The Quarterly Publication of
the British Leprosy Relief Association

LEPROSY REVIEW

VOLUME XXXVIII NO. 1 JANUARY 1967

PRINCIPAL CONTENTS

EDITORIAL OFFICE
6 HILLCREST AVENUE, PINNER, MIDDLESEX, ENGLAND

Single Issue 10s. 6d., plus postage

Annual subscription £2 sterling, (U.S. $6)

Registered Office of British Leprosy Relief Association
8 PORTMAN STREET, LONDON, W.1

LEPROSY REVIEW

VOLUME XXXVIII NO. 1 JANUARY 1967

Contents

All communications re *Leprosy Review* and all subscriptions should be sent to the Editor.

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Editorial Office: 6 Hillcrest Avenue, Pinner, Middlesex, England

Printed by Rawlinsons (Printers) Ltd., Northwood, Middlesex, England

Editorial

1. LEPRA LEPROSY CONTROL PROJECT IN MALAWI. On 20 October the General Secretary of Lepra, Air Vice-Marshal W. J. Crisham, C.B., C.B.E., attended in Blantyre, Malawi, the ceremony of the laying of the Foundation Stone of the Lepra Leprosy Control Project centre building by President Banda of Malawi. We are glad to quote from *The Times* of London their comments about the event.

'*From our own Correspondent—Blantyre, Oct.* 19.

President Banda will tomorrow lay the foundation stone of the British Leprosy Relief Association's control centre in the grounds of the Queen Elizabeth Central Hospital, Blantyre, and thus consolidate a scheme which will lead a world drive against leprosy.

The project, which will cost £42,000 a year, is being financed by voluntary contributions from the British public.

A report of a survey said the scheme would point the way to the long-term solution of the world leprosy problem. "This problem, far from diminishing, is most likely increasing, despite all efforts by governments, missions and other organizations", it said. "In the world as a whole today, only one leprosy sufferer out of every five has any chance of receiving treatment."

More people than ever before were subject to overcrowding and low standards of hygiene, which contributed to the spread of the disease, the report added. The Malawi project was an important step forward.

10-year aim

The project area has a population of a million, which includes 10,000 leprosy sufferers, and the aim of the control centre is to eradicate leprosy from Malawi within 10 years. Among the guests at tomorrow's ceremony will be Air Vice-Marshal W. J. Crisham, the association's general secretary, who said: "We plan to demonstrate to the world from Blantyre that leprosy can be cleared from an endemic area. Thanks to President Banda's knowledge and understanding of the problems involved, we should be able to do valuable work for the whole of mankind."

The unit will function under Dr. B. D. Molesworth, the leprologist, who will send out teams to identify all infectious patients in villages and treat early patients to prevent deformity.

Our Medical Correspondent writes:—

The Blantyre leprosy centre is the latest development in an imaginative campaign sponsored by The British Leprosy Relief Association. The southern region of Malawi has been chosen for the project, which was launched in May last year and was endorsed by the World Health Organisation, because it offers the required number of leprosy patients in a compact and readily accessible area. A further factor in favour of Malawi was the interest shown by Dr. Banda.

Not the least significant feature of the scheme is that it puts leprosy at the centre of the medical services of the country—and not at the periphery in inglorious isolation as has so often been the case in the past, and still is in too many countries.

As treatment will be largely on an out-patient basis carried out by mobile teams there are only 36 beds in the centre. In addition it will provide laboratory, physiotherapy and research facilities. Among its other important activities will be the training of Africans in anti-leprosy and laboratory work.'

In his speech President Banda paid tribute to the British Leprosy Relief Association for their vision in planning this Project and to the Brown Memorial Trust Fund for providing the money for the buildings to house the Project. He recalled that Malawi lies in the leprosy belt of the world and all Malawians can remember people in their villages who suffered from leprosy and for whom nothing could be done even by witch-doctors. Fortunately for the leprosy sufferers medical science can now do a great deal and this Project hopes to reach as many of these people as possible and treat them, and the President called on everyone in Malawi to co-operate with the staff of the Project so that this scheme 'will not only serve as a treatment centre but also a spring or fountain of hope for thousands and thousands of people who otherwise might be doomed'.

Our Prayers for Malawi. At this juncture when the Project in Malawi has had the Foundation Stone laid and is about to begin active work, it is fitting that all who believe should start and continue with prayer for the grace of our Lord and success to the whole project in bringing solid aid to leprosy sufferers.

We publish the report of the visit of the General Secretary, Lepra, to Malawi on p. 63.

2. ELEP. An important step forward in the struggle against leprosy in the world was taken

at Berne, Switzerland, on 24 and 25 September, 1966. A meeting of representatives of some 11 Leprosy Societies (from Switzerland, Germany, Belgium, Britain, France and Italy, with an observer from Scandinavia) decided unanimously to recommend to their various home councils that a Bureau for Co-ordination should be established. This Bureau would act as a clearing-house for disseminating information about anti-leprosy activities and projects, and would attempt to prevent duplication of effort in leprosy work.

The Headquarters of the Bureau would be established in Brussels, and Monsieur Pierre van den Wijngaert was appointed Honorary Secretary. The expenses of equipping and running the Bureau would be borne by member-organisations. Other voluntary Societies in Europe, with similar aims, would be welcomed as members of ELEP.

A Medical Commission (consisting of Drs. S. G. Browne, Fr. Hemerijckx, M. Gilbert, together with L. P. Aujoulat) was appointed to advise ELEP on professional matters, especially on priorities in leprosy projects and on possible areas of joint action.

Any move designed to harness the tremendous amount of active goodwill towards leprosy sufferers must be welcomed. Voluntary agencies still have an indispensable role to play in the struggle against leprosy, channelling as they do both considerable financial resources and dedicated persons into places where these can be valuably utilised.

3. RECENT FRUITFUL TRAVELS OF DR. S. G. BROWNE. Dr. S. G. Browne, O.B.E., has recently completed a tour, sponsored by The Leprosy Mission (to which he is Medical Consultant), that has taken him from London to Korea via Ethiopia, and back.

In Addis Ababa he took part (together with Professor Paul Brand and others) in negotiations concerned with the All-Africa Leprosy Rehabilitation and Training Centre, and attended the Annual Meeting of the Board of Directors.

Immediately after these meetings, he took part in the Second Seminar on Rehabilitation in Africa, organised by Professor Oscar Barry of the Haile Selassie I University Medical School. Drs. Felton Ross and Pfaltzgraff also presented papers on various aspects of leprosy. Professor Brand and Dr. Price contributed to the lively and fruitful discussions, and Drs. Antia and Dastur and colleagues presented their findings on nerve lesions in leprosy.

From Ethiopia, Dr. Browne flew to Korea via Hong Kong. Both in Taegu and in Seoul, he conferred with leprosy workers and lectured to professional audiences. With colleagues working with The Leprosy Mission, he visited the Mission's excellent installation adjacent to the Taegu Medical School, and discussed the future pattern of collaboration between the Mission and the University and Government authorities.

He stayed for a short time at the Isle of Happy Healing, near Hong Kong, and advised on various aspects of the leprosy programme both on the island itself and in Hong Kong, where the Department of Health is grappling with the problems posed by leprosy patients who no longer present viable forms of *M. leprae* in their skin but who require prolonged periods of supervised treatment.

From Hong Kong, Dr. Browne flew to India, where he advised on future policy in the Purulia district, where Dr. Ernest Muir did some of his finest work. From the parched plains of northern India to the flooded paddy-fields of the south proved a rapid and dramatic transition. In Madras, Dr. Browne visited Karigiri and Vellore, conferring with medical and surgical colleagues and proffering advice to enhance their excellent work in various fields.

An all-too-brief visit to the All India Leprosy Research and Training Institute at Chingleput, where he took part in a seminar with all the senior staff, completed the tour.

After a few days in England, Dr. Browne took off again: this time to Eastern Nigeria, where he plans to review and assess the patients taking part in the drug trials he initiated in the leprosy settlements associated for this purpose with the Research Unit at Uzuakoli.

4. Subscribers to *Leprosy Review* are reminded that payment is now due for 1967, Vol. 38. Please remit as soon as possible to the Editor, *Leprosy Review*, 6 Hillcrest Avenue, Pinner, Middlesex, England. The January issue will be mailed to all regular subscribers, but subsequent issues cannot be mailed until payment is received for the full subscription for the year.

IMPORTANT NEWS

5. Forthcoming Ninth International Congress of Leprology. Dr. S. G. Browne, Secretary-Treasurer, International Leprosy Association, has asked us to insert the following notice:—

The Ninth International Congress of Leprology will be held in London in 1968, from September 16 to 21. This preliminary notice is published so that all intending participants will be able to make their plans accordingly. Details of the programme will be published as soon as they have been decided by the Council of the International Leprosy Association. Simultaneous translation will be provided in English and Spanish.

S. G. Browne,
Secretary-Treasurer,
International Leprosy Association.

Lep. Rev. (1966) **38**, 1, 7-10

Drug Trials in Leprosy

some unemphasized factors

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Perusal of the voluminous literature on drug trials in leprosy is liable to produce all too often the impression that any drug has a great variability of therapeutic action: there is a disturbing imprecision and lack of uniformity of criteria. Apart from certain obvious reasons, such as small series, pairing difficulties, retrospective controls, inadequate period of observation, etc., these wide variations may be due to hitherto unemphasized causes, which will form the subject of this paper.

In drug trials, we are not only concerned with academic considerations but also with the practical problems of treatment of the individual suffering from leprosy. Fortunately at this stage we need enter into no theoretical speculations regarding the precise mode of action of the drugs employed. It is possible to investigate the effectiveness of a given drug and determine its place in therapy without having first answered the innumerable questions that plague the biochemist, the immunologist and the epidemiologist.

Although non-lepromatous leprosy is probably commoner in the world as a whole than lepromatous, it is the latter that constitutes the greatest challenge from most points of view, and for drug trials it is essential that the participating patients should be suffering from this form of leprosy. If a drug is to be effective in leprosy, its effectiveness must be conclusively shown in the lepromatous form. A drug effective in multibacillary disease may also accelerate clinical clearing of lesions in paucibacillary forms. To become a practical alternative to existing drugs, a new drug must show its superiority in no uncertain way—economic considerations quite apart. A merely marginal advantage in reducing somewhat the contagious stage of the disease, or in shortening slightly the total time of treatment necessary, or in diminishing the incidence of complications in no very definite way—this marginal advantage may admittedly indicate a limited usefulness in selected patients (for example, as a second-line drug in cases of intolerance or proved resistance), but cannot indicate that it will have a place in the treatment of a global disease affecting many millions.

In non-lepromatous disease, the varying degrees of tissue reaction to the infection—ranging from hypo-ergy to hyper-ergy—are frequently unstable and unpredictably changeable, and constitute an unknown series of variables in any trial; patients suffering from these forms are therefore best excluded from all pilot and restricted trials.

Less obvious in its bearing on therapeutic results is the kind of lepromatous leprosy and the extent and depth of the subcutaneous granuloma involved. These factors may be directly related to the duration of the infection in the individual; they are also related to the rapidity of progress of the infection and of the tissue reaction to the infection. As a result, the sheer mass of the granuloma, replete as it is with mycobacteria in globi, that must be acted upon in some way by the therapeutic agent, varies tremendously from patient to patient. Moreover, the obvious clinical appearances—macular, nodular, or infiltrative—may by no means run parallel with the amount of granuloma as revealed by histological examination. Thus, a series of trial patients may be excessively weighted in either direction, and neither careful clinical examination nor simple bacterioscopic

findings (by the slit-smear technique) nor even the histology of a few biopsy specimens (possibly atypical) may reveal the true overall picture of the extent of the tissue changes due to leprosy in the individual patient. The effectiveness of a drug may thus be masked by the mass of granuloma to be effected, and a real and marked reduction in the concentration of *M. leprae* may fail to be indicated by the bacterial index as ordinarily determined. Another aspect of the same problem concerns the concentration of bacilli in the depths of the sites smeared; the material actually examined, obtained as it is by the hazardous method of smearing, may be unrepresentative and thus give misleading impressions of the rate of decline of the index.

These considerations apply especially when results of drug therapy from Africa are compared with those from, e.g., South India, or the Philippines, where lepromatous leprosy is on the whole more severe, more resistant to therapy, more subject to reactional episodes, and more likely to be accompanied by severe eye and nerve complications. The granulomata are more succulent and florid, and the response to standard drugs as well as to newer drugs is apt to be less good than in Africa.

Degenerative changes in the bacilli indicative of non-viability may provide earlier information and more useful pointers to the effectiveness of a drug than the bacterial index; but here again, standard smearing procedures do not always produce consistent or uniform or comparable results. It may be that bacilli in different situations in the body or at different depths in the granuloma are affected to different degrees by the medication or by the complex tissue response consequent on therapy—to put it no more precisely than that. A higher proportion of bacilli from the nasal mucosa may continue to stain as solid rods than those from ear-lobes or skin.

Standard smearing techniques fail to reveal persistent foci of morphologically normal bacilli located in nerve trunks and deep organs (lymphatic glands, liver, bone marrow, etc.), which represent concealed and inapparent concentrations of viable bacilli from which reactivation of the disease may occur. Histological examination of the deep cutis may furnish suggestive evidence—in the presence of viable bacilli in the nerve fibrils—or in the endothelial cells of small blood vessels, of the existence of infection of the deeper organs, but it may not do so. Standard techniques do, however, furnish valuable information concerning the slowness of the removal of non-viable acid-fast material from the body, and there is much clinical and histological evidence concerning the immunological importance of the presence of dead matter in the tissues.

Another aspect of this problem concerns the notation employed to indicate the degree of improvement attributable presumably to the drug used. Because of its apparent precision and its arithmetical expression, the bacterial index at each site examined is accorded an importance that outweighs clinical features that are less easily represented numerically. Scales for expressing the bacterial index should be uniform from one country to another. Emphasis on the bacterial index presumes a bactericidal or bacteriostatic action of the drug investigated, which may be a fact, but which is by no means the whole explanation of its action or a precise indication of its value in limiting or reducing the complex tissue response to acid-fast foreign matter, living or dead. Thus, reduction of the generalized lepromatous infiltration may be a valuable indication of the success of chemotherapy, but this is difficult to indicate precisely by any one criterion, or by any combination of the recordable data at our disposal—clinical, histological, photographic. The human memory cannot retain accurate picture images of more than a limited number of patients under trial, say 30 or so.

