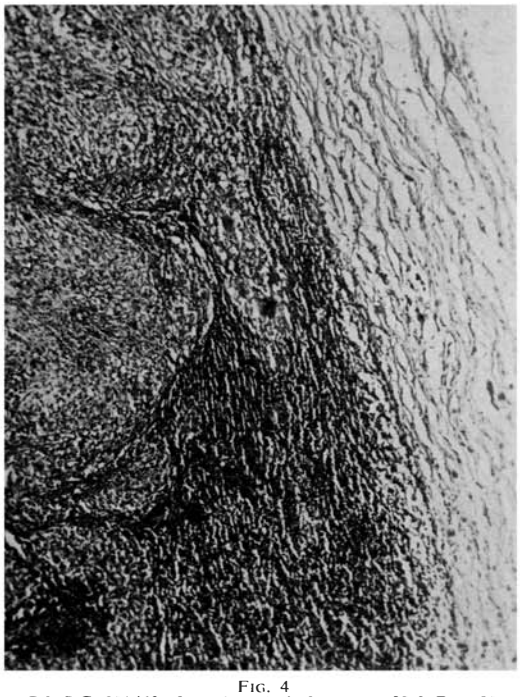


FIG. 4
G.L.S.C. 201/63—Lymph node in Leprosy. H & E × 80.
Illustrates lymph node showing follicular hyperplasia with pale epithelioid cells thickening of capsule with A.F.B. 5% positive.

FIG. 5
G.L.S.C. 201/63. H & E × 80.
Skin in leprosy—shows collections of histiocytes at one end.

deferens shows evidence of infiltration, with few chronic inflammatory cells—A.F.B. positive. Testis—Fibrosis, thickening of Basement membrane—A.F.B. positive. Hydrocele fluid—nil particular—Bone marrow autolysed.

Note: Though the testis and adnexa with other biopsy specimens were sent the pathologists overlooked the histopathological study of the epididymis.

Patient 3—G.L.S.C. No. 105/59. V.N.B. Age 38 years. Indian Christian, educated, Government employee, married, 2 children. History of leprosy 25 years. History of lepra reaction 15 years.

Patient first examined by Dr. Cochrane at Vellore during early 1948—has been under regular treatment since then. His first attack of epididymo-orchitis was during October, 1963, and the present attack in June, 1967—the duration of attacks being 15 and 12 days respectively. On both occasions the patient was under the author's observation and treatment. He exhibits marked gynaecomastia of the right breast and has been impotent and sterile for the past 8 years. The patient did not consent to testicle biopsy.

Patient 4—G.L.S.C. No. 280/64. S. S. Sahib Age 35 years. Muslim, illiterate, sharescropper, married, 5 children. History of leprosy 15 years. History of lepra reaction 7 years. Semblance of libido present.

Apart from his acute epididymo-orchitis the patient had marked cervical lymphadenopathy and lepromatous infiltration with development of an extensive patch over the right forearm in a skin area previously scalded in early childhood. Both the nipples and surrounding skin area were bilaterally infiltrated.

The patient was willing to have biopsy but refused orchidectomy. The following biopsy specimens were taken: (*a*) Testis with tunics; (*b*) Epididymis with tunics; (*c*) submandibular lymph gland; (*d*) lepromatous patch from scalded skin area.

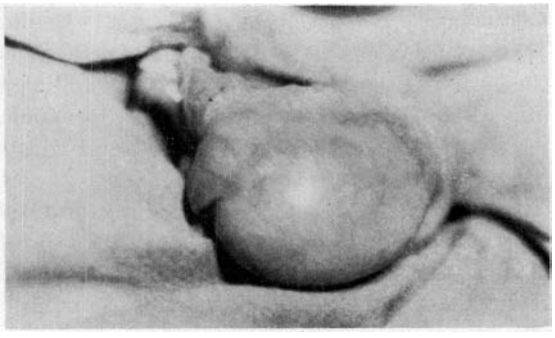
Clinical photographs a, b, c, of the testis and the epididymis *in situ* were taken.

Report of histopathological studies by Dr. Sundarasiva Rao, M.D., Professor of Pathology, Government Ramnarayan Ruia Medical College, Tirupathi:—

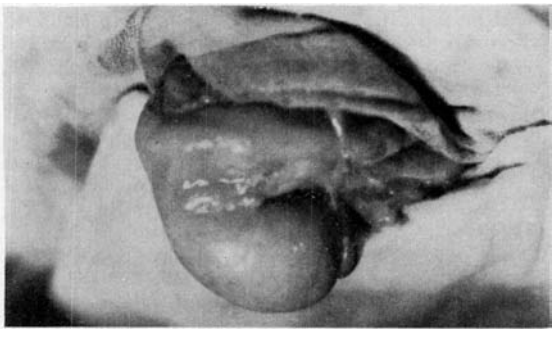
Testis—Marcoscopic size $2'' \times 1\frac{1}{4}'' \times 1\frac{1}{4}''$. Surface—smooth and glistening. Colour—bluish white. Consistency—soft and vascular with no nodules felt—epididymis enlarged and hard, particularly globus minor. A few delicate adhesions present between body of epididymis and testis proper.

Testis with tunics: Marked thickening of tunics with atrophy and wide separation of tubules. Hyalinized connective tissue with diffuse round cell infiltration and foam cell collections in the perivascular areas present between the tubules. The predominant change is a granulomatous infiltration of the interstitium with fibrosis and atrophy of seminiferous tubules. There is no actual increase in the interstitial cells.

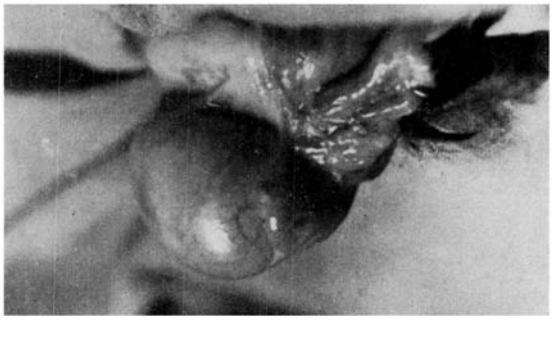
A.F.B. were seen both intra- and extracellularly, in the interstitial tissue as well as inside the tubules. Vangieson showed moderate increase of connective tissue in tunica albugenia and peritubular areas with dilated blood vessels.



a
G.L.S.C. 280/64.
Left testis and epididymis with tunica vaginalis *in situ* —both enlarged—surface smooth and glistening with a few blood vessels seen running transversely over testis.



b
Parietal layer of tunica vaginalis incised and testis and epididymis exposed. Globus major and body moderately enlarged. Globus minor markedly enlarged and glistening. Delicate adhesions present between the testis and epididymis.



c
Another view of both these structures, showing relative enlargement and vascularity.

Epididymis with coverings: Showed connective tissue with dense diffuse chronic granulomatous infiltration around the vessels and obliterating them. The tubules look normal with moderate thickening of intertubular connective tissue. A.F.B. mostly extracellular were seen in the tunics only, sparing the epididymis proper. No actual chronic inflammatory cell infiltration and presence of A.F.B. could be made out in the epididymis proper. It looks as though the tunics only are involved sparing the epididymis.
Submandibular lymph gland: Sections showed necrosis, epithelioid and giant cell reaction, with follicle formation. Few sections examined did not reveal A.F.B. organisms. However, considering the large number of foam cells, the lesion is only probably lepromatous.
Lepromatous patch from scalded skin area: There is atrophy of skin with flattening of papillary layer. Diffuse inflammatory round cell infiltration in perivascular, periglandular and perineural layers present with granulomatous changes.
All sections were examined after H & E, Vangieson and Acid Fast staining.

DISCUSSION

Testicular lesions are frequent in leprosy and their incidence in the different types have been admirably dealt with by Kobayashi (1920), Mitsuda and Ogawa (1937), A. L. Fu r iss (1956), Job and Macaden (1963), V. R. Khanolkar (1964) and H. W. Wade (1963).

Acute epididymo-orchitis in leprosy is non-sexual and non-venereal in origin and needs to be stressed. The author's series of 4 reports of patients confrms the occurrence of testicular lesions during repeated lepra reactions in advanced lepromatous leprosy. Ridley (1960) states in this connection 'that the reactions occur at the sites of small, pre-existing, lepra-cell granulomata'. It is as unfortunate as it is regrettable that the epididymis has not been studied at all save for the single autopsy study of the structure by A. L. Fu r iss (1956). Some of the most important physiological functions of spermatozoa 'like motility, maturation and spermatotrophic action occur in the epididymis which acts as a store house for them', Sampson and Wright (1965).

During repeated lepra reactions there is a flare-up with bacteriemia and widespread blood-borne dissemination of 'bacterial showers', and the testes become hypersensitised and receptive for the lodgement of *M. leprae*. The epididymis too participates in such a pathological process.

