Lepr. Rev. (1974), **45**, 334-341

Leprosy and the Community

LEPRA–LEPROSY CONTROL PROGRAMME, MALAWI ANNUAL REPORT 1973

1973 was the eighth year of the comprehensive leprosy control project organized by LEPRA in Malawi with Dr B. D. Molesworth as Director. Dr Molesworth's annual report for 1973 includes the following.

GENERAL

The whole approach to leprosy work in Malawi has undergone a radical change and various projects which had been under discussion for some time became realized. With the visit of Mr F. Harris, Director, LEPRA London, in March, all facets of the work were discussed and in the outcome virtually the whole country can be brought under close coverage.

In general terms:

(i) The Northern region work will become the responsibility of LEPRA and to this end a group of houses were purchased from Messrs W. & C. French Ltd, who were relinquishing them on completion of their contract. These are at Chilumba, on the Lake shore, 40 miles south of Karonga. This will make an ideal headquarters for the work which, in the first phase, will be in the Chitipa, Karonga, Chilumba and Rumphi districts. Dr Gjalt is in charge and moved there in October.

(ii) The Central Region is the site of a new scheme for the outpatient treatment of both leprosy and tuberculosis. This work is being undertaken with the co-operation of D.A.H.W., The German Leprosy Relief Association, and is financed by them with the assistance of the Order of Malta, and LEPRA being responsible for the field work. This is a very important advance and, if proved successful, could completely alter the approach to tuberculosis treatment in the country. Dr Warndorff is in charge and began work there in July. At present the project is confined to the districts of Lilongwe (the new Capital) and Mchinji, but will expand to the rest of the Central Region. The Leprosarium at Kochirira will provide ward accommodation and will be the base for one mobile unit. At Mua the Mission Leprosarium has begun mobile work in the surrounding area and the wards are to be improved while the "residential" accommodation is reduced and finally discontinued. Mua is on the railway and is now connected with a good bus service to Balaka.

(iii) South of these areas and north of the original LEPRA project area, the country is divided north to south by the Lakes Malawi, Malombe, and the Shire River. The new leprosy hospital at Balaka, built by the Daughters of Wisdom, is now operational and Dr Krenzien is in charge. One outpatient circuit is already in action and a second is planned which between them will cover the land to the west of the divide, the work based on Likwenu and

started and run by Mr Walters, will continue, and will expand northwards to include all Malawi territory to the east of the Lake/River division. The wards at Likwenu will be retained while the housing accommodation will be discontinued, and cases requiring surgery or more specialized treatment will be transferred to Balaka. Thus, Balaka will be seen to be at the hub of road and rail communication and forms the centre of this large and densely populated area of work.

(iv) To the south again comes our original project area now reaching the stage of integration with existing health facilities but over which we shall retain surveillance.

(v) Finally, the very difficult area of the Lower River (Shire) which has become the care of the Seventh Day Adventists, using their leprosy wards at Malamulo, and setting up outpatient work in the valley.

All this work will be coordinated by LEPRA working in close collaboration with the Ministry of Health.

PROJECT AREA

As the case load has diminished, it has been possible to modify the original circuits with push bicycles being used (three replacing one Land Rover), and in charge of three cycles is a Medical Assistant using a motorcycle. This has proved successful and the more personal approach has shown in the attendance figures. The work of reviewing and, where possible, discharging, has continued.

NORTHERN REGION

Since Dr Gjalt only moved to his headquarters at the end of October, the work has been largely one of settling in and becoming acquainted with the area and the people. This has been mostly confined to the coastal area from Chilumba to Karonga. Staff and equipment have been gradually built up and the radio link has proved of great value.

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CENTRAL REGION

This part of the work is now six months old. Housing and temporary office accommodation were obtained and vehicles arrived from U.K. Work has begun on the new Centre. Progress has been made in the localizing of both leprosy and tuberculosis patients, somewhat hampered by hold-up in the secondment of staff due to the outbreak of cholera requiring all available health personnel. Mobile treatment runs are being planned which include both leprosy and tuberculosis patients. The role of Mua Leprosarium has already been mentioned.

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BALAKA

With the arrival of Dr Krenzien in June, the outpatient work is on a firmer basis with known "cases" being reviewed and new admitted. Hitherto these had not been seen by a doctor. Half the ward accommodation was given over to cholera cases owing to an explosive outbreak in the area.

Vehicles are available and a second circuit is planned westward to the border.