Another little-appreciated factor causing variation in the therapeutic response is the phase of the leprosy process that happens to be in the ascendant when treatment is initiated. There is some spontaneous variation in the concentration of *M. leprae* in the skin and nasal mucosa, apart altogether from detectable differences between adjacent sites smeared. These variations may be at times correlated

with the waxing and waning in the apparent clinical activity, which is the obvious result of the tissue response. They may also be correlated with the proportions of degenerate forms as seen in slit-smear material examined. In general, the proportion of morphologically normal forms in untreated patients is higher in Africa than in Malaya.

The normal processes of degeneration and phagocytosis may be accelerated by factors other than the drug given. Thus, a trial may be vitiated if a disproportionate number of patients in one or other phase—progressive, or stationary, or regressing—is included; good results may be attributed to the drug in question whereas they are really due to the inherent variability of the disease. The degree of vascularisation and consequential fibrosis of a lepromatous granuloma may also have a bearing on the rapidity of the therapeutic response to a given drug. It is known that in rare cases of untreated lepromatous leprosy, all the bacilli may be degenerate in form, whereas in others all may be morphologically normal. Again, standard smearing techniques may fail to disclose bacilli in undoubtedly active lepromatous disease.

The variation in immunological response provides a parallel in non-lepromatous disease; it is known that during an acute generalized reactional phase in tuberculoid leprosy, the Mitsuda reaction may be temporarily negative—which phenomenon suggests an 'exhaustion' phase comparable with that in lepromatous leprosy, whether erythema nodosum is present or not.

It is not yet possible to do more than suggest that it is unlikely, on the analogy of other mycobacteria, that *M. leprae* should prove to be a single species, without races or strains showing biochemical and pathogenic differences. Such differences, if they are ultimately shown to exist, would go far to explain certain variations in the results of drug trials. Indeed, the possibility will open up of differentiating races or strains of *M. leprae* on the strength of different susceptibilities to chemical compounds, considered of course in relation to the other investigative procedures already in use for cultivable and inoculable mycobacteria.

The influence of hormonal and nutritional states on the course of lepromatous disease is sufficiently well recognized by leprologists engaged in drug trials. Care must be taken as a general rule to exclude children and adolescents, pregnant or lactating or menopausal females, and ill-nourished adults. The mere fact that a recently-admitted patient enjoys a better diet and regular meals, and enters upon a more sheltered life, and often attains an equable mental attitude to his disease—may all possibly have some bearing on the bacteriological and clinical course of leprosy. Such factors, operating inconsistently in small series, may vitiate a therapeutic trial if unrecognized.

The frequency and severity of reactional episodes often disturb the leprologist as well as the participating patient. It is difficult to see how these can be avoided, given the high expectation of such episodes in any series of lepromatous patients, especially the lighter-skinned, and the undoubted effect of anti-leprosy therapy in precipitating or accentuating such reactions. 'Comparable' series may not be comparable from one country to another because of the differing incidence of unpredictable reaction.

The influence of climatic factors operating during the course of a trial has often been suspected, but is difficult to prove. High temperature and high relative humidity may together coincide with the appearance or exacerbation of lepromatous lesions, just as intercurrent disease or pregnancy or parturition may apparently precipitate both leprosy and reactional episodes in lepromatous disease. Similarly, it is conceivable that seasonal variations in the immunological state of individual patients may account for some of the differences shown in one centre as compared with another.

Finally, the controversial subject of drug resistance must be mentioned briefly. Resistant forms of *M. leprae* may theoretically develop either spontaneously or as the result of therapy.

It is now possible conclusively to demonstrate such resistance. True resistance may rarely vitiate trials in small series of patients, but the not infrequent transient reappearance of morphologically normal bacilli may complicate the evaluation of a drug as well as its possible bactericidal role.

Another complicating factor is the occurrence of the different varieties of sensitivity reaction, which may affect up to 3% of patients in some African series.

To sum up, the fact that obvious and serious differences in the results of therapeutic trials do exist, is not a matter of surprise considering all the complicating factors involved; what is surprising, is that a considerable measure of agreement has been attained in different centres in widely differing circumstances.

SUMMARY

Various under-emphasized factors may complicate trials of drugs in lepromatous leprosy, and even vitiate the results. Such factors concern the extent of the lepromatous granuloma, the phase of activity of the disease process, the variability in bacillary concentration and perhaps bacillary morphology from one site to another and from different depths in the granuloma, the complexity of the tissue reaction to leprosy infection, the inherent variability of the disease, etc.

Despite these variables, a consensus of expert opinion may be reached concerning the value of a reputed bacteriocidal or bacteriostatic drug in leprosy.

Lep. Rev. (1966) **38**, 1, 11-14

The Effect of Procarbazine on Leprosy

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INTRODUCTION

Following our experience of the effects of cyclophosphamide on leprosy and on the acute reactions of leprosy (Davison *et al.*, 1964) it was decided at the end of 1963 to investigate the effect of procarbazine on this disease and its complications.

Procarbazine (N-isopropyl-alpha-(2-methyl-hydrazino)-p-toluamide hydrochloride N.S.C. 77213) is a methylhydrazine derivative of established value in the treatment of Hodgkin's disease. (Falkson *et al.*, 1965.) It has been shown to suppress immune reactions (Hoffmann la Roche & Co.) so that even if no antibacillary effect could be predicted, it was hoped that it would suppress erythema nodosum leprosum (E.N.L.).

MATERIALS AND METHODS

Eleven patients, 10 with lepromatous and 1 with reacting tuberculoid leprosy (no patients with borderline leprosy were included in this series) were treated with procarbazine. All patients received concomitant treatment with dapsone (average of 600 mgm. weekly) and 7 patients received intermittent prednisone for E.N.L. The age, sex and main clinical features of each patient as well as previous treatment are shown in Table 1.

At the start of treatment with procarbazine 4 of the 10 patients with lepromatous leprosy were recent admissions and had heavy infiltration of the skin with
nodules. The remaining 6 lepromatous patients had been given standard anti-leprosy therapy for from 107-292 weeks before the treatment with procarbazine was started. In these patients the lepromatous infiltrations were already diminishing, but they suffered from severe and continuous E.N.L.

Procarbazine, 50 mgm. by mouth 3 times per day, was given to the patients until the white cell count fell below 4000 per sq. cm. When the white cell count again rose above 6000 per sq. cm. treatment was resumed. Blood counts were done at weekly intervals. In Table 1 the total dose of procarbazine and the duration of administration is shown for each patient.

RESULTS

Despite the fact that leukopenia was induced in 10 of 11 patients no significant objective improvement was seen in the acute reactions of leprosy. Two of the 6 patients with erythema nodosum claimed that their lesions were less painful during procarbazine administration.

Reacting tuberculoid leprosy can be expected to resolve within months on standard treatment alone so that the improvement observed in patient No. 1 cannot be ascribed to procarbazine. Of the 10 patients with lepromatous leprosy there was marked clinical improvement in patients Nos. 2, 3, 4 and 5 who were new admissions with heavily infiltrated lesions. When procarbazine was discontinued their lesions continued to regress on dapsone alone. No unexpected change was observed in the 6 patients who had already been on treatment for long periods of time and whose infiltrations had already lessened previously.

Although the average bacterial indices† decreased in all patients following procarbazine

* In receipt of a grant from the National Cancer Association of South Africa.

† The bacterial index is calculated as follows: Smears are taken from 4 sites of affected skin. These are graded from ½ (fewer than 10 bacilli in any one slide) to 4+ (hundreds of bacilli per field). The highest possible count would therefore be 16 when the results of the 4 specimens are added together.

TABLE I

RESULTS OF TREATMENT OF LEPROSY WITH PROCARBAZINE

No.	Age	Sex	Previous Treatment: Type of Leprosy	Previous Treatment: Duration in weeks	Previous Treatment: Drugs	Clinical Findings at start	Duration in weeks	Total dose in gm.	Lowest white cell count per sq. cm.	Concomitant Treatment	Results	Average Bacterial Indices: Before	Average Bacterial Indices: After
	44		Reacting Tuberculoid		Dapsone	Heavy spongy macules face, raised macules trunk and limbs	36	17.85	2000	Dapsone	Acute reactions during treatment. Lesions eventually flat and paler	7	0
2	30	M	Lepromatous		Dapsone	Generalized infiltration of skin; many raised plaques	68	56.70	2450	Dapsone	Marked flattening of lesions after 3 months. No reactions	13	10½
3	38	M	Lepromatous	0	None	Heavy infiltration with nodules	38	16.8	2150	Dapsone	Marked clinical improvement after 5 months. One mild reaction (E.N.L.) 14 during treatment. Giddiness	14	13
4		M	Lepromatous	0	None	Generalized infiltration; nodules on face	49	44.1	4000	Dapsone Prednisone	Marked regression of nodules after 7 months. Transient rash apparently due to dapsone. When dapsone temporarily discontinued, mild E.N.L. started	16	13
		M	Lepromatous	0	None	Heavy generalized infiltration with rugae plaques and nodules	62	39.0	2450	Dapsone	Marked clinical improvement after 5 months. Occasional mild E.N.L. from start	16	
	32	M	Lepromatous	168	Dapsone Cyclophosphamide Prednisone	Subsiding generalized infiltration of skin. Severe continuous E.N.L.	36	25.2	2000	Dapsone Prednisone	No significant improvement in E.N.L.		
	48	M	Lepromatous	292	Dapsone Prednisone Thiambutosine Cyclophosphamide	Subsiding generalized infiltration of skin. Severe continuous and ulcerating E.N.L.	36	30.45	4100	Dapsone Prednisone	No improvement in E.N.L. Attacks leprous neuritis	0	0
8	50	M	Lepromatous	208	Dapsone Prednisone Thiamazole Cyclophosphamide	Subsiding generalized infiltration of skin. Recurrent E.N.L.	36	37.8	6050	Dapsone Prednisone	No improvement in amount of E.N.L. E.N.L. less painful		
	60	M	Lepromatous	208	Dapsone Prednisone Cyclophosphamide	Generalized infiltration of skin. Severe recurrent E.N.L.	36	31.5	3150	Dapsone Prednisone	No improvement in E.N.L.	4	
10	25	M	Lepromatous	168	Dapsone Prednisone Cyclophosphamide	Generalized infiltration of skin. Almost continuous E.N.L. and leprous neuritis	36	24.15	2300	Dapsone Prednisone	No objective improvement in E.N.L. but less painful. Neuritis remained severe	2	
11	40	M	Lepromatous	107	Dapsone Cyclophosphamide Prednisone	Generalized infiltration with nodules. Severe E.N.L. and neuritis	22	17.85	2850	Dapsone Prednisone	No improvement in E.N.L. or neuritis. Died of tuberculous bronchopneumonia. White blood count 11,400 at time of death		

treatment, this was not beyond what might have been expected from dapsone alone. The bacterial indices for each patient are shown in Table 1.

One patient, No. 11, died during the time that he was receiving procarbazine. He was not leukopenic at the time of death and post mortem examination revealed lepromatous leprosy and caseating tuberculous bronchopneumonia. The only disadvantageous effect apart from leukopenia was giddiness in 1 patient (No. 3), for which the treatment was stopped.

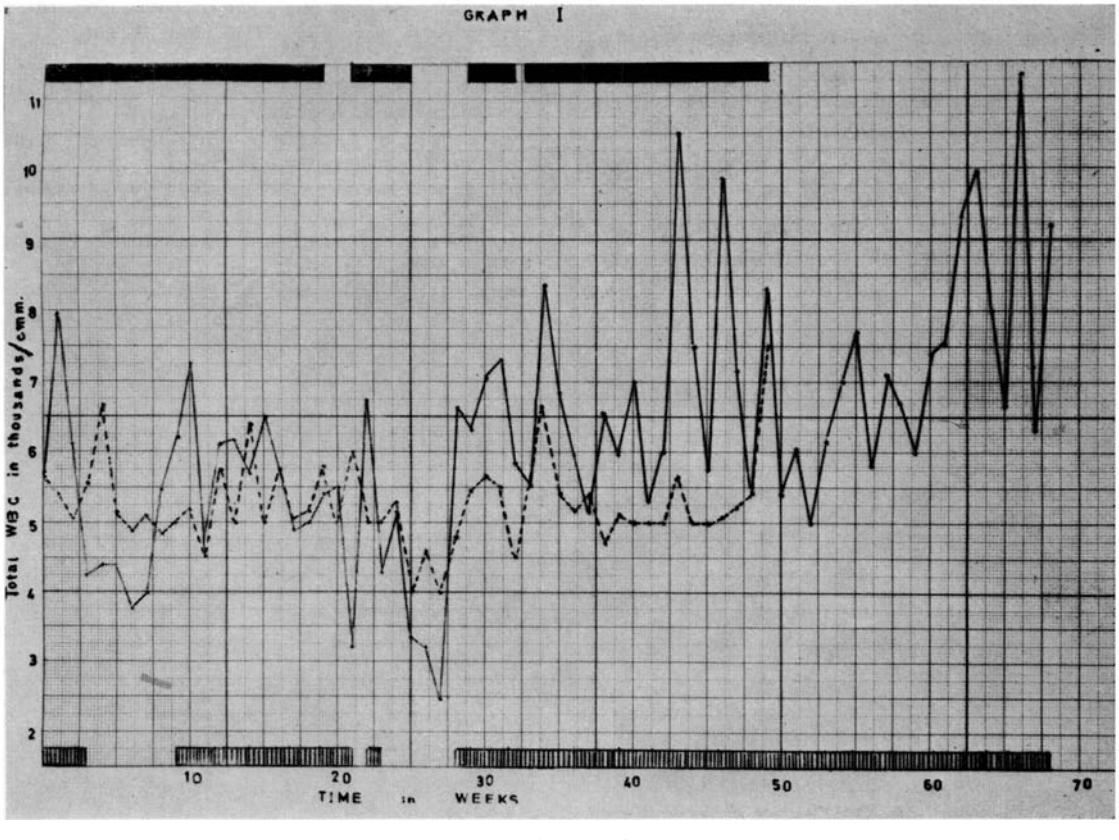
The lowest white cell count for each patient is shown in Table 1. Figure 1 shows the changes in the white cell count during procarbazine treatment in patient No. 2. Dapsone was not found to inhibit the development of leukopenia in patients receiving procarbazine, whereas dapsone inhibits the development of leukopenia in patients receiving cyclophosphamide. (Davison *et al.*, 1964.)