These phenomena, though rare, do occur and are observable clinically and should be designated as epididymo-orchitis, instead of being termed as mere lepromatous orchitis. Such involvement would appear to be concurrent and simultaneous. It is suggested that future studies of the testis in leprosy should include the study of the epididymis as well irrespective of types. Further, such studies ought to be mandatory especially during reactive phases 'as the search of periodical literature of the past 30 years has beell unrewarding and the occurrence of such lesions is not well documented in the literature'. H. W. Wade (1963).

SUMMARY

Four patients with acute epididymo-orchitis in advanced lepromatous leprosy in reaction were clinically studied by the author and are presented.

ACKNOWLEDGEMENTS

I am deeply indebted to the 2 patients for their cheerful, intelligent and willing cooperation and consent to parting with their testes. I would particularly like to thank Dr. D. J. Reddy, M.D., Director, Upgraded Institute of Pathology, Drs. Sundarasiva Rao, M.D., and C. Rajaram Mohana Reddy, M.D., Professors of Pathology, and Dr. K. Vasantha Rao, M.S., Assistant Professor of Surgery, Kurool Medical College, for their active collaboration, help and advice.

I further wish to acknowledge my deep gratitude to the staf members of the Government Leprosy Subsidiary Centre, Kurnool, particularly Sri M. Danaiah, B.A., Senior Medico-Social Worker, without whose dedication this original work would have been well nigh impossible. The same applies to Sri L. Ramaiah, B.A., for his patient revision of several drafts before fnally typing this article.

In conclusion, I wish to tender my grateful thanks to Dr. I. Bhoosan Rao, M.D., Director of Medical and Health Services, Andhra Pradesh, Hyderabad, for his kind permission to publish this article.

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J. C. HATHAWAY, M.D.

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Within the past few years sulphonamides have been given a trial in the treatment of leprosy in various areas of the world. Most of these trials have been short series of patients and the results have been equivocal.

Fourteen patients with lepromatous leprosy were treated at Hale Mohalu Hospital (Leprosy facility of the State of Hawii) with n' acetyl sulphamethoxypyridazine (Acetyl Kynex, Lederle) from 15 December 1965 to 15 March 1967. All 14 patients were heavy lepromatous patients who had not responded to sulphones or had been intolerant to them.

The medication used was an orally administered suspension of the drug containing 250 mgm. per 5 cc. The dosage was 10 cc. daily for 1 week and 5 cc. daily thereafter for a minimum of 10 months and after that the dosage was cut to 5 cc. twice a week. The complete length of treatment was 15 months. Of the patients, 8 were pure Hawiians, 5 were part Hawiian, and 1 was Portuguese. The BI (scale 0-6), using the scraped incision method and the standard Ziehl-Neelsen acid fast stain, was 6+ in 12 patients and 3+ in 2 patients. All were adults, Ñmen and 6 women.

T elve of these patients, the ones with 6+ BI showed no clinical improvement and have been in almost continuous progressive leprosy reaction. Four of them have been unusually severe. Due to the lack of response to treatment it was decided to discontinue this study after 15 months. Skin snips with standard scraped incision technique made at monthly intervals continued to show 6+ BI in all.

The other 2 patients were the ones who showed only 3+ BI at the start of treatment. Of these 2 patients, 1 gradually improved and in about 6 months was clinically arrested. The sulphonamide was continued but dapsone (Avlosulphon) was begun cautiously - 25 mgm. once a week and gradually increased until afer taking this for 6 months, she tolerated 25 mgm. daily. At the end of 15 months the sulphonamide was discontinued and the patient has continued to stay clinically quiescent on 25 mgm. dapsone daily. Her BI has gradually improved and her last 3 scraped incisions showed 1+ BI. She is being continued on dapsone 25 mgm. daily.

The other patient showed less than 3+ BI at the start of treatment. She became almost clinically quiescent in about 5 months but was not entirely clear until after a year's treatment. Due to the fact that this patient has biopsy-proved amyloidosis of her kidneys the dose was reduced to 250 mgm. twice a week after 6 months' time. Her last scraped incision on March 1, 1967, showed 1+ BI. We have continued her on 250 mgm. twice a week. Due to her kidney condition and proved marked intolerance to sulphones she was never given another trial of dapsone.

There were no ill efects of any kind during the time of treatment that could be attrib ted to the medication. Urinalysis and complete blood counts were carried out every month and liver function tests every 3 months. None of these showed anything abnormal that could be attributed to the medication.

CONCLUSIONS

No conclusions can be drawn from such a small number of patients, but it would appear that under the conditions of this study, the use of n' acetyl sulphamethoxypyridazine has very little efect on severe sulphone resistant lepromatous leprosy but may be useful in less severe patients. No ill efects were apparent.

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Mrs. S. KARAT, m.b.b.s., f.r.c.s.(edin.)

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PART I

Causes of Dehabilitation

The advent of DDS and other specifc anti-leprosy drugs brought in their wake a change in the attitude towards the patients sufering from leprosy. The possibility of eradication of leprosy by early detection and adequate treatment of all patients led people to seek new methods of appro[ch to the problem of leprosy. The age-old principle of compulsory isolation and segregation was found to be inefective as this method encouraged the undeformed and those with no subjective discomfort to go underground and thereby defeated the purpose of such a programme. The 'Brand' era brought hope and courage to patients not only because of the achievements of reconstructive surgery for paralytic deformities, but by the recognition of anaesthesia and misuse as the major cause of the much-dreaded trophic ulceration, loss of digits, and the gross deformities that one usually associates with leprosy. This knowledge not only helped the patients to learn to protect their anaesthetic limbs from mechanical and unrecognised trauma, but also helped to take away from the minds of medical personnel and the informed public, the fear and dread of leprosy that was based on the hopeless state of the ugly deformities associated with leprosy. The mystery that surrounded the process of destruction of the limbs was solved.

Thus gradually we have begun to realise that 'Leprosy can be cured and deformities can be prevented or, if need be, corrected.' (Karat, 1966.) The policy of segregation gave place to desegregation and domiciliary treatment programmes forleprosy control. But the principles of rehabilitation have not kept abreast of the march of these events. During the last 2 decades a great deal of thought and planning has gone into devising efective ways of rehabilitating patients who had lost their 'family roots' owng to a prolonged period of isolation from their relatives and friends, and in that period had developed varying degrees of disfgurement, deformities and disabilities. Once their disease was arrested and deformities corrected, the natural sequence was to fnd suitable means of gainful employment and restoration to normal social relationships. This was soon realised not to be an easy task.

However, with the greater outreach of domiciliary treatment, the old concept of 'Rehabilitation' of leprosy patients was not changed. B ,"0(" !#ĺ 4*($ĺ "#ĺ "(% ")+ĺ) ,"0(")ĺ*" # ĺá ,ĺ , ĺ&,"#3ĺ#3ĺ*" %#ĺ !>ĺ6"#"3 4 # ĺ!>ĺ(*%!$+ĺ*" # $ĺ ĺ $ĺ # 5 "0(ĺ ," ĺ*% 5 # !#ĺ !Yĺ) ,"0 1 " !#ĺ $,!'1)ĺ 0 ĺ , ĺ *% 4"%+ĺƇ%$ ĺ$ *ĺ #ĺ"((ĺ% ,"0(" !#ĺ*%!3_4 4 $ĺ ¬!%ĺ(Hϑ%ǯ$Ąĺ*" # $ĺ

There are 2 aspects that need to be considered. First, the recognition of the causes for dehabilitation of a patient. Second, the early recognition of these factors, and dealing with them before they cause dehabilitation.

CAUSES OF DEHABILITATION

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7"2Ǒ ª!NNǑ !>Ǒ ꝑ¥Èŭ ¿ 5 Ǒ N ÃN" !#Ǒ ǰyǑ *" #/Ǒ 4* %" '% Ǒ "#)Ǒ ú% NN'% Ǒ are the most di f cult handicaps for the patient to overcome, To this may be added a low threshold to injury by the tissues, and the lack of adequate inflammatory response, which is to some extent controlled by nervous reflex mechanisms. Unrecognised injury caused by sharp or blunt instruments or by repetitive minor trauma results in a primary wound which the patient is unaware of till bleeding, deformity or an ulcer draws his attention to its presence. The uninitiated patient does not know that he has to substitute vigilance and deliberate care for the protective function of a painful limb. Lack of pain and subjective discomfort result in further insults and trauma heaped on an already injured tissue and the condition rapidly deteriorates. The patient's cortical centres are 'blind' to the insults and injury that are constantly occurring in the battlefeld, from which the lines of communication to the cerebrum are severed. The battered cells collapse one by one and their desperate cry from the battlefeld is not heard by the o f ce of the high command. No reinforcement, either vascular or humoral, is forthcoming, and the lonely tissues, isolated fronl the headquarters with no reinforcement to fght and no way of withdrawing from their battlefeld to protect and treat its casualties, perish at the enemy's hand. The enemy advances and faces very little resistance till he reaches thc outpost, which still retains its communications. Immediately the defence is mobilised and every possible help rushed to the scene of warfare. It is not rare to see such a patient who gives a history of grossly infected fngers with dead bone and necrotic tissue in the hand unattended for several days until infection and cellulitis ascends up the forearm to a sensitive area, where the immediate inflammatory response, pain, cellulitis and often adenitis drives the patient to travel miles to the hospital for help.