LIKWENU

Whilst Mr Walter has continued to run the leprosarium and the outpatient

circuit attached, preliminary planning has been undertaken for the extension of the work northwards. Money was made available for capital expenditure from a legacy in America and half the recurrent costs have been promised by the American Leprosy Mission with LEPRA underwriting the remainder. Mr Walter is due to retire early in 1974 and Mr Buller will take over his work and that of the extension.

LOWER SHIRE

This has proved a problem area. The preliminary work was encouraging and then lapsed owing to the attempt to cover too much ground to start with. Then in October cholera broke out making movement very difficult. At this time, Mr Howson went on leave. Fortunately, Mr Knutsen, a final year medical student from Oregon, was able to give four months service during which two runs were worked out and a great deal of village work done. This has proved a most valuable start and the methods can now be extended.

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STATISTICAL REPORT

Total cases registered	13,027
Still on treatment register	6,246
Total discharged by end of 1973	2,574

Patients charted

1973	1972	1971	1970	1969	1968	1967	1965 & 1966
536 (4%)	635 (5%)	806 (6.5%)	1022 (8%)	1243 (10%)	2335 (18.5%)	2918 (23%)	3532 (29%)

Patients under treatment by sex and class

Lepromatous		Non-lepromatous		Total
male	female	male	female	
1251(20%)	704(11%)	1741(28%)	2550(41%)	6246

New cases 1973 by sex and class

Lepromatous		Non-lepromatous		
male	female	male	female	
101(21%)	48(10%)	157(32%)	176(37%)	482

(54 cases previous treated but unregistered brought this total to 536.)

The trend in 1972 has continued. New cases are now only 4% of the total. Patients under treatment have fallen in numbers as a result of discharges, mostly of tuberculoid cases. This has led to an increase in the lepromatous rate and the male rate.

Participation in two general hospital skin clinics has led to the discovery of 197 cases of leprosy.

SCHIEFFELIN LEPROSY RESEARCH SANITORIUM, KARIGIRI, S. INDIA ANNUAL REPORT 1972-73

The Schieffelin Leprosy Research Sanitorium, for the past 19 years the principal research centre of the Leprosy Mission, is one of the leading leprosy research and teaching institutions in India. Its annual report for 1972-73 lists 29 papers

contributed to scientific journals during the year. It is not surprising that at the centre where Paul Brand undertook some of his historic work, there should be a continuing emphasis on the surgical aspects of leprosy, both reconstructive and preventive. Under the leadership of Dr D. A. Ranney, 266 orthopaedic and plastic operations were carried out, while the Department of Physiotherapy and the Orthopaedic and shoe workshops both continued their large scale and varied activities. On the medical and laboratory side, Professor Job's relationship with the hospital has continued, and every department has indeed set the highest standards in a research orientated hospital.

The extensive leprosy control project in Gudiyatham Taluk, started in 1962, is of particular interest, in that a population of over 400,000 is being kept under continuous surveillance for leprosy in a carefully planned project. In 1970, the estimated leprosy prevalence was 26 per thousand. The first survey of the population was completed in 1966. New cases detected since then are as follows.

Year	No. of new cases	Below 15 years of age	Lepromatous rate (%)
1967	546	37%	11.7
1968	440	38%	10
1969	400	38%	14
1970	963	43%	12
1971	923	38%	11
1972	828	30%	8.6

These figures exemplify the problems of leprosy control in India.

Teaching has been undertaken by all departments, and embraced doctors, physiotherapists, occupational therapists and health workers from several countries.

During recent years the hospital has owed much to the wise and dedicated leadership of Dr P. V. Kurian, and we offer good wishes both to him in his retirement and to Dr Ernest Fritschi who succeeds him.

Field Workers' Forum

TREATMENT OF REACTIONS IN LEPROSY

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Reactions comprise the most serious group of medical complications occurring during the course of treatment of leprosy. Hitherto, their classification has been controversial, the mechanisms of the different types unknown and treatment largely empirical. They have frequently caused prolonged morbidity and hospitalization of leprosy patients, and have often resulted in unsightly scarring and sometimes permanent deformity.

*Reprinted from Proceedings of the 6th Singapore-Malaysia Congress of Medicine, 1971.

Classification and Differential Diagnosis

Collaborative work by the Leprosy Research Unit, Sungei Buloh, initiated in 1967 and still continuing, has shown that the majority of reactions may be classified into two aetiological groups (Waters *et al.*, 1971). The principal points of differentiation are listed in Table 1.