DISCUSSION

Dapsone (sodium 4'-4' diamino diphenyl sulphone) both brings about resolution of the lesions of leprosy and causes the bacilli to disintegrate. This response to dapsone may however only follow after years of treatment in the lepromatous type of the disease. During treatment acute reactions are apt to occur which may be debilitating. Although these reactions also occur without treatment, they are more common and more pronounced during treatment with dapsone. A drug is therefore needed which will cure the disease more rapidly without worsening the acute reactions. Many of the complications of lepromatous leprosy appear to be hyper-reactive phenomena. A drug which could supress these phenomena during dapsone administration would be of value.

E.N.L. is an acute reaction which occurs in about 30% of patients with lepromatous leprosy and occasionally in borderline patients. It is thought to be either the result of an allergic reaction to the breakdown products of leprosy bacilli, or to be a stress phenomenon (Muir, 1962).

Because cyclophosphamide markedly inhibits antibody production (Berenbaum, 1960, 1961 and 1962) a clinical trial with this agent in leprosy started in 1960. It was found that when large doses were used, although the lesions



Legend to Graph I

TOTAL WHITE CELL COUNT AND TREATMENT IN PATIENTS NOS. 2 AND 4

.....White cell count in Patient Number 4.
■ 150 mg. procarbazine/day, Patient Number 4.
▬▬ White cell count in Patient Number 2.
III 150 mg. procarbazine/day, Patient Number 2.

regressed considerably, the bacillary content was not affected. Large doses of this agent did however inhibit acute reactions such as E.N.L. When small doses of cyclophosphamide (100 mgm. per day for from 98-146 days) were administered concomitantly with dapsone, no beneficial effect was observed from the cyclophosphamide.

Recently Mathews and Trautman (1965), after presenting evidence that leprosy has features of a collagen disease, suggested investigating the efficacy of antimetabolites in leprosy. They claimed extremely encouraging results in a limited number of patients following the use of azathioprene and methotrexate in patients complicated by erythematous exacerbation or necrotizing vasculitis.

The immuno-suppressive properties of cytostatic drugs vary with total dose and concentration. Because of the side effects involved in using a high dose of procarbazine (leukopenai, thrombocytopenia, nausea, vomiting, etc.) only a low dosage (150 mgm./day) was thought safe in this trial. Within this dose range no significant immuno-suppressive effects were observed in our leprosy patients.

SUMMARY

Eleven patients with leprosy were given low doses of procarbazine with dapsone from from 22-68 weeks. In 2 of 6 patients with severe recurrent E.N.L. the lesions became less painful, but no objective improvement was observed. In 5 patients with infiltrated lesions, resolution may have been hastened by the addition of procarbazine to standard treatment. Procarbazine did not significantly affect the bacterial indices.

This paper is published with the permission of the Secretary of Health, Department of Health, Republic of South Africa.

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The Classification of Leprosy

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INTRODUCTION

This article is an attempt to add to the recent discussions on the classification of leprosy, especially the contribution by Leiker (1966) and to further develop his thesis, seeking clarification of this important problem. Most recent writers, including Leiker (Ridley 1962, Cochrane 1964) have accepted the basic concept of a spectrum of disease in leprosy. However, there is still a great deal of confusion as to the position of specific cases in this spectrum, and more especially is there confusion in the use of terms which are not universally accepted nor uniformly defined.

Frequently, due to erroneous concepts about classification, workers have come to faulty conclusions about many aspects of leprosy. Such conclusions must be in error if based on wrong postulates and concepts of the pattern of disease. A notable example of this is the recent article 'The Onset and Pattern of Deformity' by Mallac (1966). This is an excellent article attempting to refute the old concepts of 'trophic' causes of disability. But in spite of its being a very real contribution to the literature on disability in leprosy, there still remains the implication of the inevitability of deformity in leprosy. The belief that deformity is some inscrutable concomitant of leprosy that may in any patient suddenly arise to curse his future with an irreparably disabling stigma has not been removed. Dr. Mallac fails to show that this is not the case, primarily because he does not fully acknowledge the direct relationship of disability to the classification of leprosy.

There is a fundamental need to understand the classification of leprosy in order to gain a satisfactory concept of the evolution of disease as well as to understand its epidemiology. In fact, when we shall fully understand the concept of disease manifestations as they relate to host resistance there will undoubtedly be a clarification of our understanding concerning the epidemiology of leprosy; at present an area of considerable speculation and conjecture based on inadequate premises and faulty theories. Much more importantly, adequate case handling and treatment are based to a great extent on a complete understanding of classification for, as Leiker explains, there are a number of aspects of treatment and management which are clarified and simplified by accurate classification.

Let us list those factors relating to management:—

1. Infectiousness. The more resistance there is to the *M. leprae* manifested by the individual, the less likely the bacilli will propagate in numbers adequate to cause an infectious state.

2. Complications. There are certain types of leprosy in which complications are never seen. There are others in which they are greatly to be feared. Specific types of complications are related to specific types of disease, thus complications can be anticipated and usually avoided. Certain reactions occur only in tuberculoid leprosy, and others only in lepromatous. The potentiality can be predicted if we clearly understand the position of a patient on the spectrum of disease.

3. Specific therapy. Due to varying responses to treatment there is need to attack differing types of disease with different schemes of treatment.

4. Duration of treatment is directly related to the severity of the disease, and this is adequately depicted in a proper classification.

5. Prognosis of a patient can be more accurately predicted when there is full understanding of the exact placement in the outline of classification.

SOLUTIONS TO THE EXISTING PROBLEMS IN CLASSIFICATION

In the following suggestions there is little, if any, new subject material, but rather an attempt is made to take accepted facts and co-ordinate them into a unity of understanding in order to form a connected and logical whole.

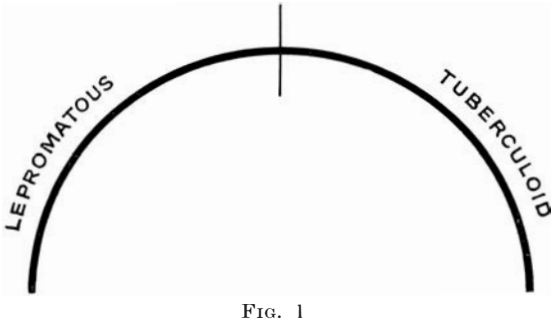

FIG. 1

First, since it can be accepted that there is a spectrum of disease, let us make a diagram to express that as in Fig. 1, with the lepromatous portion to the left and the tuberculoid to the right. It is possible to divide essentially all cases of leprosy into these two categories, but it leaves far too much confusion and would be of relatively little help in clinical management. A still simple classification, but slightly more helpful, includes a third and intermediate group of cases between the lepromatous and the tuberculoid, which it seems would best be called dimorphous (see below), having manifestations of both polar types of disease, Fig. 2.

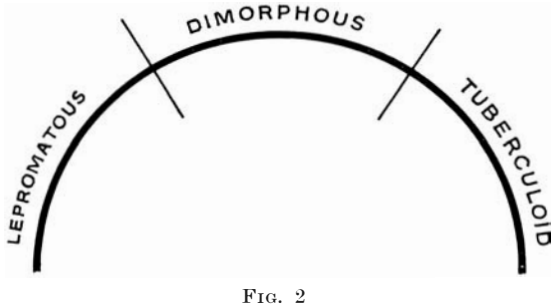

FIG. 2

There are several factors which have at times been implicated as the etiology of the variations in the manifestations of leprosy. The three most commonly discussed are the host, the bacillus and the environment. The last of these is perhaps the easiest to rule out. It is very doubtful if there are variations in leprosy that are due to a geographic differential *per se*. At times it has been suggested that perhaps there are differing strains of *M. leprae*, and this would be a means whereby there could be varying manifestations in different geographic locations. However, there is recent evidence that such is not likely the case (Rees 1965). This work shows that bacilli from different areas of the world all give a similar growth response when inoculated into the footpads of mice. A much more likely reason for such variation in disease pattern lies in the genetic variations of mankind—the host. Thus races and individuals differ in their response to the introduction of *M. leprae* into their bodies. Although we do acknowledge such a difference, yet it should be minimized, since though there are racial differences in the position on the spectrum where the majority of patients may be situated, yet the entire gamut signs and symptoms of leprosy is seen in every race. One generalization can be made here that the severity of the manifestations of disease are in an inverse relationship to the depth of pigmentation of the skin. However, there are always exceptions that do not follow this pattern of the 'average' case, and in a large group of patients of any racial group there are demonstrated all aspects and varieties of the disease.

It is noteworthy that this suggested classification is fully in accord with clinical manifestations of disease, and cases can be categorized on a clinical basis. And it also agrees with the differentiation of patients on a bacteriological, immunological or histological basis. If there is a seeming discrepancy in the findings by any of these diagnostic methods we must look further until every patient can be fitted into the total scheme without disagreement in any aspect. This is all part of a total pattern of disease and must ultimately fit together logically (Ridley 1962).

This classification also has a logical relationship to the evolution of the disease. See Fig. 3. Upon contact the great majority of individuals

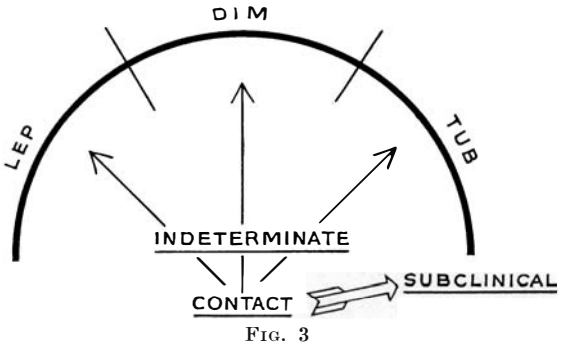

FIG. 3

are either totally resistant to infection or else develop a sub-clinical involvement. What actually happens in instances where an individual does not develop overt infection can at present not be determined. In a relatively small proportion of contacts disease becomes manifest as an indeterminate, insignificant and often overlooked hypo-pigmented and hypo-aesthetic macule. During this stage there is an interaction between the bodily defences and the bacilli which determines the ultimate development of a specific type of disease evolving from the initial indeterminate macule.

The indeterminate macule is *not* a part of the spectrum of leprosy, but is a stage in the development of the disease, as noted in Fig. 3. The presence of disease is not always acknowledged at this stage and quite a few patients are only recognized when the full-blown disease appears. It may well be, as Leiker states (Leiker, 1966), that not all patients go through an indeterminate phase, but this is very difficult to establish with certainty. Again, quite frequently adequate resistance is developed at this stage in the evolution of disease so that it does not progress beyond being indeterminate. This is especially true of patients treated in this early stage. In those not recognized and treated there is an ultimate determination of 'balance of power' between the bacilli and the host, and where resistance is higher moves towards the Tuberculoid side of the spectrum, and with weaker factors of resistance moves toward Lepromatous disease. Indeterminate leprosy as conceived by the South American leprologists (Azulay, 1965) is too large a group of patients including many that should be classed Maculo-anaesthetic, Macular Dimorphous, and Macular Leproma. For purposes of treatment and prognosis it is worthwhile to keep this group restricted to lesions which show vague hypo-pigmentation of a relatively small number of lesions having somewhat indefinite borders, slight hypo-aesthesia or normal sensation, and no bacilli seen by usual means of determination.

The difficulties we have in understanding each other concerning classification will be solved if we have a unified mental picture on which we can base our understanding. For this reason I have attempted to represent diagrammatically the spectrum of leprosy so that we all can more clearly understand just what we are discussing. If all concerned have a common mental image upon which to build further discussions, this skeleton can ultimately be built up into a body of complete understanding. Admittedly there are still areas lacking in clarity, but with these basic concepts perhaps we can work together in filling in the areas of confusion and misunderstanding. I would be the first to recognize that some of this diagram may need alteration to fit the total picture as it is eventually developed.

THE SPECTRUM OF LEPROSY

To visualize adequately the spectrum of leprosy one needs a series of several diagrams which make up a composite and superimposable whole. Fig. 4 depicts the spectrum of the major types of

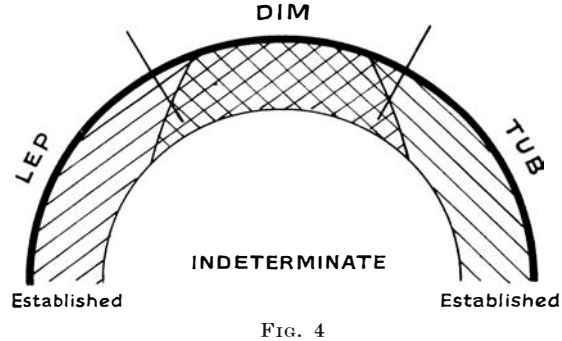

FIG. 4

disease, and the fact that there is a graduation from one type to another. At either end of the spectrum is a group of patients in whom the type of disease is firmly established or fixed, and never alters under any circumstances.

Following common usage as much as possible we will term the large groups of leprosy lesions 'types', e.g., Tuberculoid, Dimorphous and Lepromatous. Since indeterminate lesions are not actually a part of this spectrum of disease, let us use the term more appropriate for a heterogeneous category and call it a 'group' of lesions. For the further division of the three major types let us use the term 'variety'. This follows as closely as possible the terminology used by Cochrane (1964) in his textbook.

At the far right of the spectrum is the established or fixed tuberculoid variety. This is an inoculation type of lesion similar to the 'butcher's tubercle' of tuberculosis (Cochrane, 1964, p. 303). There is an extreme tissue response presumably at the site of inoculation of sufficient number of bacilli to cause a tissue defence reaction. The site of inoculation is infiltrated and surrounded by an intense cellular reaction that walls off and destroys the invading bacilli. This invasion causes the marked infiltration and erythema of this lesion which thus looks much like a *single* reacting Major Tuberculoid lesion. There is so much response to the presence of bacilli that they are very rapidly killed off and removed by the macrophages and thus the lesion disappears rather promptly, whether treated or not.

At the far left hand side of the spectrum is the established leproma. Here there is evidence of a marked lack of bodily resistance. We cannot say an absolute lack of resistance since we as yet have no satisfactory means of making a quantitative determination of this resistance. It is well known that there are in the blood of lepromatous patients large amounts of gamma globulins, but their relationship to the attempt of the body to remove the bacilli is not at present known. The diagnosis of this type of disease is evident only during the clinical course. It is slowly progressive to serious lepromatous involvement, and even with treatment, it shows relatively poor response. However, the lack of resistive powers is evident in that there seldom or never is any evidence of reaction. Thus there is no neuritis nor erythema nodosum leprosum; however, there is very slow but steady improvement under therapy.