Excessive use of an insensitive limb can produce injury by deep seated blisters and necrosis of soft tissue. This method of causation of plantar ulceration is well recognised and accepted and does not need further description (Price, 1959).

7O2Ǒ ª!NNǑ !>Ǒ ȝ# Ǒ !'¿,Ǒ "#)Ǒ ; % !3#!N NǑ a f cts fner and more delicate fnger movements. Artisans like goldsmiths and watch repairers are greatly handicapped, but experience has proved that, with practice, a great amount of skill can be regained.

Loss of sweating due to destruction of the nerve supply to the sweat glands coupled with dimunition or loss of sebaceous secretion results in hard, dry skin with a tendency to hyperkeratosis. Small and large fssures develop in the a fected area. Often fssures around the edge of the sole of the foot get deeper in areas of high pressure, and form the starting point of a deep perforating ulcer (personal observation).

2. ű"%"1+N NǑ

Paralysis in leprosy forms the next major cause of disability. Paralysis produces both functional disability and ulcerations due to high pressure areas resulting from defective mechanics of function. The fnger tip injuries in ulnar paralysis and the ffth metatarsal head ulcer in foot drop are familiar examples. In addition, neglected paralytic deformities result in secondary contractures which are often permanent and severely disabling, and in which the best surgical procedures can only produce mediocre results.

3. T !%0) +Ǒ

Morbidity due to general ill-health may also contribute to the dehabilitation of a leprosy patient. His capacity to be gainfully and competitively employed are impaired and hence he may fnd himself out of a job, home and family surroundings and driven to become a beggar.

The systemic manifestations of leprosy are o f en unrecognised. Patients with leprosy are apparently more likely to have anaemia, oedema, hypoproteinanaemia, malabsorption, kidney disorder, endocrine disturbances, amy-

loidosis, etc., which, singly or in combination with each other, reduce the longevity of patients su fering from leprosy as well as contributing to the morbidity and sub-normal health of these patients.

4. A$¯&, !(! í &"(ů L" '$ $ů

In spite of all the advances in the management of leprosy, the stigma and fear of leprosy are still very much ingrained in the very fabric of our society. The person who gets leprosy is o fen haunted by the fear of detection and isolation from his fellow men. Often, this fear of ostracism by society and the family causes considerable mental agony and psychological trauma. It is not uncommon to fnd a patient who has a minor deformity, but has broken down under the psychological strain and has not found the courage to retmn to useful living. He becomes introspective, depressed, hostile and anti-social.

5. Õ#") Á'"& $ů!>ů ůØ $ # ůA" 8#ů!C ď, õ :+ů

(i) The prolonged period of therapy needed with DDS necessitates repeated attendance and sometimes hospitalisation extending over a period of many years. ' his naturally upsets the patient's routine and his work.

(ii) The problem of nerve destruction even while under therapy, and sometimes due to the therapy, is often neglected, and needs further study and careful management.

(iii) The unsolved problem of chronic reactors forms a major problem for a fairly small proportion of patients.

(iv) The lack of simple care and preventive measures for anaesthetic limbs, as part of the larger control programmes, is a major defect of the present control progeammes. Anaesthesia and paralytic limbs are left uncared for to run their natural comse, and the limbs of an uninitiated patient are permanently and severely deformed and disfgured due to misuse and disuse.

6. l$!(" !Ãů"Ã)ů ; ő8 í" !#ů!CůA!$ 5 ůA@ Æ $ů

The age-old principle of isolating and segregating positive patients over a period of many years in sanatoria dislodges them from their family and society and makes it impossible for a large number of them to return to useful living. Lack of vocational training during this period adds to this problem. Often, a patient who has stayed in a sanatorium for many years has developed a 'deformed personality' which makes his re-entry into an unfriendly society still more di cult and it'olates him further from society.

7. Ž!ç ¼(ů Aġ lj') & ů "#)ů Õ3#!8¼#& ů

Social prejudices and ignorance contribute m ch to the dehabilitation of leprosy patients. The 'persecution' that is often meted out unconsciously by almost every section of society makes it hard for the patient to have normal social relationships. A patient with identifable deformities, or a patient with no deformity but who attends a special clinic or hospital for leprosy patients often faces the possibility of being thrown out by his own immediate family circle and by his neighbours, and be forced to leave his home. Occasionally, patients leave their home and become destitutes and beggars in their attempt to avoid embarrassment and serious social consequence for the rest of the members of the family.

PART II

MEDICAL AND SURGICAL ASPECTS OF PREVENTIVE REHABILITATION

It is more and more being recognised all over the world that rehabilitation starts at the stage where prevention of disabilities can be e fective. This should be the basis of our approach in leprosy, but unfortunately, in the large majority of areas this aspect is all but forgotten in the planning and management of both individual patients and in the leprosy control programmes.

What about patients who are already disabled and dehabilitated? There are now an estimated 10 million patients su fering from leprosy. The majority of these are in what are

called 'under developed' or 'developing' nations. The number of patients with deformities is estimated to be something between 20 and 25% of the total patient load (W.H.O.: Polambakkam). The majority of these patients are unemployed or under employed. These countries with their limited resources and a high percentage of healthy unemployed will find sheltered workshops and expensive rehabilitation projects practicable only to a very limited extent. In addition, the majority of the patients are in their fourth and fifth decades, are not amenable to learning new trades and unwilling to move out of familiar surroundings. Moreover, the sense of belonging to their families and society is one of the basic needs of leprosy patients, and tearing them away from such an environment cannot be justified even when balanced against material sufficiency and security.

In such a situation it would be considered ideal if patients could return to their own jobs, their families and social set-up, provided they have obtained special training and help to overcome their disabilities. It is such a programme that we designate as 'Re-education for Re-settlement' rather than rehabilitation.

MEDICAL MANAGEMENT

Maintenance of the integrity of the function of peripheral nerves during anti-leprosy therapy should be the concern of every leprologist. This much neglected, ill-understood and in most instances completely ignored, complication of the disease is the chief cause of morbidity in leprosy. Often the word 'neuritis' is used to indicate pain and tenderness over the nerve trunk which most often is not directly related to the functional integrity of that nerve. The insidious onset of anaesthesia or paralysis without any pain in the affected segment of the nerve is often missed. It is important to record the motor and sensory function of the peripheral nerves routinely and periodically during treatment. The need to recognise patients who show a greater predilection for nerve involvement and to treat such patients with drugs other than DDS, such as Thiosemicarbazone and CIBA 1906, during the initial 12 to 18 months should be more strongly emphasised. Anti-inflammatory drugs like Chloroquin could be usefully given in combination, sometimes preceding the institution of specific anti-leprosy drugs. All patients with borderline leprosy, patients with disseminated tuberculoid leprosy, and lepromatous leprosy with a tendency to painful enlargement of the nerves or paralysis or a previous history of ENL need such special care. In addition, acute paralysis or an acute tender nerve anywhere should be considered as a serious form of 'reaction' and a definite contra-indication to the use of DDS. In such patients anti-inflammatory drugs and such other measures to control the acute phase should be instituted in an attempt to restore nerve function. Lack of such serious notice of nerve dysfunction in the mass treatment programmes results in a large number of casualties sustaining permanent injury to peripheral nerves resulting in anaesthesia or paralysis.

This problem will continue to increase with the mass treatment programme until the medical and paramedical personnel begin to look beyond the results of skin smears for bacilli and the disappearance of skin lesions as their criteria of results of treatment, and take time and care to assess the peripheral nerve function during active anti-leprosy treatment.

Early treatment of even minor hand injuries with splinting and provision of microcellular rubber for adaptation of tools and for footwear for patients with anaesthetic feet should be available for every patient.

Every ulcer should be treated with plaster of paris immobilisation and provided with microcellular rubber footwear. The problem of dehabilitation will multiply and worsen in every control programme unless these measures are adopted as routinely as DDS therapy.

In our control programme in the Gudiyatham Taluk, a simple programme of ulcer treatment followed by the issue of microcellular rubber footwear resulted in a 65% reduction in the incidence of ulcers within 2 years, a drop in unemployment from 66% to 9% among the 101 patients cured of plantar ulceration and 90% of these patients attributed their ability

to return to work to the use of microcellular rubber footwear.

Lack of such care to prevent and treat deformities in a domiciliary treatment programme results in loss of confdence by the patient in the doctor's ability to 'cure' him with DDS. A patient who has to be persuaded to take therapy for a minimum period of 5 years or all his life does not understand the mysterious 'bacilliary index' that the doctor assures him is improving when no care is taken of recurrent trauma and infections resulting in trophic ulceration and the unrelenting progressive destruction of his limbs. To the patient, deformity is leprosy. The indisputable lack of the patient's confdence in such a treatment programme is one of the causes of the large percentage of absenteeism that is the basic "veakness of every control programme.