TABLE 1

Comparison between the two main groups of "reactions" occurring in leprosy

	Erythema nodosum leprosum	Lepra reaction
Type of leprosy in which reaction occurs	Lepromatous and small numbers of borderline lepromatous	Whole of leprosy spectrum except polar lepromatous and polar tuberculoid
Relationship to treatment	Treated patients greatly exceed untreated	Untreated ("Downgrading Reaction") patients. Treated ("Reversal Reaction") patients
Manifestations	Crops of painful papules developing in a few hours and lasting a few days. Successive crops may occur over many months or years	Leprosy lesions themselves gradually become swollen and erythematous (new lesions may also appear); reaction lasts for weeks or months
Complications	Neuritis, iritis, orchitis, lymphadenopathy, arthritis, proteinuria	Ulceration of skin, neuritis
Histology	Vasculitis, polymorph infiltrate, fragmented leprosy bacilli	No extraneous infiltrate
Change in leprosy classification	Does not occur	Untreated patients–shift toward lepromatous. Treated patients–shift toward tuberculoid
Aetiology	Immune complex disease	Change in cell medicated immunity against *Myco. leprae*
Suppressed by	Steroids Thalidomide Clofazimine	Steroids Clofazimine

The first group, usually known as *erythema nodosum leprosum* (ENL, lepromatous lepra reaction), occurs in more than 50% of lepromatous and small numbers of borderline- lepromatous patients, principally during treatment. It consists of episodic eruptions of painful red papules, usually accompanied by fever and malaise, and neuritis, orchitis, iritis, lymphedanitis, arthritis and proteinuria may also occur. Histologically there is polymorph infiltrate and vasculitis. We have produced good evidence that ENL is due to the formation of

immune complexes consisting of mycobacterial antigen, immunoglobulin and complement (Wemambu *et al.*, 1969; Waters *et al.*, 1971). The second group, usually named "Lepra Reactions", occur in all types of leprosy save polar lepromatous (LL) and polar tuberculoid (TT). Here the leprous skin lesions themselves are inflamed for many weeks or months; clinically and histologically they are consistent with the type of leprosy the patient is suffering from or developing, and there is no extraneous inflammatory infiltrate. Ulceration of the skin and neuritis are not uncommon complications. In general, the end result of such reactions is a shift in leprosy classification; an untreated patient who develops a lepra reaction becomes more lepromatous ("Downgrading Reaction", Ridley, 1969); whereas treated patients become more tuberculoid ("Reversal Reaction"). There is substantial evidence from our lymphnode studies (Turk and Waters, 1968, 1971; Waters *et al.*, 1971) and from experimental leprosy (Rees and Weddell, 1968) that such reactions are associated with changes in cell mediated immunity against *Mycobacterium leprae*.

Treatment of Severe Reactions

The following recommendations summarize 12 years experience and six controlled clinical trials in reactions performed at the Leprosy Research Unit.

(1) ENL

It is traditional to reduce dosage or to stop completely treatment with dapsone (WHO Technical Report, *Leprosy,* 1966), to give anti-inflammatory drugs and stibophen; and in very severe ENL to give steroids, although the risk of steroid toxicity is great.

We disagree completely with stopping effective anti-leprosy treatment because: (1) We find no evidence that the incidence and severity of ENL is less on low dosage as compared with high dosage dapsone (Waters, 1968). (2) In a double blind study in established ENL, restarting dapsone after a period off anti-leprosy treatment did not result in an immediate worsening of the reaction (Pearson and Helmy, 1973). (3) Even in the most severe prolonged ENL, the reaction always eventually dies away, perhaps after several years, provided that effective anti-leprosy treatment is continued. (4) Prolonged stoppage of dapsone allows the small numbers of persisting viable leprosy bacilli present to multiply, increasing the patient's load of mycobacterial antigen and thereby increasing the total duration of the reaction.

Therefore we continue dapsone in full dosage throughout ENL. If the ENL cannot be adequately controlled by anti-inflammatory drugs and stibophen (i.e. if there is prolonged fever and malaise or if any complications such as iritis or neuritis develop) then there are three alternative regimens.

(A) Dapsone plus prednisolone. Steroids very rapidly control ENL, they can be given to nearly all patients, but because they are usually required in high dosage (e.g. 20-60 mg prednisolone daily, and one patient required 160 mg!) for many months or years they frequently result in significant steroid toxicity, and we have seen several patients with collapsed vertebrae due to steroid osteoporosis.

(B) Dapsone plus thalidomide. Thalidomide quickly and effectively controls nearly all cases of ENL (Sheskin, 1965; Pearson and Vedagiri 1969; Waters, 1971). The drug has immunosuppressive properties, although its exact mode of action is unknown, and there is no dose for dose relationship with prednisolone.