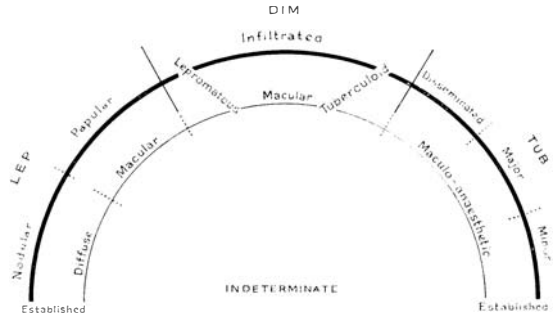

FIG. 5

The most perplexing aspect of this composite diagram is the naming of the various types and varieties of disease. In the accompanying diagrams we have tried to use terms that are most commonly accepted. The lower curving line in the diagram, Fig. 5, represents those lesions which do not incite infiltration as part of the host response, but in some other way alter the characteristics of the skin, such as its colour, the contours of the surface, its appendages (hair, sweat glands) and its tactile sensation. The upper curve represents lesions which produce any infiltration and elevation of the skin of an involved area.

Beginning at the far right side of the diagram are the least severe types of disease. Having already discussed the established tuberculoid, let us consider the other tuberculoid lesions. First there is the Maculoanaesthetic variety, the name describing the character of this lesion. Although this covers a large area in the diagram, it probably does not involve an equivalent number of patients. It is difficult to distinguish from Indeterminate leprosy, and some authorities will call a lesion maculo-anaesthetic whereas others will call it indeterminate, and yet others a tuberculoid macule. Dharmendra (1962), Indian leprologists and others tend to broaden this category to include larger macules with associated neural involvement, which are better considered as part of the Dimorphous type. It would appear preferable to include in maculoanaesthetic only benign patients in which there is never nerve involvement leading to disability. Where there occurs one or a few macules in

which there is unquestioned anaesthesia, no elevation of the surface, and a clear-cut margin they should be placed in this category. As the number of lesions increases there is a shift to the left on the diagram, and an increased potential severity of disease.

In considering the elevated tuberculoid lesions, the first is the Minor Tuberculoid. It occupies the right side of the spectrum just next to the established tuberculoid. It has been clearly defined and accepted universally, and we need not attempt a description. Next to minor tuberculoid should come Major Tuberculoid, although in many patients the differentiation lacks significance for clinical management. Howbeit, it is distinctly a more severe variation in the manifestation of disease. Its characteristics, appearance and location are generally agreed upon, so there is no need to include a description here.

To the left of major tuberculoid is the group of Disseminated Tuberculoid lesions, in which there can be a profusion of lesions which individually appear to be minor or major tuberculoid in appearance, but because of the large number of involved areas, this must be considered in a separate group due to the potentiality for complications, and the need for more prolonged therapy. This is the variety of disease nearest to the Dimorphous, but still in the clearly tuberculoid portion of the spectrum, and therefore the lesions begin to take on the characteristics of dimorphous leprosy. The number of lesions is greater, the edges are less clear-cut, there is less loss of pigmentation, and the tendency for severe neural involvement increases greatly. In this variety the problem of neuritis becomes especially significant although it can be a complication of Major Tuberculoid disease as well, but it is there often limited to single nerves only.

It should be noted that there is no category of reactional tuberculoid in the spectrum, as this is not a true variety of leprosy. When there is an upset of the host-bacillus balance and an increase of defence activity on the part of the host cells there is an increased infiltration and lesions increase in induration. If such lesions were originally on the macular 'line' they simply move centrifugally into that of the infiltrated lesions. 'Transient' is the key word, as the lesions never remain in a category that could be called Reactional, but rather reaction is a temporary phase in the manifestations of disease, and the signs and symptoms will once again revert to those seen prior to the reaction.

Next in degree of severity are the Dimorphous lesions. First of all we should explain the use of this term. The etymology of the word signifies 'two-types' and Dimorphous leprosy encompasses a group of lesions which have some of the characteristics of both polar types of disease. Very frequently the term Borderline is used synonymously, but there is considerable confusion associated with this word since some leprologists use the term for all the cases we categorize as dimorphous, and others use the term only for a restricted portion of the dimorphous spectrum. Since there is this confusion in the usage, and since it is not a suitably descriptive term, I would prefer to omit it altogether.

Dimorphous patients comprise a most significant part of the spectrum of leprosy. If properly conceived this type extends further to the right, and to the left into the tuberculoid and lepromatous portions of the spectrum, and includes a larger proportion of patients than is commonly included in this category. There is good reason thus to broaden this portion of the spectrum in order to include those patients not fully lepromatous, as they respond to treatment more satisfactorily than does true lepromatous leprosy, but yet there is more potential for early and extensive neural damage. This usage is equivalent to Ridley's (1962) term Borderline, which is not used in a restricted sense as it is by the Latin American workers. To include an increased number of patients to the right, e.g., towards tuberculoid leprosy, also brings into the category those patients in whom there is great potential danger of neural destruction. Thus it becomes possible to include in the Dimorphous type the greater majority of patients where nerve involvement is a likely possibility. Thus to lump these cases together in one category

makes for simplification for less skilled workers, and they can understand that caution must be exercised in one category of patients, namely Dimorphous.

As yet we have inadequate terminology for the varieties of patients who are included in dimorphous. It is clumsy to have to say 'Macular Tuberculoid Dimorphous', 'Infiltrated Lepromatous Dimorphous', etc. But the dimorphous type should clearly be split into four distinct varieties, as to whether the lesions are raised or flat, and whether they tend to have predominant tuberculoid or lepromatous characteristics.

The Macular Dimorphous has been recently termed Low Resistant Tuberculoid by Leiker (1964). This terminology, although descriptive, is confusing since it implies that this variety is a part of the tuberculoid spectrum, whereas it is clearly a manifestation of dimorphous disease. Leiker himself suggests this when he states, ' . . . unless a subgroup of borderline (Dimorphous?) leprosy toward the tuberculoid side of the spectrum is created, it is more nearly correct to include these cases in the tuberculoid group'. Such a variety as he mentions is, in fact, that which I propose. He goes on to say that macular dimorphous lesions fit into the low-resistant tuberculoid group. Rather I would say that they are one and the same thing.

Macular dimorphous leprosy is most important because of the high proportion of patients developing severe deformative complications. The skin lesions, although pronounced in most patients for a period of time, are relatively transitory. Dimorphous macules are large hypopigmented patches involving large areas of the skin surface. It probably never occurs as a single macule. The outline of a lesion may be bizarre with an irregular border. The superficial nerve trunks may be markedly involved but usually do not show as great hypertrophy or nodularity as in the infiltrated tuberculoid area of the spectrum. The involvement is manifest, not so much in hypertrophy of the nerves, as by anaesthesia and paralysis. It is from this group that the great majority of mutilated patients with quadrilateral involvement arise. Activity of the disease is relatively transient, but rapid, leaving the patient with severe disability, there being marked neurological deficits in sensory, motor and autonomic nerves. This group is often misdiagnosed as indeterminate. However, indeterminate leprosy *never* causes disability prior to its progression into one of the specific types of disease manifest on the spectrum.

The Dimorphous Infiltrated lesions are those usually called Borderline. There are characteristics of lepromatous disease in that they tend to show more symmetry than any of the lesions thus far discussed. The centre of the lesion is more elevated than the edge, and there is less likelihood that they will be anaesthetic. These lesions readily tend towards the lepromatous pole if there is a decrease of resistance. In these, too, there is always a multiplicity of small lesions. Their small size and large number differentiate them from any of the types heretofore described. The use of the term Borderline for this type of case in a very restricted sense by the South American workers is confusing to those of us who see very many Dimorphous cases. They use the term Borderline only for a very restricted group of lesions somewhere near the very centre of the Dimorphous Infiltrated spectrum (Alonzo 1959, Azulay 1965).

The final category of disease—Lepromatous—is that found to the far left on the spectrum. There are two types of infiltrated lesions, and two that do not show marked infiltration. The non-infiltrated lesions are the Lepromatous Macule, nearer the dimorphous type, and Diffuse Lepromatous leprosy. Individual lepromatous macules may resemble closely the indeterminate macule, but they are distinguished by their multiplicity, symmetry and the presence of bacilli in a smear. There is an area here in which confusion as to the diagnostic category readily occurs. There is similarity in appearance to the dimorphous macule, as well as to the indeterminate macule, which are closely adjacent to the lepromatous macule. These all fade off imperceptibly into each other. Although clinical differentiation may be impossible, a definitive diagnosis should be feasible with evaluation of

other diagnostic means, such as the smear, immunology and histology.

Diffuse Lepromatous leprosy is very difficult to recognize as it causes so little alteration in cutaneous characteristics until at an advanced stage with loss of eyebrows, diffuse infiltration, nasal septal involvement, etc. There may be a slight increase in erythema, and a smooth, glossy surface to the skin, but there are no areas of distinct hypo-pigmentation. It is in this portion of the spectrum that cutaneous endarteritis and arteriolar occlusion occur, producing the Lucio Phenomenon. Although this is a very serious complication in some lighter skinned races, it does occur occasionally as a localized and limited lesion in the darker skinned as well.

It is feasible to divide arbitrarily the infiltrated lepromatous lesions into two varieties, because this division is of some prognostic value. The group nearer dimorphous is named Papular Leproma, with the infiltration manifest chiefly by small lesions, the majority of which are less than 5 mm. in diameter. There may be some larger papules, and some diffuse infiltration, but the most evident lesions are the well-defined papules which almost appear pedunculated, since they are so markedly elevated. The only purpose for distinguishing this variety from the final one is that this type of disease responds to treatment considerably more rapidly than does the Nodular Leproma. There is also a greater tendency for lepromatous reaction, and erythema nodosum leprosum to occur in papular than in nodular lepromatous leprosy.

The last grouping, Nodular Lepromatous Leprosy is manifested by larger infiltrations than those seen in the papular leproma. Here the majority of the lesions are larger than 5 mm. diameter, and there may be large nodules and plaques of infiltration. In this variety there is less likelihood of early complications, but slow unremittant neural involvement is usual.

To the far left of the spectrum is the Established Leproma, already discussed. The only means of differentiating this from the Nodular Leproma is in the clinical course of the disease. (It may be that with time and experience a histological differentiation will be possible.) In the fixed leproma there is a slowly progressive disease with no period of exacerbation or remission. There is a steady increase of areas of peripheral anaesthesia which goes unnoticed by the average patient. Without therapy there is a steady down-hill course and increasing evidence of serious complications. If treatment is given there is a slow and gradual improvement which is not marked by episodic complications. However, treatment will undoubtedly be required for life as there appears to be no attempt to develop bodily defences in this variety of leprosy.

As yet we have not mentioned Neuritic (or polyneuritic) Leprosy. Cochrane (1964) states that potentially there are neuritic patients associated with all divisions of the spectrum, which patients do not show obvious cutaneous changes. However, I am inclined to agree with Leiker (1966) that probably there are no neuritic patients which do not at some stage show cutaneous lesions. If sought for assiduously such lesions or their residua can invariably be found. I believe that patients most commonly called neuritic actually arose initially as dimorphous macular lesions in which the evidence of cutaneous disease has disappeared but there is still activity or the results of activity such as scarring and fibrosis in the large superficial nerves. Thus in the categorization of neuritic disease one should attempt to determine the original type of skin involvement, and place the patient in the pattern of disease most appropriate.

In order to demonstrate how extremely important is a correct classification of leprosy in order to draw any significant conclusions about this multi-faceted disease, let us again refer to Dr. Mallac's 'Onset and Pattern of Deformity in Leprosy' (1966). According to Dr. Mallac, indeterminate leprosy has the least potentiality for deformity, yet in actuality, indeterminate, if correctly defined, is a group of patients in whom deformity *never* occurs unless it is transformed into one of the definitive

types of leprosy. Dr. Mallac uses the conventional definition for indeterminate leprosy which is little more than a 'waste basket' for macular lesions.

He also records that deformity on the average occurs in $2\frac{3}{4}$ years in tuberculoid leprosy. It would be preferable to divide the tuberculoid into its varieties and note specifically the ones where deformity is a common occurrence. It never occurs in maculo-anaesthetic leprosy, properly defined, and it never occurs in Minor Tuberculoid patients. In major tuberculoid it may occur as related to an extremity on which lesions are found. Thus it may occur on one limb alone, and seldom involves all 4. Dr. Mallac's usage of Borderline is like that of the South Americans. Thus it coincides with only a very limited part of the Dimorphous spectrum. This definition includes only relatively few patients, whereas dimorphous properly conceived includes a large grouping, and also one in which there is a high incidence of deformity. This should include the dimorphous macular lesions as well as those which are infiltrated.

After reviewing the literature Dr. Mallac concludes that 'no single test emerges as a reliable means of predicting the potential for deformity', and on this we fully concur. However, he does not carefully relate incidence of deformity to the spectrum of disease accurately conceived, which process aids immeasurably in determining a prognosis concerning disability. This work is a very real contribution to the literature on rehabilitation in leprosy, and the stress he lays on early diagnosis and treatment is quite correct. Just one thing more should be added to his work that is of extreme significance, and that is that with correct classification of a patient, leading then to therapy related to the type of disease, *at an early stage*, deformity is preventable in all except a small minority of dimorphous patients.

It is of utmost importance to remember that there are no absolute boundaries dividing the various types and varieties of leprosy, there is simply a gradual progression from one category into the next.

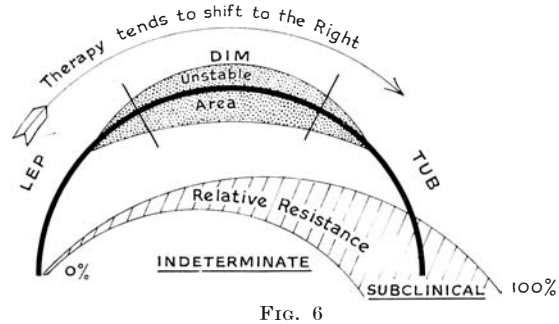

FIG. 6

There are three factors related to this composite diagram of Classification that can be readily superimposed on to the picture to add to its significance. These all relate to matters already referred to, and need little comment. The factors are: 1. host resistance, 2. disease type stability, and 3. response to therapy, and these may be added to the diagram as in Fig. 6.