With the advent of the efective domiciliary treatment programmes compulsory segre [ttion and isolation as a method of leprosy control is slowly disappearing. Such a programme imimedately reduces the number of patients who need special rehabilitation because of prolonged institutionalisation. All the same, the stigma and horror associated with leprosy and the resultant callous ostracism of suferers from this disease will not change to any signifcant degree until such time as leprosy is recognised for what it is - namely, just a bacterial disease like any other and not a divine curse. Such an awareness and recognition must necessarily lead to the logical step of integration of leprosy into the general stream of medicine. When leprosy loses its mystic and divine connotations in the minds of professionals and laymen, then naturally leprosy treatment and control must become an integral part of the medical care ofered by all general hospitals and general practitioners.

Further, the early patient with a single patch and no subjective symptoms whom the paramedical worker or the doctor has sought out and persuaded to take treatment, needs a place where he can go for treatment without the serious social consequences of being recognised as a leprosy patient and this cannot be the leprosy clinics in our present social context. Unless this problem is solved the problem of the large measure of absenteeism which is presented universally in all the leprosy control programmes will not be solved. Thus the early patient will not get the best that recent advances in leprosy work can ofer.

SURGICAL MANAGEMENT

When the medical management has failed to prevent nerve dysfunction disfgurement and deformities result. The patient then presents himself with anaesthetic limbs and deformities of greater or lesser degree.

The methods of correction of paralytic deformities by tendon transfer and the correction of disfiguring deformities by plastic surgery are well established and publicised and hence do not need further elucidation.

It is sufcient to add that at present the available facilities are grossly inadequate. At the same time the correction of paralytic deformities by tendon transfer is a specialised job needing an adequate period of training and experience for the surgeons and physiotherapists who undertake this work. Each stage of the surgical management needs experience, skill and technical excellence. The criteria for selection for surgery, pre-operative physiotherapy, the high standard of asepsis needed for such surgery, the perfection of sUgical technique with its necessary modifcations to suit individual limbs of patients, and the all-important post-operative re-education period with constant supervision by a qualifed physiotherapist and repeated survey and review by the surgeons arc essential to obtain excellent results. The author has seen many a patient who sought help because a previous operation had failed. It is obvious that failure is not due to major faults in technique but due to small errors in management resulting in disastrous consequences.

Three major principles should always be borne in mind, namely: -

1. Tendon transfers and plastic operations can be done only once and re-operation on a failed procedure rarely gives satisfactory results.

2. It is not useful to do these operations unless the best possible results are obtained. A patient who had pre-operative clawing of 75° fexion is very slghtly better of with an improvement of 45° fexion post-operatively and, from what wc have observed, these insu f ciently corrected deformities deteriorate in subsequent years to pre-operative lcvels.

3. The surgeon should resist the temptation to adopt the attitude that 'something is better than nothing'. Faced 'ith a large number of patients to cope with and inadequate facilities for surgery, this attitude may appear justifable, but in our experience insuficient correction and unsatisfactory post-operative re-education almost invariably result in deterioration of the limb to its pre-operative level. It is not uncommon to fnd such a hand some years after operation functionally worse than its prcoperativc condition.

SUMMARY

A changed orientation in relation to the rehabilitation of leprosy patients is presented. The main theme of the paper is the prevention of 'dehabilitation' of leprosy patients by reeducation for re-settlement concurrently with comprehensive medical care (including adequate facilities for reconstructive and plastic surgery) administered through the domiciliary treatment programmes.

The etiological factors in relation to 'dehabilitation' of leprosy patients are discussed in detail. A rational medical and surgical approach to preventive rehabilitation is described. Particular emphasis is laid on the careful choice of drugs in medical treatment and on the possibilities of reconstructive surgery both as a procedurc to restore normal and near-normal function and as a 'salvage' procedure.

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A v v n A w o t

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Deformity and the resulting disfgurement of the extremities and face is the main factor responsible for the difculty in the rehabilitation of leprosy patients. Functional disability is also a factor, but one which is more easily overcome. Ever since surgical reconstruction of these deformities was developed by the pioneering work of Professor Brand in the Department of Reconstructive Surgery in Leprosy of the Christian Medical College and Hospital, Vellore, a new hope has been made available for such persons who were hitherto considered hopeless from the point of view of rehabilitation. Even though, however, a nearly normal function of hands and feet which were badly afected can noV be restored, there remains the very serious hazard of residual anaesthesia. This shows itself to be a real problem when such patients are asked to perform any form of manual labour. Sixteen years ago, in VeHore, an experimental Rehabilitation Centre was established where young men between 15 and 25 years of age were admitted for varying periods to learn to use their hands and feet in doing a variety of jobs including carpentry, toy making and manufacture of articles from perspex, etc. To minimise the hazards of injury to the anaesthetic extremities, modifcations were made to their tools.

A SURVEY OF THE RESULTS

In leprosy as in other conditions which give rise to disability, it is extremely important to prevent the patient from becoming dehabilitated and consequently care has been taken in the selection of patients for admission to the Rehabilitation Centre. The criterion for admission has always been a degree of deformity which rendered the boy unable to gain admission to a regular school and also boys who have either been rejected from their home environment or otherwise unable to secure the means of livelihood. We would like to stress the great importance of not taking young people out of a normal school in order to train them in vocation. It is of extreme importance that as far as possible, any patient for whom there is normal provision in his home environment should remain in that environment.

The aim of the Centre has been two-fold, viz., to teach the patient the use of his hands and feet without the danger of injury and further deformity and to teach him a trade or skill with which he can earn a living. Great stress has been laid upon the practising of exercises to prevent

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contracture and the daily inspection of hands and feet to detect early signs of injury or infection and the importance of reporting immediately any injury sustained. In this way, a new "Reflex of caution" is initiated so as to replace the loss of the protective refexes initiated in normal individuals by the sensation of pain.

In the selection of suitable vocations for patients with anaesthetic extremities it was recognised that the normal mechanisms of protection are two-fold. One is by the conscious knowledge of impending dangel', and the other by the possession of the faculty of pain. For example, in the use of a sharp instrument a normal person does not rely on his sense of pain to inform him of the danger of the instrument. He relies on his knowledge that the instrument is sharp and must therefore be handled with caution. This knowledge is common knowledge to everybody. On the other hand, in the matter of handling hot objects the information obtained from the sensory nerve endings on the part of the body in contact with the object is the information upon which the reflex withdrawal is efected. If the sensory nerve endings are defunct this information is lacking and burns are sustained. Similarly in the production of blisters due to handling tools in the performance of heavy work, the normal individual relies on the sense of soreness which precedes the onset of the blister. If this soreness is absent the blister forms unknown to the patient. Thus, the choice of a trade suitable for leprosy patients should involve, as far as possible, the avoidance of processes involving heat and the use of protective devices and modifcations of tools to prevent friction blisters. The type of skills introduced in the Centre, therefore, were: -

1. Carpentry.
2. Toy making.
3. Manufacture of articles from perspex.

In addition to these, small scale kitchen gardening and poultry keeping were also taught. All the boys attend evening school so that the emphasis on reading and writing has been maintained.

''he Centre consists of thatched houses with brick and mud plaster walls, white-washed and provided with adequate ventilation. The object of this is to avoid divorcing the patients from their normal village environment as much as possible. The workshop equipment was such as to involve the minimum use of power-driven tools although in later years it has become recognised that the almost universal availability of electricity has made the use of power less undesirable than it was 15 years ago.

During their stay in the Centre the boys are taught their trade and financial credit is given to them as soon as they are able to produce marketable goods. This credit is allowed to accumulate in their names and they are only issued pocket money as required. The total accumulated saving is given to the patient on discharge from the Centre either in the form of cash or in the form of a set of tools to serve as a means of continued productivity.

DISCUSSION OF FINDINGS

It will be noted (Table 1) that the percentage of follow-up obtained was 74.6. In every follow-up analysis of leprosy patients that we have so far conducted we have experienced great difculty in contacting the patients after discharge and this fgure is exceptionally good.

TABLE 1

	Total	Follow-up
No. of persons interviewed ..	30	30
No. of persons circularised ..	45	
No. of replies received ..		26
Total numbers contacted ..	75	56

Percentage of follow-up: 74.6%

Of the 56 patients who were followed-up ÌÂ patients were found to be unemployed (23%) (Table 2a). This fgure was rather higher than we had expected. In some of these cases the family circumstances were sufciently satisfactory so that the line of least resistance was depending upon the family. Two members were defnitely known to have resorted to begging. The entire patte r of public opinion which we

attempt to inculcate in the Rehabilitation Centre is that begging is the worst possible mode of existence and therefore it was disappointing to fnd that even as small a number as 2 had resorted to this. These 2 boys were without any family and presumably were driven to this plight out of desperation. Subsequently one of these 2 was re-admitted for treatment of ulcers and is now working on a piece-work basis in the Splint Workshop attached to the Christian Medical College Hospital. Of the employed group, the large fgure of 31 out of 56 (55.4%) were working under conditions which must be called protected industry, since all the institutions in which they are working are specifcally intended for disabled persons (Table 2b).