The one toxic effect we have seen is occasional mild allergic dermatitis (easily controlled with anti-histamines); drowsiness is largely avoided by giving the main dose of the day at 4 or 6 p.m. We have no evidence of neurotoxicity, and indeed thalidomide seems particularly valuable in ENL neuritis (Sheskin *et al.*, 1969). It is frustrating that such a generally safe and effective drug, which would enable many ENL patients to return home and to work, cannot because of its teratogenic properties, be given to premenopausal females, and should only be prescribed under most carefully supervised conditions. Initial dosage is 300-400 mg daily, usually reducing to a maintenance dose of 50-200 mg daily.

(C) Clofazimine (B663). This rimino-phenazine derivative has both anti-mycobacterial and anti-inflammatory properties (Vischer, 1969). Therefore it can be given by itself in the treatment of ENL. Although it causes occasional mild diarrhoea it appears to be a safer drug than either prednisolone or thalidomide, is applicable to all patients with ENL, and is especially valuable for out-patient treatment. It has two disadvantages;

(a) it causes a deep red-brown discolouration of the skin, unpopular in light-skinned patients;
(b) it is slower acting than the other two drugs, and may not adequately control the most severe cases of ENL.

Pettit (1967) has shown that 100 mg daily was insufficient dosage for his patients, although Helmy (1971) has found good response with 300 mg daily in a less severe group of patients. The dose should not exceed 400-500 mg daily (Working Party, 1969) and if this fails to give adequate control then additional treatment with small doses of either prednisolone, or (in male patients) thalidomide should be given.

In summary; the treatment of ENL depends on the individual patient's circumstance, but the reaction may usually be well controlled, and many patients are now able to return to work on treatment.

(2) LEPRA REACTION

Adequate treatment is important, as patients may rapidly develop ulceration of the skin, leading to a bad cosmetic result, and neuritis producing temporary or permanent nerve damage.

Effective anti-leprosy treatment should be initiated (in "downgrading reactions") or continued (in "reversal reactions"). If anti-inflammatory drugs and stibophen prove inadequate, the great majority of reactions may be quickly and easily controlled with prednisolone in relatively low dosage, e.g. initial dose of 20-30 mg daily, which may usually be reduced to 10-15 mg daily after a few days. Steroids may have to be continued for several months, but toxicity is uncommon.

Clofazimine is also effective in most cases of lepra reactions, although it acts less rapidly than steroids, and may be given as sole treatment or else substituted gradually for prednisolone once initial control has been achieved. But thalidomide has no significant effect, and should never be used in this group of reactions.

UNCERTAINTIES IN TREATMENT

In ENL it is traditional to give the minimum dose of the chosen drug just sufficient to suppress the reaction. However intermittent neuritis may occur, and very rarely renal damage and/or amyloid disease. The possibility that either mono or dual therapy (i.e. clofazimine and/or thalidomide and/or prednisolone) in

dosage above the minimal reaction-suppressive dose may give better long term results is being considered.

In lepra reaction, progressive nerve damage may rarely develop despite treatment with steroids and/or clofazimine in dosage which adequately suppresses all signs of reaction in the skin. This is being investigated.

Nevertheless with the greatly increased understanding of reactions in leprosy obtained within the last three years, both the immediate comfort and the long term prognosis of the reaction patient is very greatly improved.

Summary

From experience gained in the Leprosy Research Unit, Sungei Buloh, over the last 12 years, and from six controlled drug trials, schemes of treatment of the two main groups of reactions in leprosy are described. The importance of continuing effective anti-leprosy treatment in *erythema nodosum leprosum* (ENL) is emphasized. The relative value of steroids, thalidomide and clofazimine in ENL, and of steroids and clofazimine in lepra reactions is discussed.

Acknowledgements

The Leprosy Research Unit, National Leprosy Control Centre, is administered jointly by the Malaysian Ministry of Health and the British Medical Research Council. I am grateful to the Academy of Medicine, Singapore, for permission to reprint this communication.

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Addendum

In a series of recent papers, Godal and his colleagues have produced, good evidence that reactions in polar tuberculoid leprosy, whether treated or untreated, are due to the development of very adequate cell mediated immunity. Therefore the treatment of such reactions is similar to that described for "Reversal Lepra Reactions".

Field workers without indirect access to clofazimine and thalidomide are under a great disadvantage in treating severe ENL. It would appear highly desirable for regional centres to be set up in leprosy endemic areas, possessing adequate supplies of these drugs, to which patients suffering from severe ENL could be referred.

[a] See Helmy, H. S., Pearson, J. M. H. and Waters, M. F. R. (1971). *Lepr. Rev.* **42**, 167.