The resistance of the individual to disease is high on the right side of the spectrum, so high in fact that in the great majority of exposed individuals no obvious disease becomes manifest. Thus we have the 'Sub-clinical' category. Host resistance gradually lowers as we proceed toward the left, and thus disease becomes more and more severe.

In consideration of type stability we note that the central area of the spectrum is the least stable, and a patient can shift in his manifestations quite readily. On the other hand the

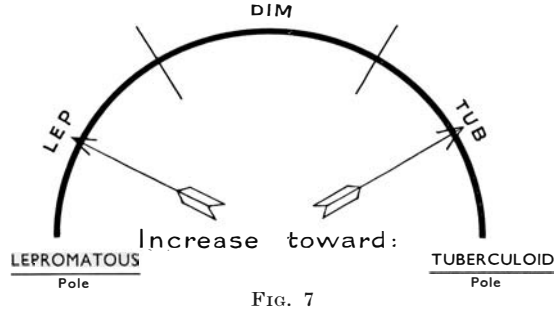

FIG. 7

1. Number of lesions.
2. Symmetry.
3. Bacilli.
4. Smoothness and lustre.

1. Definition of edge of lesion.
2. Hypopigmentation.
3. Size of individual lesion.
4. Anaesthesia.
5. Lepromin positivity.
6. Response to therapy.

disease at the very poles of the spectrum is absolutely stable. The closer to the centre of the spectrum, the more likely a loss of 'balance of power' between disease and host. The disease may shift to the left with any stress such as intercurrent illness, undue physical activity or even psychic trauma. Conversely, an increase of resistance in an individual tends more to the type of disease to the right.

Finally, concerning therapy we can state that adequate and effective treatment tends to shift the type of disease to the right hand side of the spectrum.

A further diagram which may aid in determining the site of a patient in the spectrum of disease is noted in Fig. 7. Note that the characteristics of leprosy lesions which increase as disease moves towards the left or becomes more nearly lepromatous, are the number of lesions, the symmetry of lesions, the number of bacilli present, and the smoothness and shininess of lesions. The farther to the right we go in the classification the more marked are the following characteristics: definition of the edge of the lesion, hypo-pigmentation, size of individual lesions, anaesthesia, lepromin positivity, and the response to therapy. Alterations which appear in the histology as a patient appears to the right or left in the diagram could also be discussed here, but we have not included it in our present considerations.

SUMMARY

The similarity of opinion held by a majority of present-day workers on the matter of classification of leprosy is noted, and an attempt is made to bring together various divergent viewpoints into a united whole by a co-ordination of the thinking of several authorities.

Emphasis is laid upon the logical basis for a spectral concept of leprosy related directly to the establishment of a balance between host resistance and bacillary multiplication.

The logical classification is diagrammatically presented in order that workers may develop a uniform concept of the spectrum of leprosy on which further information can be developed as it becomes clear.

The types and varieties of leprosy making up the total spectrum of disease are briefly described, and their relationship to one and another are established in the spectrum.

It is pointed out that without an adequate understanding of a proper classification of leprosy, many aspects of this disease, most importantly as related to management and therapy, remain unclear. Thus a plea is made for still further development and elucidation of the subject of classification.

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Acute Lepromatous Ulceration of the Skin

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A great deal has been written regarding the exacerbated phases in the various types of leprosy. Recently Tolentino (1965) presented an excellent summary of the clinical features of acute manifestations of leprosy at the research conference in Washington. A comprehensive discussion on exacerbated phases in leprosy can also be found in the report of the panel on reaction at the VIII International Congress of Leprology (Rio, 1963).

It is generally agreed that there are three fairly well defined groups of acute manifestations in lepromatous leprosy (Cochrane, 1964; Tolentino, 1965; Tijiri, 1955), namely:—

(1) *Acute Lepromatous Infiltration* or acute exacerbation of lepromatous leprosy during which the disease progresses rapidly. At this stage there may be striking increase in generalised infiltration of the skin with thickening of the skin and erythema; in some others, infiltrated plaque-like lesions with sloping edges and/or nodules may appear, especially over the face and ears.

(2) *Erythema Nodosum Leprosum* which is characterised by the appearance of painful, erythematous nodular eruption usually associated with systemic symptoms such as fever, anorexia, arthralgia and swelling of the feet; and

(3) *The Lucio Phenomenon* which is a special manifestation reported almost exclusively from Latin American countries. 'It is described as a necrotising vasculitis beginning as purpuric lesions that become necrotic in the centre and break down into ulcers. It is observed chiefly in advanced cases with diffuse lepromatous infiltration.' (Tolentino, 1965).

We are here describing another acute manifestation in lepromatous leprosy hitherto inadequately documented. This is characterised by an abrupt spread of lepromatous infiltrated lesions which quickly ulcerate in the centre of the lepromatous plaque or nodule and the patient presents with a large number of skin ulcers with very little systemic disturbance.

Patient No. 1—*R.R.: S.L.R.S.* 7861. Male aged 45 years; was first seen at S.L.R.S. on 2.11.65 with a 7-year history of lepromatous leprosy. One month prior to arrival at S.L.R.S., there was a sudden flare up of the disease with appearance of new raised lesions over the trunk and limbs, some of which ulcerated. There was no other systemic symptom.

On Examination: The patient was found to have advanced lepromatous leprosy with loss of eyebrows, enlargement of ears, early depression of nose, gross infiltration of the skin from head to foot, and bilateral ulnar paralysis. There were a large number of infiltrated, raised lesions with elevated centres and sloping edges, of variegated size and shape (Figs. 1 and 2). A number of these lesions had ulcerated in the centre, discharging a sero-sanguinous material which, on acid fast staining, showed sheets of uniformly staining acid fast rods and globi filled with acid fast bacilli.

Patient was treated with intramuscular injections of Streptomycin 1.0 g. daily and INAH 300 mg. once a day. The skin lesions healed within a week (Figs. 3 and 4). There has been a rapid improvement in the clinical condition of the patient and simultaneously the bacterial index has come down very dramatically.

Skin Smears:

Date	B. Index	% Rods
2.11.65	5.0	75
17.12.65	3.5	10
8.2.66	2.0	
25.4.66	1.0	
20.6.66	0.87	2

Bone Marrow: Aspirate showed groups of rod shaped acid fast bacilli on 4.11.65. On 20.6.66 no bacilli could be found in the bone marrow aspirate.

Skin Biopsy: Showed the epidermis atrophic with flattening of the rete pegs. There was a clear area beneath the epidermis separating a band of inflammatory cells consisting of mostly foamy macrophages. There were also scattered collections of lymphocytes. An occasional plasma cell was present.

Acid fast stain showed numerous bacilli inside macrophages.

This picture was that of a patient with advanced lepromatous leprosy.

Patient No. 2—*S.N.P.: S.L.R.S.* 8053. Male aged 48 years; was admitted here on 9.3.66 with a 10-year history of leprosy which began with a patch on the thigh. He had taken treatment irregularly. About 2 months prior to arrival here there was a sudden flare up of the disease with the appearance of raised lesions all over the body which quickly went on to ulcerate in the centre.

On Examination there was gross lepromatous infiltration of the skin from head to foot; partial loss of eyebrows and gross oedema of the legs and feet. There were innumerable skin ulcers in various stages of evolution. Majority of these ulcers were in the middle of lepromatous, infiltrated, raised lesions (Figs. 5 and 6). Both the eyes were congested, there was corneal haziness, circumcorneal injection and yellowish-white nodules on the conjunctiva near the limbus on both sides. There was marked bilateral gynaecomastia, and both testes were atrophic.

Patient was treated with 1.0 g. of Streptomycin daily, and 300 mg. INAH once a day orally. In 14 days all skin ulcers healed, leaving papery thin scars (Figs. 7 and 8). Along with the striking clinical improvement, the skin bacillary index also came down rapidly.

Skin Smears:

Date	B. Index	% Rods
10.3.66	4.87	60
31.3.66	3.62	25
19.4.66	3.37	5
10.6.66	3.25	
8.8.66	2.62	5

Bone Marrow: Aspirate on admission to S.L.R.S., had acid fast bacilli in rod form.

Skin Biopsy: Epidermis showed some proliferation of the prickle cells. There was marked parakeratosis and some hyperkeratosis. Beneath the epithelium was seen a dense inflammatory infiltrate composed almost entirely of foamy macrophages. There were also scattered lymphocyctes and plasma cells. In one area there was an ulcer, the superficial part of which was formed by granulation tissue consisting of capillaries, polymorphonuclear leucocytes, lymphocytes and plasma cells. In the deeper area there were large collections of foamy macrophages.

On acid fast stain numerous bacilli inside macrophages were seen.

This picture was quite consistent with a lepromatous ulcer.

Patient No. 3—*Y: S.L.R.S.* 7917. Female aged 25 years; was first seen here on 6.12.65 with a 10-year history of leprosy which began with a hypopigmented patch over left arm. About 3 months ago, there was an abrupt onset of extensive skin ulceration without any systemic disturbance.

On Examination there was gross infiltration of the skin from head to foot. Thrre was enlargement of ears; early depression of the nose; and partial loss of eyebrows. There were extensive areas of skin ulceration over the trunk, limbs and face (Figs. 9 and 10) discharging sero-sanguinous fluid which on acid fast staining showed numerous rods and globi. Treatment was begun with daily injections of 1.0 g. Streptomycin and oral INAH 300 mg. once a day and in 3 weeks time all the skin ulcers healed leaving papery thin scars (Figs. 11 and 12). Along with the healing of ulcers and rapid resolution of the gross skin infiltration, the skin bacillary index came tumbling down.

Skin Smears:

Date	B. Index	% Rods
6.12.65	4.62	95
4.1.66	3.87	60
18.1.66	3.87	55
9.3.66	3.75	
23.5.66	3.00	3
26.7.66	2.05	

Bone Marrow: Acid fast bacilli in rod form seen in aspirate.

Skin Biopsy: The histological picture of the skin in this case was very similar to what was described under Patient No. 2.

The Liver Biopsy section showed small focal collections of foamy macrophages containing acid fast bacilli.

Patient No. 4—*D: S.L.R.S.* 7918 (son of Y. 7917), aged 10 years; seen at S.L.R.S. on 6.12.65 for the first time with a 4-year history of leprosy. During the last 1 year the disease spread rapidly and enlargement of the ears was noticed. About 3 months ago a number of the raised skin lesions ulcerated and would not heal.

On Examination there was gross, coarse infiltration of the skin from head to foot; enlargement of ears with nodules along the pinna; a number of raised, infiltrated lesions with sloping edges and raised centre of varying sizes and shapes all over the body, face and limbs; partial loss of eyebrows (Fig. 13). Many of the infiltrated lesions had ulcerated discharging sero-sanguinous fluid which on acid fast staining was full of rods and globi. Patient was started on treatment with daily injections of 0.5 g. of Streptomycin and 150 mg. of INAH orally. The skin ulcers healed in 2 weeks (Fig. 14).

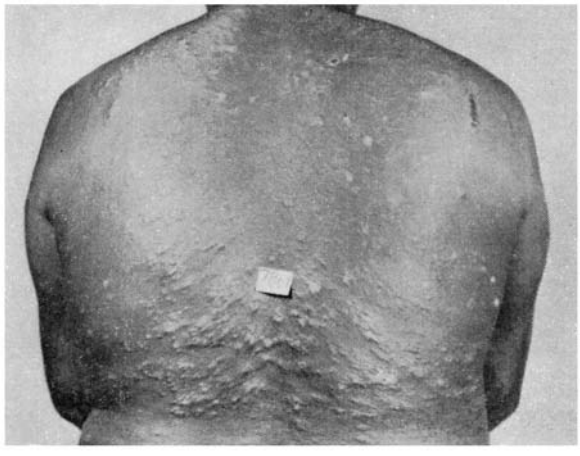

FIG. 1

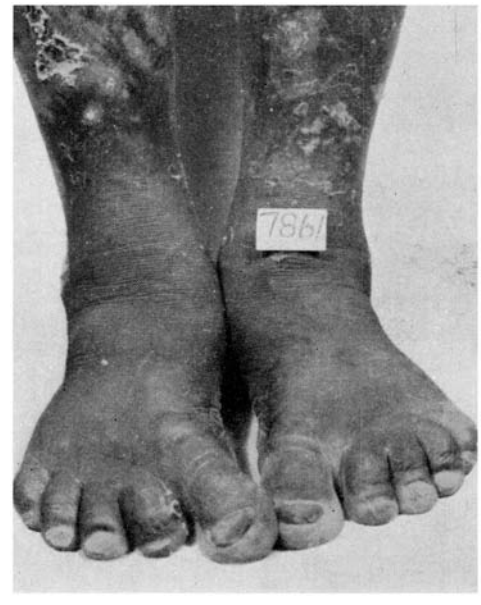

FIG. 2

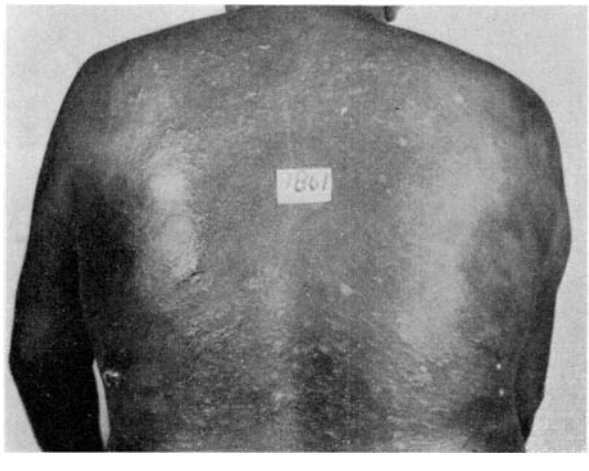

FIG. 3

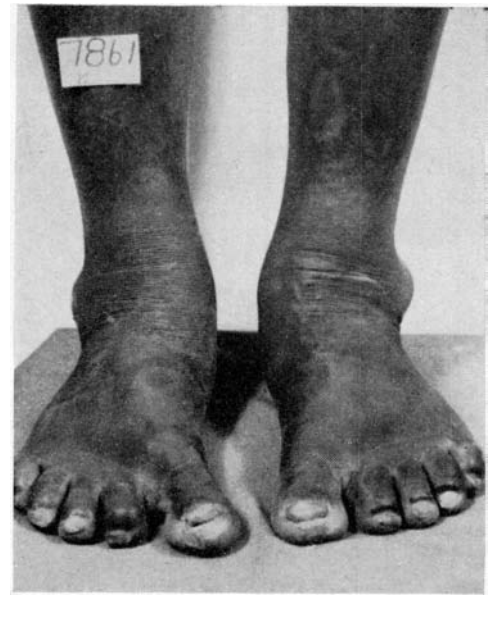

FIG. 4

FIG. 1. Shows the back on admission. Notice the infiltrated lesions on the skin, some of which have ulcerated.