TABLE 2a

Self-employed: Agricultural labourers	5	
Artisans	2	
		7
Employed in Institutions		31
Partial Employment: Artisans		2
Unemployed (dependent on others)		13

TABLE 2b

Swedish Red Cross Rehabilitation Industries	10
Government and Private Institutions	5
Hind Kusht Nivaran Sangh Socks Factory, Seplanatham	5
C.M.C. Hospital	5
S.L.R. Sanatorium, Karigiri	1
Other Leprosy Institutions	5
	31

The di f culty which these boys have evidently experienced in securing self-employment is a factor to be noted. The design of the vocations taught was such as to enable patients to be self-employed (Table 3).

TABLE 3

Carpentry	18
Toy Making	26
Kitchen Gardening	2
Poultry Keeping	2
Miscellaneous	8
	56

This aim has evidently not been achieved, and resort has, in many instances, been made to employment in a protected industry. It cannot be said that the teaching of carpentry was a total mistake since the skills that they learned in carpentry are being made use of to a very large extent by the individuals in the carrying out of their duties in the protected industries in which they are now employed. Furthermore, we can presume, although it is statistically impossible to substantiate this presumption, that this experience taught them to use tools and instruments with the least possible damage to their anaesthetic extremities. It is felt that the failure of the self-employment ideal may be related to the fact that in India the social structure is very conservative and trades tend to run in families and in communities and outside intrusion into these trades is resented by society.

TABLE 4

Total number of leprosy patients treated in the Department of Orthopaedics from September 1, 1965, to August 31, 1966		540
Female:		
Housewives	46	
Recorded as Nil	30	
		76
Males		
Agricultural labourers	100	
Agriculturists (owners of land)	72	
		172
Students		22
Teachers		4
Weavers		13
Salaried employees		50
Business		10
Professional (barbers, dhobis, doctors)		21
Recorded as nil		160
Recorded as beggars		10

An analysis of the occupation of the out-patients for one year (Table j revealed that most of our patients who form the reservoir from which the Rehabilitation Centre members are drawn were agricultural labourers. It would seem therefore important that the vocation taught must be related to the background from which the patients have come. If a person belongs to a weaving community he

should be taught weaving. Similarly, if he comes from an agricultural community his vocational training should be in terms of agriculture. In conversation with some of these patients who were interviewed we found that a number of them had sold the tools with which they were equipped on leaving the Centre. In many cases this was done only after obtaining reasonably secure employment which did not involve the use of these tools.

TABLE 5

Marital Status of Ex-Members

Single	43
Happily married	10
Married and separated	2
Widowed . .	1

A study of the marital status (Table 5) showed that only a small percentage were now living normal married lives. It is our belief that family life is an essential part of rehabilitation. Hence this subject was also investigated. Twelve members got married after leaving the Rehabilitation Centre. Forty-three members are living alone. Three members have married ex-patients and the remaining 10 have married women who have never had leprosy. Ten out of 12 married couples are living together happily. Out of these one member has concealed his previous disease from his wife and the remaining 2 are living separately on account of this disease. Out of these married couples 7 have children. The fact that successful family life has been so far denied to 45 out of 56 ex-members must remain a matter for some concern.

An attempt was made to relate the duration of stay in the Rehabilitation Centre with the ultimate rehabilitation of the patients but it was found that this did not correlate at all. To some extent this is understandable because people who stayed the longest in the Rehabilitation Centre were often those who constituted the biggest problem in job placement.

CONCLUSIONS

1. The teaching of a vocation which involves a deviation from the traditional employment of a person is probably not advisable except if the person is being taught with a view to absorption in some protected industry.

2. Self-employment of patients which is the obvious ideal, in order to be successful, must involve the return of the patient to his home environment and the pursuit of the occupation in which his family is concerned. If, for example, instead of equipping a person who comes from an agricultural background with a set of carpentry tools he is given a yoke of oxen it would be possible for him to earn Rs. 3/- per day in hiring the services of himself and his oxen to the local villagers. This has been proved experimentally in an agricultural programme upon which we have now embarked in the Rehabiliation Centre since the commencement of this study. We find that the demand for our oxen and plough in the local villages is very high and there has been no difficulty at all in the villagers accepting our patients irrespective of their deformity, if they are able to assist in ploughing the fields.

3. Poultry keeping and kitchen gardening are examples of trades which can only be carried out if a small quantity of land is available for the person and if such land is not available it is not possible for them to carry out these vocations.

How then should rehabilitation be planned in a country such as India? It is felt strongly that protected industry must feature largely in any rehabilitation programme since many of the patients are already displaced persons and not acceptable in their own community. Furthermore, most of them are landless and are therefore unable to practice kitchen gardening and poultry keeping.

In past years the idea of settling patients in small communities on pieces of land has been frowned upon. It has been stated that it is most undesirable to create 'leprosy villages'. We, however, differ from that view. We feel that small co-operative farming communities must be set up, the land being obtained from the

District Collector, and assistance given to the group to start agriculture and to supplement the income from the agriculture by small cottage industry and live stock. The advantages of this system are that the patients working together have no di f culty in producing the goods. They must be responsible mutually for the care of any of their members who are temporarily incapacitated by injury or foot ulceration. Permanent incapacitation will, of course, involve institutional care. They can be provided corporately with improved agricultural instruments such as a power tiller and a pump in the well which will enable them to cultivate the felds economically with the least possible injury to themselves. They will have a sense of independence and will probably be able to marry and start families. The children of these small communities can easily be kept under regular medical surveillance and prophylactic DDS. They must attend the local village school. This, in our experience, is not dificult because so far we have not encountered any prejudice against children who have no deformity going to schools. It is deformity that society fears and if this is absent society can easily be educated to accept these children. In the course of one generation the village will cease to carry the stigma which in the present generation they may be likely to bear. It appears to us that the advantages of this pattern far outweigh the theoretical disadvantages of the stigma persisting.

The problem of leprosy is not a small problem. In the area in which we are working the incidence is between 2 and 3% of the total population. The schemes that we envisage involve fairly large outlays of capital and allocations of land. We believe that it is necessary that such outlay and allocations be made. If the problem of the elimination of the leprosy beggar is to be taken seriously it is necessary that a patient be prevented from becoming a beggar. The only way that this can be accomplished is by a concerted e fort being made, assisted by Government co-operation, to provide for displaced persons who would otherwise have to resort sooner or later to begging. It is our conviction, based on the work that these boys have showed themselves capable of turning out, that such small agricultural communities and protected industries can be as productive as any local village community. If "he small communities are taught to take advantage of the assistance now available in the form of improved agricultural methods, improved seed and scientifcally controlled fertilising we believe that their rate of productivity w i l be higher than that of the average village community, in spite of the hazards of ulcers and injury which leprosy brings in its wake.

Believing this we look forward with faith to the time when the disabled, from whatever cause, will no longer be dependent on the community but will bear their own burden of responsibility and share in the mutual interdependence which must characterise any enlightened and democratic society.

Positive Living
Leprosy and the Spirit of Man

by T. N. JAGADISAN*

All exceptional su fering is a challenge to the spirit of man. Leprosy with its long legend of incurability, deformity and mutilation leading to ostracism of the patients, sometimes sanctioned even by religious practice, has remained through the ages a living death to the patients and a dark horror. In the past the large multitude remained indi ferent and even cruel to the leprosy patients so that, 'Man's inhumanity to Man' was seen at its worst in the treatment of leprosy patients. But this very inhumanity of the ordinary man roused a rare devotion and compassion amounting to herosim in the hearts of some of the finest spirits of mankind. In the dark life of the leprosy su ferer these exceptionally compassionate souls brought gleams of light and love. But alas ! these souls were few and far between; they were, at any rate, far too few to save the vast numbers of the neglected and despised leprosy patients who were steeped in their own despair. These brave and dedicated men - Jesus Christ, the Knights of St. Lazarus, St. Francis of Assisi, Father Damien and in recent days Mahatma Gandhi, by answering the challenge of leprosy, have ushered in a new outlook on leprosy and a new era for the leprosy patients. These men, imbued with religious spirit, saw the Divine in the lonely and forlorn leprosy patients and identifed themselves with them. Out of such compassion and identification with undeserved su fering was born the wider impetus to scientifc advent u e which resulted in an understanding of the causes of the disease, the discovery of drugs to deal with it, the measures to control the spread of the disease and ways to rehabilitate the patients.