FIG. 2. To show oedema of the ankles and superficial skin ulceration.

FIGS. 3 and 4. Same patient as in 1 and 2—after treatment. The skin ulcers have healed and the raised, infiltrated lesions have flattened out.

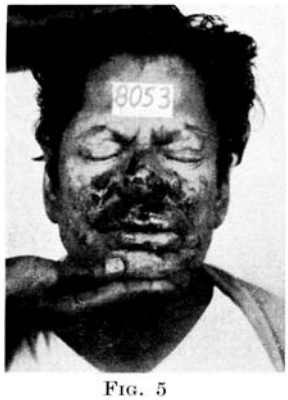

FIG. 5

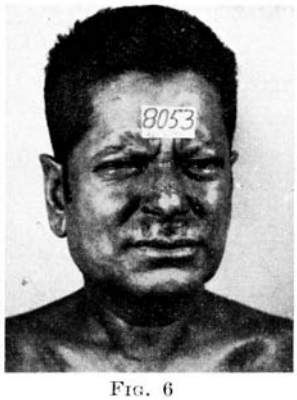

FIG. 6

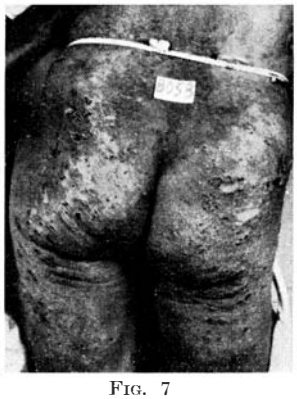

FIG. 7

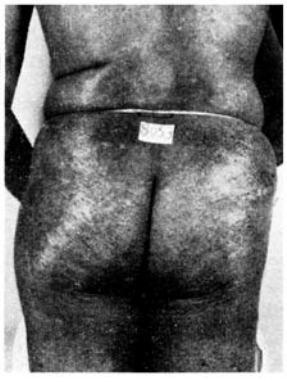

FIG. 8

FIG. 9

FIG. 10

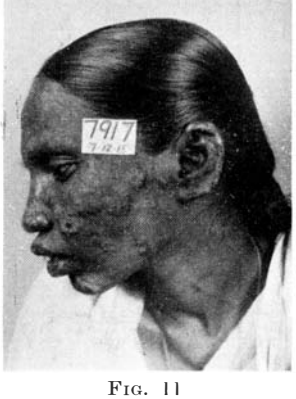

FIG. 11

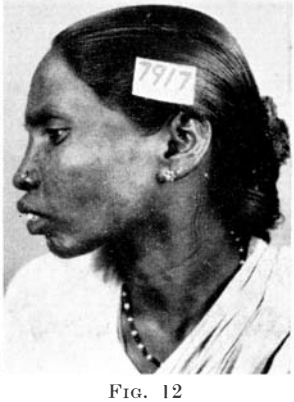

FIG. 12

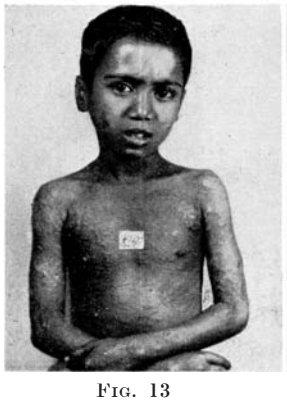

FIG. 13

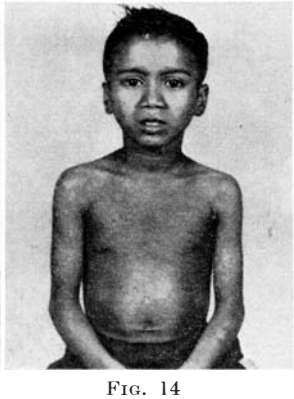

FIG. 14

FIG. 15

FIG. 16

FIGS. 5 and 7. Show pre-treatment appearance of multiple skin ulcers in association with infiltrated skin lesions.

FIGS. 6 and 8. After treatment.

FIGS. 9 and 11. Pre-treatment views to show gross lepromatous infiltration of the face and ears with ulceration.

FIGS. 10 and 12. Post-treatment appearance. The resolution of the gross infiltration seen in Figs. 9 and 11 is obvious.

FIG. 13. Before treatment—gross lepromatous infiltration and areas of ulceration are seen.

FIG. 14. After treatment—the clinical improvement is easily appreciated.

FIG. 15. Photomicrograph to show the edge of the lepromatous ulcer.

FIG. 16. The bed of the ulcer consists of a superficial layer of necrosis, a layer of inflammatory cells consisting of lymphocytes, macrophages and a few polymorphs and then a sheet of foamy macrophages containing acid fast bacilli.

Skin Smears:

Date	B. Index	% Rods
6.12.65	4.62	90
4.1.66	3.62	58
18.1.66	3.62	48
21.5.66	2.75	2

Bone Marrow: Acid fast bacilli in rod form seen in aspirate.

Skin Biopsy: Section shows a lepromatous granuloma of the skin with sheets of foamy macrophages underneath the epidermis. The inflammatory cell collections extend right up to the epidermis from which it is separated only by the basement membrane. There was no clear area between the epidermis and the granuloma.

Acid fast stain shows numerous bacilli inside macrophages.

COMMENTS

Practically everyone working in the field of leprosy would have seen patients with lepromatous leprosy in whom the disease for some reason or other suddenly begins to spread, and sometimes these lepromatous lesions ulcerate. Though one is familiar with this kind of clinical picture, we are unable to find a good description of this condition, nor any guide lines regarding management.

That these ulcers are directly a consequence of the proliferation of *Mycobacterium leprae* there is little doubt (Figs. 15 and 16). What was surprising was the rapidity of resolution of these lesions under treatment with Streptomycin and INAH, *pari passu* with corresponding drop in bacterial index.

In the patients here described, skin biopsies confirmed the presence of lepromatous granuloma in the affected area of skin. In those in whom liver biopsy had been done, there was the typical lepromatous granulomata and acid fast bacilli in the parenchymal tissue. Bone marrow aspirate also had typical acid fast bacilli one associates with lepromatous leprosy.

We would suggest that this particular behaviour pattern of the bacillus *M. leprae* may be due to 2 factors: (*a*) alteration in host immunity or (*b*) mutation of the *M. leprae*. We are inclined to support the latter suggestion since the infection responds so dramatically to Streptomycin and INAH and the bacterial clearance apparently occurs concurrently with the clinical improvement in the physical condition of the patient, unlike the usual infection with *M. leprae*.

We would strongly recommend that this kind of patient with lepromatous skin ulceration should be treated with 1 g. of Streptomycin intramuscularly daily and 300 mg. of INAH orally once a day since in our limited experience this treatment brings about rapid healing of the ulcerated skin lesions concurrently with accelerated clearance of the dead bacilli. This response may in part be due to the bacteriocidal action of Streptomycin and increased susceptibility of this strain of *M. leprae* to Streptomycin.

SUMMARY

1. Four patients with acute lepromatous skin ulceration are described, with clinical and histopathological data.

2. Acute lepromatous skin ulceration presents with a history of abrupt spread of lepromatous leprosy lesions and infiltrations all over the body which rapidly progresses to skin ulceration, without any other systemic symptoms.

3. We recommend that patients with acute lepromatous skin ulceration be treated with Streptomycin 1 g. intramuscularly daily and INAH (isonicotinic acid hydrazide) 300 mg. once a day orally. These patients respond to this regime dramatically both as far as skin ulceration is concerned, as well as their bacteriological index on skin smear.

4. The possibility of this complication being due to a mutant strain of *M. leprae* is discussed.

ACKNOWLEDGEMENTS

We are grateful to Mr. S. Jesudass for technical assistance with tissue sections; Mr. C. Dorairaj for photographs; and Mrs. L. Furness for secretarial help.

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Lep. Rev. (1966) 38, 1, 31-33

Preliminary Report on the Effects of L-Triiodotyronine, Radioactive Iodine^{131}, and Methimazole on Experimental Murine Leprosy

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Lurie *et al.*[1] have found that administration of thyroid hormones can increase the level of native resistance to tuberculosis in rabbits, and that thyroidectomy and antithyroid drugs have the opposite effect.

On the other hand, the harmful effects of iodides on the clinical manifestations of human leprosy are well known. O'Byrne[2] and Rojas[3] have reported favourable responses in the treatment of this disease with thiouracil and methimazole.

These reports would indicate a substantial difference in the effects of thyroid-related compounds on two infections produced by bacteria which are so closely related taxonomically. To further investigate these relations we treated mice with thyroid-related compounds and then infected them with another closely related mycobacteria, the Stefansky bacillus.

Seventy albino-swiss mice, 7 weeks old, were divided into 4 groups and were treated as shown in the Table I.

TABLE 1

Treatments and inoculation of the mice divided by groups

Group	Mice Number	Treatment		Inoculation* Day
		Drug	Duration (days)	
1	10	None	—	16th
2	20	Methimazole**	1st to 65th	16th
3	20	Iodine^{131}***	9th	16th
4	20	L-Triiodotyronine****	1st to 65th	16th

* 0.5 cc. of a suspension of bacilli in saline solution inoculated intraperitoneally. (Approx. 5×10^7 bacilli.)

** Methimazole (Tapazol, Lilly Lab.) was administered in the drinking water in 0.1% solution.

*** 85 microcuries in 0.5 cc. administered intraperitoneally in a single dose.

**** L-Triiodotyronine was mixed with the diet (100 microgm./100 gm. of food).

All animals were fed Purina Lab Chow.

RESULTS

Lesions were found in all surviving mice. In order to do a quantitative analysis, granulomata were counted in liver tissue[4]. To avoid investigator bias, granulomata were counted in slides labelled randomly, without knowledge of the precedence of each slide ('blind counts'). Results were expressed as number of granulomata per square mm. of liver tissue, as seen in Table 2.

TABLE 2

Average number of granulomata found in the livers of the experimental animals. In parenthesis: percentage of mice in each experimental group

Experimental Group	Mice Survival	Granulomata per square millimetre of tissue						Average of averages
		40 or less		41—79		80 or more		
		Mice	Percentage	Mice	Percentage	Mice	Percentage	
Control	10 of 10	2	(20)	1	(10)	7	(70)	118
Methimazole ..	13 of 20	3	(23)	2	(15)	8	(61)	106
Iodine^{131}	10 of 20	14	(74)	0	(00)	5	(26)	73
L-Triiodotyronine..	6 of 20	6	(100)	0	(00)	0	(00)	5

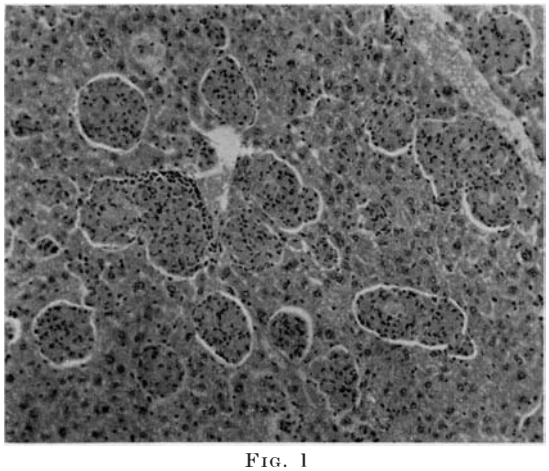

FIG. 1
Liver of mouse inoculated with Stefansky bacilli. Control group. Notice multiple granulomata. (H & H 105X.)

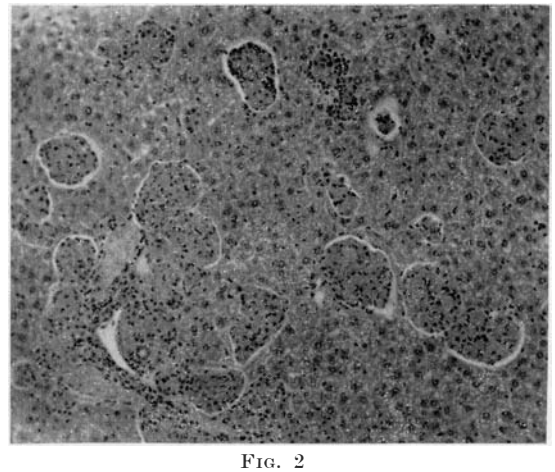

FIG. 2
Liver of mouse that received Methimazole and was inoculated with Stefansky bacilli. There is a close similarity with the control. (H & E 105X.)

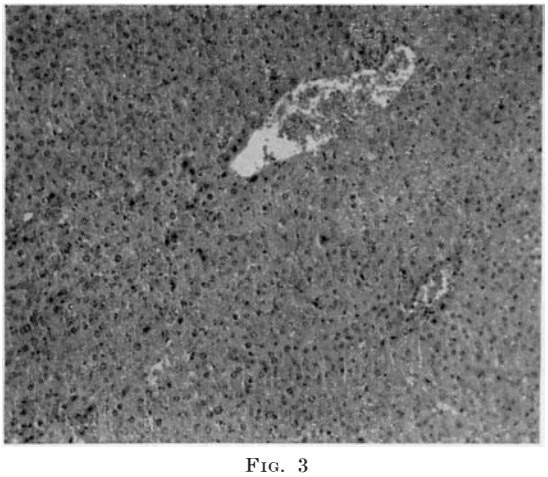

FIG. 3
Liver of mouse that received I^{131} and was inoculated with Stefansky bacilli. Notice absence of granulomata. (H & E 105X.)

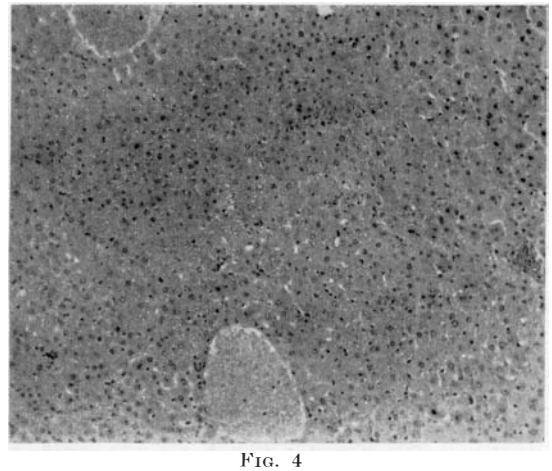

FIG. 4
Liver of mouse treated with L-Triiodotyronine and inoculated with Stefansky bacilli. Notice the absence of granulomata and the similarity with Fig. 3. (H & E 105X.)