SCIENTIFIC ADVENTURE AND COMPASSIONATE ACTION

As if to emphasise the inter-linking of scientifc adventure and compassionate action, it was about the time when Dr. Hansen discovered the leprosy bacillus in the early 1870's that Father Damien went to Molokai to live among the uncared for victims of leprosy, thus beginning a life of matchless heroism which ultimately awakened the world in an unforgettable manner to the needs of leprosy patients. It was at this time that Wellesley Bailey was paying his frst visits to the leprosy su ferers at Ambala which led to the foundation of the Mission to Lepers (uow the Leprosy Mission) which has done incalculable service in research, treatment and care of patients. The voluntary spirit behind all this early endeavour is a precious inheritance which should be preserved and enriched. For, by so doing, we shall not Olly conquer leprosy but improve the quality of life. First, and last, we should remember that leprosy work is a means of humanizing human life and giving greater depth to civilized life.

FALSE ASSUMPTIONS

The legend of leprosy, however, is only scotched, but not killed. It should be completely destroyed if leprosy is to be conquered and this ancient river of su fering is to be dried up. 'This legend is based on 3 false assumptions: that leprosy is a very contagious disease; that it is incurable; and that leprosy patients are people, apart, accursed and possessed of a special psychology.'[1] These erroneous ideas, deeply rooted in the minds of most peoples, at all levels of society, have been responsible for much a f iction of the mind and loneliness of the spirit. This loneliness that comes in the wake of the knowledge that one has leprosy has been described vividly by Perry Burgess where Ned Langord says: 'I walked

* Shri Jagadisan is the Organizing Secretary of Hind Kusht Nivaran Sangh (Indian Leprosy Association). He has devoted his life to serving the sufferers from leprosy, 'with the zeal of a friend, with the generous energy of a father, and with the exuberant affection of a mother'. It is fitting indeed that here he writes on 'Leprosy and the Spirit of Man''.

and walked through that whole night. I walked and thought and suffered. You could never believe how alone aloneness is. You have to move, live, breathe, see, hear, in the midst of millions of people, not daring to touch one of them, afraid to speak lest they become friendly - avoiding, avoiding - eternally avoiding.'[2]

CONSTRUCTIVE ACCEPTANCE OF THE ILLNESS

[illegible]

WORLD PROBLEM

With modern methods of treatment including physiotherapy and reconstructive surgery, and with an effective drug not costly and capable of being administered on a large scale, hopes have mounted of controlling the disease that has been a terror of mankind for ages. The new impetus given by scientific advances has made the nations of the world aware of the fact that leprosy is not a disease of an unfortunate few, but really a disease that afflicts millions in many parts of the world. It is now recognised that it is a world problem. The recognition has in turn generated a new urge of well-directed emotion, among the peoples of the more fortunate countries which have practically no leprosy, to organise leprosy foundations and associations not only to collect monies but also to send out trained workers who can help in the newly developing countries. Truly the spirit of man has been aroused on a world-wide scale to help in the conquest of leprosy and the wide misery, associated with it, and thereby to assert the brotherhood of man and oneness of the world. We in India are particularly grateful to the many organisations in Europe, America, Britain, Canada and Australia and other countries and on this occasion I would particularly like to express our gratitude to the spirit of helpfulness of our friends from Japan who have come forward to set up a valuable research centre at Agra.

May I warn that in the context of today we have to guard against excessive emotionalism and weakening sentiment which may stand against a rational approach to leprosy and still present a picture of leprosy work as the field of the specially dedicated, while the great need today is to make it the normal duty of the everyday physician. But we have also to guard against the danger of looking upon our leprosy campaign as a mere technical warfare against a bacillus, thereby reducing it to a soulless campaign in which the human being who happens to harbour the leprosy bacillus is forgotten or ignored. We shall be in no danger of doing this if we remember the intensely spiritual appeal of leprosy to Gandhi and his memorable words:

> 'Leprosy work is not merely medical relief; it is transforming the frustration in life into the joy of dedication, personal ambition into selfless service. If you can transform the life of a patient or change his values of life, you can change the village and the country.'

Surely Gandhi would approve of our adding 'and the world'.

ACKNOWLEDGEMENT

Gateful acknowledgement is made to the Organising Committee of the International Leprosy Seminar, Agra, January 31 to Febrary 3, 1967, for this article extracted from the Souvenir published by them in conncction with the Seminar.

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1. *WHO Chronicle*, **14**, 1, January, 1950.
2. *Who Walk Alone*, p. 70.

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Dear Sir,

Having noted (in Archives of Dermatology, Vol. 92, page 603; Society T.ansactions, 1965) that epsilon aminocaproic acid was e fective in the control of the lesions of Anetoderma of Jadassohn, I thought that perhaps this substance might have a similar e fect in erythema nodosum leprosum.

A supply of this drug was provided by Cyanamid International through the kindness of the Medical Director, Dr. Walter E. Boehm, M.D.

The aminocaproic acid (AMICAR-Lederle) was administered to ¦ů patients with lepromatous leprosy who were having signs and symptoms of erythema nodosum leprosum, and to one patient with dimorphous leprosy with severe neuritis and early foot drop.

The drug was used in dosages of up to 8 gm. daily and for periods of from 5 days to 17 weeks without any conclusive evidence of improvement in the signs and symptoms. Thus it can be concluded that this drug is of no value in the management of the reactive states of leprosy.

ROY E. PFALTZGRAFF, M.D.
Adamawa Provincial Leprosarium,
Garkida, Via Yola, N. Nigeria.

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aÌ$ůÙ!5 Âk %ů 1967.

Dear Sir,

I was somewhat surprised to note the wording of a sentence in the body of Dr. C. S. Goodwin's article in 9 *%!$+ů B 5 ?ů (1967), *38*, p. 182, which reads thus; 'Following the suggestion of Waters and Rees (1962) that the percentage of evenly stained, morphologically normal forms of *M*. â *%" ů should be calculated in routine Ziehl-Neelsen stained preparations, the term "Morphological Index" was adopted (Goodwin, 1963), and has been accepted (Pettit and Rees, 1964; Browne, 1965)'; and of the acknowledgement on p. 186 ('The author is indebted to Dr. S. G. Browne for instruction in the examination of the morphology of Tůâ *%" ů2ů

To avoid any ambiguity regarding the word 'adopted' as used by Dr. Goodwin, it should be recorded that in 1963 while on a World Health Organization Study Tour, I visited the Hong Kong Leprosarium of The Leprosy Mission (Hay Ling Chau), and on March 5 and 6 not only demonstrated to Dr. Goodwin di erences in morphology of *M*. (*%" /ů but also discussed with him at length the 'Morphological Index' as we had come to call it in Easte r Nigeria, and the method we had been using to calculate the Index. This is recorded in the 'Report of a Study Tour of Leprosy Research Centres in India and the East', which I submitted to the World Health Organization on 11th March, 1963.

In the light of our discussions at Hay Ling Chau, I suggested that the following words be inserted in the typescript draft of the booklet, 'Essentials of leprosy for the clinician'; 'In addition the morphology of the bacilli in each smear should be noted, and the percentage of morphologically normal forms, solid rods, calculated; this is known as the Morphological Index.' The revised draft was submitted for publication the following month.

Dr. Goodwin thus 'adopted' a term already in use by others. It is hardly correct to state that this term was 'accepted' by me after April, 1963, when I had previously suggested it to him.

As Cochrane says (1952): 'These changes (i.e., in morphology) have been noted for many years and they take place both in treated and untreated cases, and have been mentioned by many workers.'

The successive Annual Reports of the Director of the Uzuakoli Leprosy Research Unit to the Government of Eastern Nigeria, from 1960 onwards, make mention of the studies that provided the data for the calculation of the Morphological Index, and before 1959, Dr. T. Frank Davey had systematized the laboratory techniques on which the Index could be based.

I am, Sir, etc.

S. G. BROWNE.
The Leprosy Study Centre,
17a Willlpole Street, London, W.1.

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1. **Effect of X-Irradiation and Thymectomy on the Development of *Mycobacterium Leprae*, Infection in Mice,** by J. M. GAUGAS. *Brit. J. Exp. Path.*, 1967, **48**, 4, 417-22.

Using the mouse hind foot pad technique first described by Shepard, inocula in the order of 5.0×10^3 *M. leprae* bacteria showed a limited type of multiplication. General immunosuppressive treatment by thymectomy, potential lethal irradiation (900r. in mice then protected by marrow transplantation) or repeated sublethal doses of x-rays (420r.) produced only a slight increase in susceptibility to infection. However, thymectomy combined with 900r. did provide much higher yields of bacteria. This combination led to a maximum 16,800-fold increase of the total initial inoculum number of bacteria from its inception in contrast to a 560-fold increase in untreated controls. The nature of the host's defensive mechanism which then halts multiplication is uncertain. Macroscopic lesions were not found and there was no spread of infection from the site of inoculation.

From the author's summary.

The following 6 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1967, **64**, 7:

2. **Leprosy survey and control pilot project HMG-Nepal,** by I. B. MALI. *J. Nepal Med. Ass.*, 1966, **4**, 4, 330-38.