DISCUSSION

Mice treated with Methimazole (Fig. 2) did not show significant differences in the number of granulomata when compared with the control group (Fig. 1).

To our surprise, mice treated with radioactive Iodine^{131} (Fig. 3) had less granulomata in the liver and other organs than the controls. Apparently, even greater differences were found in the animals treated with L-Triiodotyronine (Fig. 4). In this group all of the mice had less than 28 granulomata per square mm. of liver tissue. The higher mortality in this group is probably explained by the use of excessive doses in the beginning of the experiment (400 microgm./100 gm. of food); after the reduction to the definitive dose, there were no more deaths. Further experiments are under way to examine the possible effects of the high mortality on the results of this group. The magnitude of the differences found between the L-Triiodotyronine and the control groups, however, is so great that it does not seem to be the result of mortality selection. Our results are similar to the findings of Lurie in experimental tuberculosis and seem to indicate the necessity of further investigation of this interesting phenomenon.

CONCLUSION

Our preliminary data seems to point to some 'protective action' of Iodine^{131} and of L-Triiodotyronine on experimental infection with the Stefansky bacillus.

ACKNOWLEDGEMENTS

My appreciation to Dr. P. Correa, M.D., Associate Dean, Dr. E. Hoffman, M.D., Chief, Pathology Dept., Universidad del Valle, Medical School, and Dr. H. Wahner, M.D., Radioisotops Laboratory, Hospital Universitario del Valle, who with their help and encouragement have made it possible for me to work in this project.

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Lep. Rev. (1966) **38**, 1, 35-36

Nerve Abscesses in Northern Nigeria

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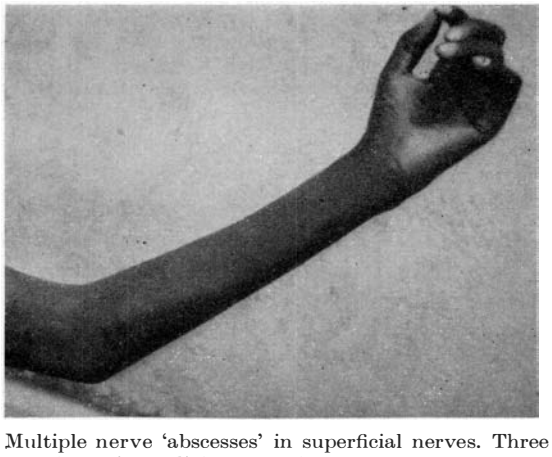
In view of the fact that the rarity of nerve abscesses in Africa is frequently commented upon, it may be of interest to report several patients seen in the last 4 years in Northern Nigeria, including 3 patients with multiple abscesses in cutaneous nerves.

Patient 1—In October, 1964, a male patient aged 22, was admitted to this leprosarium in a very debilitated condition. He had had 6 months' treatment in a local out-patient clinic. He had numerous large lesions of the tuberculoid type, markedly hypopigmented, symmetrically distributed over the face, back and buttocks, and involving the major part of all 4 limbs. The edges of the lesions were very active, and there were some satellites, as well as some smaller individual lesions of the trunk and limbs. There was extensive nerve involvement, including both supra orbitals, right auricular, both ulnars, both radials, right median at the elbow and both popliteals. There was right partial wrist drop, and complete ulnar and median paralysis, obviously of long standing, with flattening of the whole hand. There was left ulnar and bilateral peroneal weakness. In addition to the above findings, this patient had 15 small 'abscesses' in cutaneous nerves. There were 5 in the left medial cutaneous nerve of the arm, 2 above and 3 below the elbow: 3 in the same nerve on the right side, 2 above and 1 below the elbow; 3 in the superficial peroneal nerve in the left lower leg; 2 in the superficial peroneal on the dorsum of the right foot; 1 in a small cutaneous nerve in the right calf; and the largest, in the sural nerve behind the right lateral malleolus. All except the last were about the size of a pea, and contained greyish gelatinous material, which was very tenacious. The last one, about 3 times the size of the others, contained frank pus. All were incised under local anaesthetic, evacuated, the wounds closed without drainage, and they healed rapidly.



Multiple nerve 'abscesses' in superficial nerves. Three shown in medial antepradnal cutaneous nerve. *Patient* 1

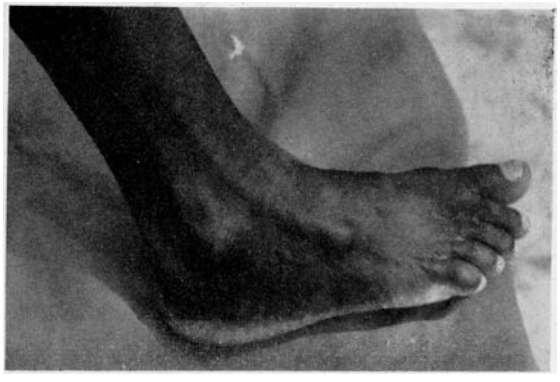
The patient was treated with Ciba 1906 for 11 months, then with Dapsone. He was most co-operative with physiotherapy, and has full recovery of his left hand and both feet. There have been no new nerve complications.

Patients 2 and 3 were seen in Bornu Province while doing relief duties at the Provincial Leprosarium, Maiduguri.

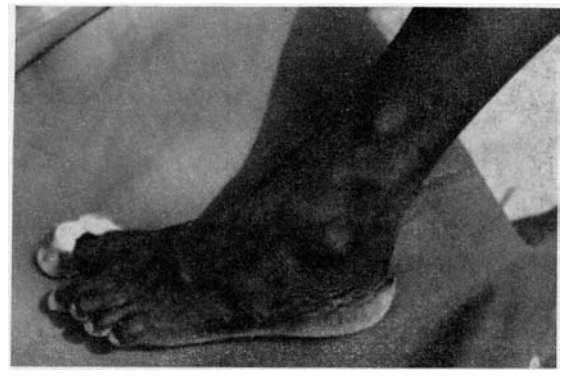
Patient 2—A boy of 12 was admitted to the leprosarium in April, 1965, with low-resistant tuberculoid leprosy. There was one very large lesion involving most of the lower back, with a few satellite lesions, and a large lesion of the dorsum of the right hand. Others were on the right side of the face, both elbows, both knees, left thigh, right lower leg. Both ulnar nerves were markedly enlarged, especially the right one.

In March, 1966, he was found to have a right mobile claw hand, with 3 moderate sized swellings in the greatly enlarged terminal branch of the radial nerve on the back of the right hand. There was also a small abscess of the lateral cutaneous nerve in the left forearm. Both superficial peroneal nerves were grossly enlarged, and each had two localised swellings in the lower part of the leg. On the right side the thickened nerve could be felt right across the dorsum of the foot to the first toe.

At operation, one of the swellings on the back of the hand contained glairy fluid, and there appeared to be a ganglion in the extensor tendon to the middle finger. The other 2 were nerve abscesses, containing frank and inspissated pus. Similar much larger abscesses were found in the legs, the left superficial peroneal being expanded into a wide ribbon above the ankle joint. Distal to this the nerve divided, and in 2 very small abscesses in one of the branches, smears of the pus showed 1 normal leprosy bacilllus and a small group of acid fast granules. Smears from other sites showed no acid fast material. All wounds healed well without drainage.



Nerve abscesses in R. superficial peroneal nerve. Also had 2 abscesses in L. ulnar nerve at wrist, and in L. superficial peroneal nerve.
Patient 3



Nerve abscesses in L. superficial peroneal nerve. Also had 2 abscesses in L. ulnar at wrist, and in R. superficial peroneal nerve.
Patient 3

Patient 3—This patient, a male aged 28 years, from the Chad Republic, had long-standing tuberculoid leprosy, but had only had treatment for a few months. He had flat, slightly hypopigmented lesions of right eyebrow, both forearms, back, left thigh and both legs. There was widespread nerve involvement, both ulnars, right median and left radial nerves being much enlarged and tender. The right popliteal and both superficial peroneal nerves were also much enlarged but not tender.

There were 2 abscesses of the left ulnar nerve on the dorsum of the hand, just distal to the ulnar styloid process. There were 2 in the superficial peroneal nerve on the dorsum of the right foot; 1 in the left lower leg, and 2 on the dorsum of the left foot. All of these were found to contain quite large amounts of creamy and yellow inspissated pus. The proximal one of the left wrist also contained some gelatinous necrotic material. Smears of the evacuated material showed small groups of acid fast granular material, but no recognisable bacilli. In this case also the wounds were closed without drainage, and healed quickly.

In addition to these 3 rather similar cases, the following patients with nerve abscesses have also been seen since 1963.

June, 1963—A male adult with tuberculoid leprosy was referred for ulnar nerve decompression, and was found at operation to have an abscess in the nerve just above the elbow.

October, 1963—A young male adult with major tuberculoid leprosy, with 1 lesion of the right arm, had 2 nerve abscesses of the ulnar nerve about midway between elbow and axilla, and 1 in the medical cutaneous nerve in the same area.

May, 1966—A male patient of 19 years was referred to the leprosarium with acute neuritis of the left popliteal nerve, which was grossly enlarged. He was found to have also great enlargement of the left superficial peroneal nerve, the posterior tibial nerve, and the saphenous nerve on the left. This last contained 3 small abscesses. The interesting feature of this case also was the fact that the only skin lesion which could be found was an apparently healed tuberculoid lesion of the dorsum and medial side of the left foot, extending upwards to just above the ankle. The skin over this area was shiny and atrophic.

June, 1966—A girl of 11 years, with reacting tuberculoid lesions, including several on the right forearm, hand and fingers, was referred to the Bornu Provincial Settlement for ulnar decompression. The nerve was much enlarged, hard and painful. At operation there was a small nodule on the outer aspect of the nerve, which contained a small amount of yellow pus, and a thin thread of this necrotic material continued upwards in nerve tissue for about 1 inch.

SUMMARY

Seven patients with nerve abscesses, some of them multiple, are described, from Plateau and Bornu Provinces of Nigeria, all of whom have been seen within the last 4 years.

Lep. Rev. (1966) **38**, 1, 37-42

A Limited Investigation into the Significance of the Site of the First Lesion in Leprosy

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INTRODUCTION

The paths by which *Mycobacteria leprae* enter the body have up to now been difficult to trace; the inability to grow the bacillus outside the human body has handicapped such investigations concerning transmission.

Muir[1] has stated that there are many instances of the disease having developed at sites of accidental inoculation.

We have as yet no proof of infection through the gastro-intestinal tract.

The possibility of insect transmission has been put forward (Moiser[2], Spickett[3]).

However, the skin as being the portal of entry is still the most widely held view and it is generally believed that skin to skin contact is the most frequent means of acquiring bacilli.

In recent years, Weddel and Palmer[4] have produced evidence to show that *M. leprae* can be disseminated by the blood stream and suggested that the organism does not enter the skin merely by contact or inunction but possibly via the respiratory or alimentary tracts. There was, however, no evidence put forward to support or refute this latter suggestion.

If the portal of entry of *M. leprae* is truly the skin, then the localisation of the first lesion of leprosy shown in the skin should be related to the point of contact in the affected individual. That is, the site of the first cutaneous manifestation of the disease should be at the point of contact of the infected individual with the contaminated skin of the infector.

In West Africa, almost every infective girl or woman has the opportunity for close and prolonged contact with children—either her own, those of related families or even unrelated families. This is because of the national custom of the females carrying the children on their backs, usually naked, and over a long period.

Although it has been the personal experience of the writer to obtain usually not more than 12% of positive answers to the question of knowledge by the patient of contact with another leprosy sufferer, it has generally been found that contact with an infected mother accounts for about 25% of such cases. A further 20% approximately attribute their disease to contact with an infected sister (Susman[5]).

Contact then between infective patients with leprosy and healthy persons appears to be the most important even if not the sole method of spread of the disease. This contact is usually direct, though may possibly be indirect, e.g., through infected clothes, bedding, etc. It is generally believed that close and continued contact is most favourable for transmission; in highly susceptible persons, however, contact of even short duration may result in the disease.

As already stated, the entry of the bacillus via the skin appears to be the most important mode of infection. The following investigation was undertaken in an attempt to find out whether further weight could be given to the assumption.

INVESTIGATION

Five hundred and ninety-seven leprosy patients, consisting of 345 men and 252 women, were closely questioned as to the localisation of the very first patch or mark of leprosy which appeared on their body. Only those who appeared to be explicit in their description were considered, doubtful answers being excluded. Thus, in fact, the first single lesions of 355 leprosy patients (198 men and 157 women) were taken into account. The patients were all from the northern regions of Togo. The following were the results obtained:—

	Men		*Women*	
	No.	%	No.	%
HEAD:				
Forehead	6	33.3	17	50.0
Cheek	8	44.5	11	32.3
Ear, nose, chin	2	11.1	4	11.8
Neck	2	11.1	2	5.9
	18	100.0	34	100.0
UPPER LIMB:				
Upper and Forearm	54	84.4	50	84.7
Hand	10	15.6	9	15.3
	64	100.0	59	100.0
TRUNK:				
Back	4	12.9	6	23.0
Chest	5	16.1	7	27.0
Abdomen	22	71.0	13	50.0
	31	100.0	26	100.0
BUTTOCKS	6		2	
LOWER LIMB:				
Thigh	33	41.8	16	44.4
Knee	18	22.8	5	14.0
Foot	19	24.0	12	33.3
Below-knee	9	11.4	3	8.3
	79	100.0	36	100.0

	Upper Limb			*Lower Limb*		
	Right	*Left*	*Total*	*Right*	*Left*	*Total*
Men	28	36	64	38	41	79
Women	28	31	59	19	17	36
	56	67	123	57	58	115

	Men		*Women*	
	No.	%	No.	%
Head	18	9.1	34	21.7
Upper Limb	64	32.3	59	37.5
Trunk	31	15.7	26	16.6
Buttocks	6	3.0	2	1.3
Lower Limb	79	39.9	36	22.9
	198	100.0	157	100.0

RESULTS

From the above tables, it can be seen that either the lower or upper limbs provide the site for the greatest number of first lesions. In men, the lower and upper limbs account for approximately 40% and 32% of the first lesions respectively, whereas in women these percentages are approximately 23 and 37 respectively. In both men and women, the trunk accounts for around 16% of first lesions, being the third site of importance in the men and the fourth in the women. In the men, the head produced nearly 9% of the first lesions, the fourth site of importance, and in the women the head was the locality of nearly 22% of first lesions, being in them the third site of importance. In both sexes, the buttocks was the site of least importance producing only few first lesions, in the men 3% and in the women about 1%.