This work has been carried out in Nepal, where little work has been done on leprosy, and Dr. Mali of Kathmandu reports on his activity in a leprosy survey and the setting up of a control pilot project in Nepal sponsored by Emmaus Suisse. A WHO short-term consultant reported a prevalence of leprosy of 10 per 1,000 but Dr. Mali found a prevalence of 5.7 per 1,000 in a village survey and 1.5 per 1,000 in a school survey. (In spite of these diverse figures it is probable, in the abstracter's opinion, that the final figure will be in the neighbourhood of 10 per 1,000 based on experience in other parts of the world where surveys have been done.) The number of patients attending for treatment has already increased greatly.

This pilot study is laying a good foundation for a controlled scheme and the success of the project ultimately depends on the interest developed by the national staff.

J. R. Innes.

Acid-fast bacilli in the bone marrow of leprosy patients, by A. B. A. KARAT. *Int. J. Lepr.*, 1966, **34**, 4, 415-19.

At the Schieffelin Leprosy Research Sanatorium in South India 413 'consecutive admissions' (apparently not all were untreated patients) were subjected to sternal puncture, 235 of the patients having lepromatous leprosy, 33 borderline, 82 tuberculoid, 10 purely neural and 53 indeterminate leprosy. Classification was based on clinical and histological features. (A more detailed classification such as that of RIDLEY and JOPLING, this *Bulletin*, 1962, v. 59, 790, might be expected in such a research sanatorium.) In 47% of the patients with lepromatous, 15% of those with borderline and 4% of those with indeterminate leprosy acid-fast bacilli (AFB) were found in the bone marrow aspirate, but none were found in patients with tuberculoid leprosy. (The density of the bacilli is not mentioned.) There was no apparent relationship between AFB in the marrow and age, or duration of the disease. It is stated that the higher the Bacterial Index (BI) the more frequently were AFB found in the marrow (but the histogram shows that AFB were found in the marrow of 76% of patients with a BI of between 2.0 and 4.0, but in 68% of patients with a BI greater than 4.0; the number of patients in each group is not reported. There is no statistical analysis of the differences between the groups). Of 8 patients with 'dimorphous' leprosy (presumably the borderline patients referred to elsewhere in the paper) who had negative skin smears, 1 patient had AFB in the bone marrow; of 53 patients with indeterminate leprosy who had negative skin smears, 2 had AFB in the marrow; and of 38 with lepromatous leprosy who had negative skin smears, 4 had AFB in the marrow.

It is suggested that bacilli in the viscera may take much longer to be eliminated than bacilli in the skin, and the presence of bacilli in the reticuloendothelial system in patients with negative skin smears may be the explanation of reactivation of the disease. The morphology of the AFB in the marrow was noted, patients with a high BI having a 'preponderance of intracellular rod forms' in the marrow. and the significance of this finding in relation to the fact that the temperature of the bone marrow is usually 2-3°F above the skin temperature is noted (the percentage of evenly stained bacilli in the marrow and skin is not reported). Exacerbation of leprosy was not accompanied by a rise in the incidence of AFB in the bone marrow. 27% of the patients with lepromatous leprosy had a megaloblastic bone marrow.

(This interesting study merits more detailed reporting and analysis, which the author intimates will be forthcoming.)

C. S. Goodwin.

Histoid (high-resistance) lepromatous leprosy, by E. W. PRICE and M. FITZHERBERT. *Int. J. Lepr.*, 1966, **34**, 4, 367-74.

In Ethiopia the histoid variety of lepromatous leprosy (WADE, this *Bulletin*, 1964, v. 61, 673) is not uncommon. Ten patients are described, 3 in detail with photographs and histological reports. The presenting symptom was in each patient facial nodules, resistant to sulphone therapy, with the general condition of the patient being 'good'. Photographs illustrate the usual distribution of the nodules in clusters in the middle of the forehead, on the cheeks, at the tip of the nose and on the chin. The ears were infrequently involved, the eyebrows persisted and the nasal mucosa was less affected than would be

expected from the degree of nasal nodulation. Flattened lesions on the limbs and buttocks are described. The skin adjacent to the nodules was remarkably uninvolved. The characteristic histopathological features of the lesions are listed. The granuloma was composed almost entirely of densely packed macrophages, some with foamy change, and a few lymphocytes were seen. Connective tissue septa occurred in large nodules, the peripheral cells of a nodule lying tangentially, while in pedunculated nodules a capsule of collagen fibres was found. The skin appendages appeared 'resistant' to the granulomatous tissue, although intraneural acid-fast bacilli were seen. The nodules were unaffected by therapy with sulphones, thiambutosine, sulphamethoxypyridazine and ditophal but they responded clinically and bacteriologically to sulphormethoxine (Fanasil, sulphorthomidine). The initial dosage was 125 mgm. weekly rising to 1 to 1.2 gm. weekly after 2 months. Treatment frequently resulted at first in oedema and ulcertaion of one or more nodules. No patients were found to have albuminuria or jaundice. Of 10 patients treated with sulphormethoxine 7 showed notable diminution of the nodules, 1 showed only slight improvement, 1 developed severe ulceration, and 1 who developed severe joint paints showed bacteriological but not clinical improvement. A table summarizes the details of each patient. The pronounced collagen reaction in the nodules is compared with the situation in nodular subepidermal fibrosis. It is suggested that this type of leprosy be termed 'high-resistance' lepromatous (but the appellation histoid has priority and is less restrictive. This report is a significant contribution to the literature of a little-known form of leprosy; but fuller details of the condition are desirable, including the morphology of the leprosy bacilli in the nodules, a more detailed bacteriological index, the lepromin reaction and a longer follow-up).

C. S. Goodwin.

5. **Calcification of peripheral nerve trunk in leprosy. Report of a patient,** by K. RAMANUJAM and G. RAMU. *Lepr. India*, 1966, **38**, 4, 185-90.

Although nerve abscesses in leprosy are 'frequent' in India, apparently no previous report has been made of nerve calcification in an Indian patient with leprosy. After a review of the literature on nerve calcification in leprosy a description is given of an Indian woman who 20 years ago had an erythematous patch over the dorsum of her right foot which subsided without treatment. The right lateral popliteal nerve in the popliteal fossa, and the musculocutaneous nerve in the lower third of the leg anteriorly were thickened and felt bony hard over a distance of 2 inches, and were not tender. There was no motor deficit in the leg or foot. Skin smears revealed *Mycobacterium leprae*, and the lepromin reaction was strongly positive. Histological examination of the musculocutaneous nerve revealed a hyaline homogeneous mass with only a few nerve fibres in one small area. No acid-fast bacilli were seen. Four radiographs demonstrate the calcified nerves. The mechanism involved is suggested to be dystrophic calcification in the wake of abscess formation.

C. S. Goodwin.

6. **Les thérapeutiques spécifiques actuelles de la lèpre** (The specific treatment of leprosy), by J. LANGUILLION. *Med. Trop.*, 1966, **26**, Spec. No., 131-56, 24 figs. on 6 pls.

After a brief but useful historical introduction to the modern treatment of leprosy, this long review summarizes existing knowledge concerning the principal drugs now used against the disease (excluding those employed in reactional states).

Pride of place is accorded to dapsone, and the mono- and di-substituted sulphone derivatives. The mode of action, dosage and toxicity of members of this series of drugs are reviewed, together with practical advice on methods of administration of the oral and injectable forms of dapsone. The results of treatment are briefly catalogued. The section on thiambutosine provides unexceptionable data arranged along similar lines. The author's interest in the long-acting or depot sulphonamides is reflected in the length and authoritative nature of this section, which gives the best (if somewhat over-enthusiastic) résumé available of the use of this series of drugs. An excellent selection of paired photographs—'before and after'—follows the letterpress.

As a work of reference, this article is of value in providing a reasonably comprehensive survey of the drugs at present available for the treatment of leprosy. It is of less use as a guide to treatment, and provides neither criteria for critical comparison nor indications for choosing one drug rather than another.

(The author's conclusion that lepromatous leprosy is never cured—a conclusion based on the persistence of acid-fast bacilli in the deep organs—will sound unduly pessimistic to many, while his assertion that the sole test for true cure is the 'negativation' (*sic*) of the Mitsuda reaction is either a misprint (for 'positivation') or an impossible ideal—or both.)

S. G. Browne.

7. **Dapsone assay based on Schiff base formation,** by L. LEVY and L. J. HIGGINS. *Int. J. Lepr.*, 1966, **34**, 4, 411-14.

Dapsone is used in the treatment of leprosy and malaria in doses that result in extremely small tissue and blood concentrations and there is need for a more sensitive method of assay. A method is described, based on the phenomenon of Schiff base formation between 4-dimethylamino-benzaldehyde and dapsone, which is more than twice as sensitive as the commonly used Bratton-Marshal method. A comparison of the 2 methods is made with the use of standards and blood from one patient under treatment with dapsone. The method is admittedly relatively complex, and measures 'free' dapsone only. However, conjugated dapsone is present in only minute amounts and is probably biologically inactive.

S. M. Parrack.

The following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1967, **64**, 8:

8. **Genetic influence in leprosy,** by P. MOHAMED ALI. *Indian J. Publ. Hlth.*, 1966, **10**, 4, 145-55.

This paper shows from studies conducted from the

Central Leprosy Teaching and Research Institute, Chingleput, S. India, that the incidence of leprosy is in part genetically determined. During the past 4 years a census survey in a heavily infected district of Madras State in a population of 200,000 showed that factors like sanitation, housing conditions, economic status, literacy, nutrition, had no significant influence on the incidence of leprosy; there was no correlation between the patients and the size of the family; and there is no basis for the theories of adult insusceptibility and the necessity of prolonged contact for contracting the disease.

The following facts are cited in support of the genetic theory: 1. The significant difference in the sex ratio vis-à-vis lepromatous leprosy particularly. 2. The 2 decisive periods when infection was found to occur. 3. The greater concordance among the monozygotic twins in the incidence of the disease. 4. The tendency of the disease to cling to families. It is concluded that there is a dual aetiology for leprosy—infection with *Mycobacterium leprae* and an inherited individual susceptibility. Certain suggestions with regard to anti-leprosy campaigns in the light of a genetic basis for the disease are also given.

J. R. Innes.

9. **Incubation period of leprosy,** by K. V. N. Prasad and P. Mohamed Ali. *Indian J. Med. Res.*, 1967, **55**, 1, 29-42.

'1. The data collected on the multiple-patient families during the course of a general leprosy survey in the Chingleput District of Madras State are utilized in the estimation of the incubation period of leprosy.

'2. The changes in the incubation period are studied in relation to the sex and type of leprosy of the Index patients and age and sex of the secondary patients.

'3. The incubation period is the same whether the index patient is male or female.

'4. Although no clear-cut significant results are obtained in all patients, a consistent difference is observed in the incubation periods between the 2 sexes, always being less in females.

'5. There is an association between the age and the age at onset of disease in an individual and the incubation period is more in adults when compared to children.

'6. In all the categories considered, the incubation period is longer with lepromatous type index patient when compared to the non-lepromatous index patient.

'7. Though there is no significant difference between the estimates of the incubation periods among the corresponding categories of the secondary patients in 2 types of index patients, we observe a notable difference between the estimates in the 2 types. Since the significance is not clear, it is difficult to explain the observed difference on the basis of the available data.

'8. The incubation period is the longest in the case of adults having lepromatous type of leprosy as index patient, its value being 85.3 months.

'9. The incubation period is shortest in the case of female children having non-lepromatous type of leprosy as index patient, its value being 29.6 months.'

10. **Leprosy prophylaxis,** by P. Fasal, E. Fasal and L. Levy. *J. Am. Med. Ass.*, 1967, **199**, 12, 905-8.

At the Leprosy Clinic of the U.S.P.H.S. Hospital in San Francisco during the last 7 years 198 family contacts of patients with lepromatous leprosy have been examined, and 16 have developed leprosy, an attack rate of 8.08%. The previous policy of 'watchful waiting' has now been changed to a programme of BCG vaccination of all contacts, except those with 'large' tuberculin reactions or pulmonary lesions found by chest radiography. Repeated tuberculin testing with revaccination of non-converters will not be carried out. The reasons for this new policy are delineated. The relative value of prophylaxis with dapsone or BCG is discussed. The reduction of the risk of infection by 51.2% with the use of prophylactic dapsone in bacilliferous leprosy contacts (Dharmendra *et. al.*, *Lepr. India*, 1965, v. 37, 447) is compared with the reduction of the risk of infection by 79.9% when BCG was given to contacts of all forms of leprosy (this *Bulletin*, 1966, v. 63, 413). An analysis is also made of 3 other, admittedly incomplete, studies of BCG prophylaxis when the reduction in risk of infection ranged from 88%-95.5%. The suppression of multiplication of *Mycobacterium leprae* in mouse footpads by BCG (this *Bulletin*, 1965, v. 62, 880) is cited in support of the BCG policy. (No other reports on dapsone prophylaxis are mentioned.)

C. S. Goodwin.

The following 3 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1967, **64**, 9:

The etiology of erythema nodosum leprosum, by J. H. S. Pettit and M. F. R. Waters. *Int. J. Lepr.*, 1967, **35**, 1, 1-10.

'An appeal is made for recognition of patients of erythema nodosum leprosum and designation as such. A study of 60 patients of ENL has confirmed earlier suggestions that the reaction appears only when the great majority of leprosy bacilli in the patient's tissues are no longer viable. This, in conjunction with other findings, emphasizes the fact that incrimination of the sulfone drugs as the causative agent of the reaction is untenable. Therefore the cessation of sulfone treatment during the course of ENL is not only illogical but is potentially dangerous to the patient's progress in that it allows any residual viable bacilli to propagate and extend a previously controlled infection.'

(There is a full reviewed discussion of the literature, with 45 references.)

12. **Erythema nodosum leprosum in borderline leprosy. Report of a patient,** by A. B. A. Karat, C. K. Job and S. Karat. *Int. J. Lepr.*, 1967, **35**, 1, 17-24.

The authors describe a patient with borderline leprosy who developed erythema nodosum leprosum (ENL) during a phase of exacerbation of the disease. Previously it was thought that ENL does not occur in this form of leprosy and this is the first report of the association of ENL with borderline leprosy. The paper is well illustrated with photographs and photomicrographs.

J. R. Innes.

13. **The treatment of eythema nodosum leprosum with B663. A controlled study,** by J. H. S. Pettit. *Int. J. Lepr.*, 1967, **35**, 1, 11-16.

The author has tried to establish a method whereby controlled investigations may be used to assess the value of a treatment in erythema nodosum leprosum (ENL). He studied severe cases which needed a high dosage of anti-inflammatory hormones and found evidence that the riminophenazine derivative B663, in a dosage of 100 mgm. daily for 6 days a week over a period of 14 months, had no dramatic effect on the alleviation of ENL, and that the cessation of sulphone therapy does not demonstrably speed the diminution of the reaction. The results are compared with those by Browne (this *Bulletin*, 1965, v. 62, 421; 1966, v. 63, 1344) in Nigeria who was using 3 times the dosage given by the present author.

J. R. Innes.

The following 4 abstracts are reprinted, with permission, from *Trop. Dis. Bull.*, 1967, **64**, 10:

14. **Über filamentös-myzeliale Globi des** *Mycobacterium leprae* (Filamentous-mycelial globi in *Mycobacterium leprae*), by V. Aplas. *Zentbl. Bakt. I. Orig.*, 1967, **202**, 4, 497-502.

The author has examined a cutaneous lepromatous lesion in frozen sections stained by his modification of prolonged staining with Giemsa. By this method extracellular globi of filamentous and mycelial forms, resembling actinomyces were demonstrated. These forms were shown to be non-acid-fast, were chromophobic and did not stain by the usual histological methods. They were demonstrable by prolonged Giemsa stain, by Sudan black, and in unstained sections could be shown as doubly refractive by polarized light.

(This observation was made on a single patient. It would be interesting if it could be confirmed on a series of patients.)

R. L. Vollum.

15. **Blood groups and leprosy,** by F. M. Salzano *J. Med. Genet.*, 1967, **4**, 2, 102-6.

This is an analysis of published work, with some 50 references. The author concludes that there is no indication 'of any differential susceptibility to leprosy or its form among the carriers of different ABO and Rh phenotypes. In relation to the ABO system the data are sufficiently numerous to rule out any important contribution of genes in this system to the variance in this attribute. Information concerning other systems is still too scarce and need not be considered here.'

16. **Leprosy and ABO blood groups,** by G. Singh and D. Ojha. *J. Med. Genet.*, 1967, **4**, 2, 107-8.

'ABO blood groups were studied in 633 leprosy patients and compared with 2,583 controls. No relation between blood groups and susceptibility to disease was observed. Lepromatous and non-lepromatous groups of patients did not differ significantly as regards pattern of ABO blood groups.'

17. **[Histological study of the derma in patients with leprosy during treatment,]** by K. P. Popov and Gia-Kulen Nguen. *Vest. Derm. Vener.*, 1967, **41**, 5, 27-30. (In Russian.)

The English summary appended to the paper is as follows:—

'The authors examined 205 patients with leprosy, of whom 62 were over 7 years from the onset. Histologic changes in the derma after treatment with DDS, rimiphone, streptomycin, novocaine and penicillin are described. As a result of treatment sclerosis of the derma is formed and leprous infiltrates are resolved, indeterminate leprosy yielding to treatment readily while lepromatous leprosy is more difficult to treat.'

sII4, d5 ds5hC

The Flowering Wilderness, by Wilfred H. Russell, B.A., 88 pages, 31 illustrations, published by The Leprosy Mission, 7 Bloomsbury Square, London, W.C.1., price 3s.

'The Flowering Wilderness', with a foreword by Sir Maurice Hallett, G.C.I.E., K.C.S.I., is a fascinating account of the growth and development of the Faizabad Leprosy Home and Hospital in India, from its formal opening in 1938 to the celebration of its Silver Jubilee. It is recommended for careful reading about good work for leprosy. If Gandhi were alive today he would delight in this work and carefully read it.

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