It has been observed from personal experience that women tend to be more conscious of lesions on the face than men and also tend to draw attention to lesions on the buttocks and thighs less frequently than do men, and unless specifically examined for such lesions these can be missed. In this investigation, reliance was placed on the patient's own story and it is probable that these facts might explain the increased number of first lesions accounted for on the head in women and the lesser number on the lower limbs and buttocks.

It can also be seen from the above tables that in both sexes there was no significant difference in the localisation of first lesions on the 2 sides, that is in the right and left of either upper or lower limbs. Horton and Povey[6] showed no difference in the distribution of lesions in the 2 hands in their series.

Furthermore, the tables show that in the head, the forehead and cheek each account for more than one-third of lesions; in women, in fact, the forehead accounted for half of such lesions. In the upper limb, over 80% of the lesions were upper- and fore-arm as opposed to hand lesions. In the trunk, the abdomen was the main site of first lesions, then the chest and, least important, the back. The thighs accounted for over 40% in the lower limbs, then the feet, the knees, and below-knees in diminishing frequency.

The following shows a comparison of the above results with those obtained in adults by Horton and Povey[6] in their investigation in South India:—

	Men	*Women*	*Total*	%	*Horton and Povey* Total	%
Head	18	34	52	14.6	14	10.8
Arms and Hands	64	59	123	34.6	42	32.3
Trunk, Buttocks and Thighs ..	70	44	114	32.1	39	30.0
Legs and Feet	46	20	66	18.7	35	26.4
	198	157	355	100.0	130	100.0

This table shows a very similar comparison in the 2 investigations and fits in with the facts that, in both, the children are usually naked and in close contact with their mothers by being carried on the back or are handled to a great extent by their mothers (or sisters).

Correlation of above findings with the facts concerning contacts

In Togo, as in many other countries, it is the custom for babies to be carried on the backs of their mothers from 8 to 10 days after birth until the child is 2 to 3 years old. Often, this period is extended until the child reaches 5 years of age, especially where the mother has no younger children. It is deemed a pleasure for the mother to carry the infant in this way when she has no other babies.

In northern Togo where this investigation was undertaken, the child is generally naked when carried. The mother may be naked also above her waist with a cloth enclosing the child's body around her own. In many cases, however, some

cloth is worn by the mother, in which cases the child's trunk is not, therefore, always in direct contact with the bare skin of the mother. Often, also, the legs of the child are held directly against the skin of the mother's side and back under the mother's cloth, the front of the infant's trunk being directly against the mother's bare back only when the upper part of the mother's body is quite nude. When the mother is thus unclothed the child's bare arms are directly in contact with the mother's lower chest but otherwise the arms may be outside or inside the mother's cloth. Even when the mother does cover the upper part of her body, the baby's head (cheek or forehead) is in contact with the bare back of the neck of the mother, especially in the bigger children.

Hence, in the north of Togo the most likely areas of contact, the above conditions being considered prevailing in the mother and infant, would appear to be, in order of diminishing frequency, the legs (especially the thighs) closely followed by the arms (especially the upper- and fore-arms), then the trunk (principally the abdomen) and then the head (mainly the forehead and cheeks). The buttocks are obviously not involved much in this question of skin to skin contact.

Thus, the findings shown in the above tables appear to fit in largely with these facts concerning the actual areas of contact between mother and child. Furthermore, it has been stated that the mother/child contact appears to be the most important one ascertained in the history of contacts. Also, sister/child may be the second important contact relationship, and it is a fact that often the infant is carried by its older sister for a large part of the time when not carried by the mother. This is the case even where the sister is only a few years older and, of course, the carrying of the infant is executed in the same manner.

Rogers and Muir[7] have stated specifically that children are particularly liable to infection and this has been supported by many leprologists including Cochrane[8], Doull[9] and Chaussinand[10]. Other field workers have agreed with this postulate (Languillon[12], Susman[5]). Browne[13] states that 'No age is exempt from leprosy', but also 'In comparable communities, a higher proportion of leprosy infection in the younger age groups will be disclosed by examination of all children'. Other workers, however, have refuted the fact 'that the majority of persons acquire leprosy . . . before the age of 20 . . .' (Mohamed Ali[11]).)

Recent work (Spickett[14]) has produced evidence strongly suggesting that there are human genetic factors involved in the epidemiology of leprosy. Such genetic factors were considered as playing an important role in the determination of the susceptibility to leprosy by previous workers such as Aycock, Rotberg, Steiniger and Kinnear Brown. However, although strong evidence has now been produced supporting this possibility and further study is needed in this field, one must not lose sight of the fact that environmental factors play a very important part in relation to leprosy.

SUMMARY

From this very limited investigation into the localisation of the first lesions appearing in leprosy patients in northern Togo, there is an indication that the sites of such lesions, when ascertained as accurately as possible, show close correlation with the actual sites of contact of the patient, generally with the mother in infancy and early childhood. This, therefore, lends support to the generally held opinion of portal of entry of the leprosy bacillus through the skin brought about principally by skin to skin contact.

ACKNOWLEDGEMENTS

My thanks are due to Dr. J. K. E. Amorin, Directeur des Services Administratifs et Sanitaires, Togo, for permission to publish this paper, and to the Catholic Mission Sisters at Koloware leprosy village in northern Togo for their assistance.

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ADDENDUM

THE REPUBLIC OF TOGO

A decree was signed on July 21, 1966, by President Nicholas Grunitzky of the Republic of Togo creating in the service of the Ministry of Public Heath a 'Committee of Assistance to Leprosy Sufferers' (Comité d'Aide Aux Lépreux). This Committee includes the Minister of Public Health or his representative as President, and the following as members: the Minister of National Education or his representative, the Minister of Social Welfare or his representative, the Director of Public Health, the Chief of the Service of the Major Endemic Diseases, the Chief of the Service of the Anti-leprosy Campaign, and representatives of the Red Cross, Evangelical Mission, Catholic Mission and Moslem Community. The Committee is charged with the following functions in Togo:—

1. To find ways and means of coming to the aid of leprosy sufferers.
2. To sponsor the various anti-leprosy campaigns.
3. To supervise the distribution to the leprosy sufferers of gifts collected.
4. To provide for the social re-integration and rehabilitation of cured leprosy sufferers.

The Committee has already held two meetings under the chairmanship of the Minister of Public Health and to which the Leprologist, Dr. I. A. Susman, was invited to attend. The first meeting was in the way of an inaugural one to introduce members to each other and to outline the aims of the Committee. It also permitted the Leprologist the opportunity to draw attention to the present position with regard to leprosy in Togo and the problems encountered and envisaged.

The second meeting, also under the chairmanship of the Minister, was called to put before a large audience of representatives of many organisations concerned with welfare, charity, sport, arts, drama, crafts, etc., the draft of the programme of the anti-leprosy campaign leading up to the next World Leprosy Day in January, 1967. This was mainly to discuss ways and means of raising funds for the fight against leprosy. The programme included the formation of Regional Committees responsible to the central committee in Lomé, conferences and discussions throughout the country to medical and paramedical staff and to teachers, who would then give talks to the general population and particularly to schoolchildren, film shows about leprosy, records to be made and played of traditional songs by leprosy patients, sermons in the various churches with leprosy as their theme on the two Sundays preceding World Leprosy Day. In addition, it was proposed to organise, throughout the country, dances, cinema shows, musical and theatrical concerts, fairs and tombola, football matches, boxing and basket-ball as well as making public collections.

On World Leprosy Day itself (which is normally the last Sunday in January) various activities would take place including appeals by

the President of the Republic, by M. Raoul Follereau, founder of the Order of Charity and of World Leprosy Day (recorded) and by the Minister of Health. The distribution of gifts to the patients at the two leprosy villages and various treatment centres by a delegation of the Committee of Assistance to Leprosy Sufferers was also planned. The press and radio would be invited to take an active part in all these manifestations.

The anti-leprosy programme in Togo forms part of the Service of the Anti-yaws, Anti-leprosy and Anti-smallpox Campaign under the Ministry of Public Health. Until October, 1965, leprosy had been included in the campaign of the World Health Organisation directed principally against yaws and smallpox. Case-finding had been carried out by the teams of this campaign. Treatment for leprosy was available in all the hospitals and dispensaries throughout the country.

Since October, 1965, a Leprologist (Dr. I. A. Susman, formerly of the Gambia and Ghana) was assigned to Togo by the British Government under the British Bilateral Technical Assistance Scheme to Non-Commonwealth Countries in order to give a special priority to the leprosy problem.

It is estimated that there are 20,000 to 30,000 persons suffering from leprosy in Togo—a prevalence of 10 to 20 per 1,000. This is a high prevalence and it includes disabled and burnt-out patients and those still requiring to come under treatment.

Severe difficulties have been experienced in the campaign up till now because of lack of competent supervision by reason of absence of suitable means of transport for the supervising staff, who also have been insufficient in number.

It has been decided that a campaign founded on static clinics giving D.D.S. to as many patients as possible will be the most efficient method of approaching the problem in Togo. This arrangement will be an integral part of the general medical and health services, making use of the personnel already existing. The general supervision of the project, in addition to the Leprologist in charge, must be implemented by specially trained personnel (the 'contrôleurs-lèpre' or the 'agents-techniques').

Unicef are providing Mobylettes as a means of transport for these supervising staff.

Reorganisation of the two leprosy villages in existence (about 700 patients) and of all the treatment centres is at present in the process of being carried out. Stress is also being laid on propaganda and health education in the leprosy field by various means which include specially prepared posters, booklets and pamphlets.

It is hoped that in the near future it will be possible to carry out some sample surveys in several different regions of the country in order to obtain a better idea of the true pattern of leprosy in Togo than has been hitherto available.

Lep. Rev. (1966) **38**, 1, 43-44

Partial Sublimis Transfer

Suggestion for New Type of Leprosy Hand Surgery

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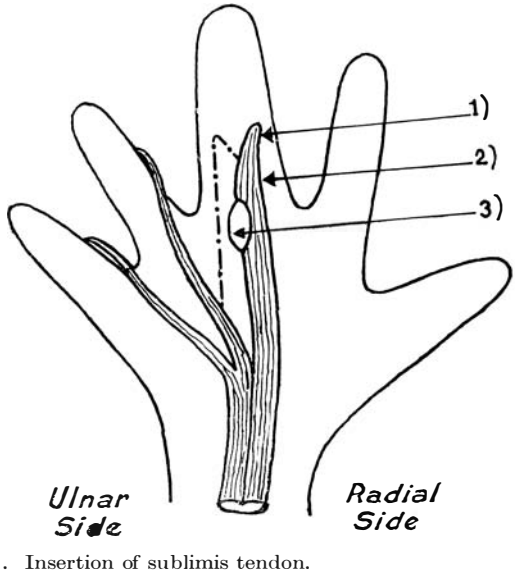
From 1959 to 1966 research was made at the Sacred Heart Leprosy Hospital, Kumbakonam, Madras State, India, in order to find more suitable methods for claw hand rehabilitation.

Long term observation of the old sublimis transfer operations have shown the opposite deformity after 1 or 2 years. These over-correction deformities are mainly due to the complete removal of the sublimis tendon and are prohibitive in the case of fingers with normal mobility. In order to prevent these sublimis removal deformities ingenious procedures have been developed by P. Brand, Vellore. The sublimis tendon is left in situ and a prolonged tendon of the extensor carpi radialis brevis is connected with the paralysed finger extensors.

The new suggestion: Why transfer a whole sublimis, where half is enough? One half of the sublimis tendon is used for the extension of the finger-joints of 2 adjacent (=neighbouring) fingers. This partial sublimis transfer cannot work on one and the same finger, because the remaining half will flex the finger-joints, whereas the transferred half would extend them and interfere.



1. Insertion of sublimis tendon.
2. Chiasma-part of sublimis tendon.
3. Profundus canal.

EXAMPLE: *Clawing of ring and little finger* (very common in leprosy). Ulnar half of long finger sublimis is split off, pulled back into the palm and divided in 2 tails. Each tail is passed through the lumbrical canal and stitched into the extensor expansions of ring and little finger, giving extension to the finger-joints. Radial half of long finger remains in situ, preventing sublimis removal deformity.

Detailed description of the PARTIAL removal of the sublimis tendon.
(Without damaging the flexor sheet proximal profundus canal !)

1. Terminal anaesthesia at the base of long finger. Bloodless field by tiny rubber-band, distal MP joint*. Ventrolateral incision at level of proximal finger joint. Flexor sheet opened. In maximal flexion of MP joint* the ulnar tail of the sublimis tendon is pulled out by dental hook. Ulnar tail is held by assistant. Chiasma-part of sublimis tendon pulled out and lifted, so that the 'bottom' of the chiasma and the vinculum is visible. Now the vinculum is cut. Complete detaching of all the vincula is essential, otherwise the sublimis tendon cannot be pulled out.
2. In maximal flexion of wrist and MP joint*: the whole sublimis tendon is pulled out, until the profundus canal is visible. Under control of the eye the chiasma part of the sublimis tendon is split from the profundus canal towards the insertion. Radial and ulnar tails of the sublimis tendon are thus separated.
3. Only now ulnar half is detached from the insertion. Undetached radial half is pulled out and fixed by assistant. Loose ulnar tail is caught by mosquito forceps. By simple pulling on the mosquito forceps the sublimis tendon is rent in two tails, backwards from profundus canal. Extreme flexion of wrist and MP joint* will make this splitting procedure easy and will give a nice long rent far back into the palm. Flexor sheet proximal profundus canal remains untouched.

* Metacarpo-Phalangeal joint.

'Two-finger deformity.' Clawing of ring and little finger.

4. Under local anaesthesia incision in the distal fold of the palm. Sublimis tendon is taken out from the flexor sheet. The rent in the tendon is identified (extreme flexion of the finger-joints very helpful !). Now the loose ulnar-half can be pulled out separately into the palm. A second time the ulnar half is torn back and cut into two tails. Each tail is passed by tunnel forceps through the lumbrical canal and stitched into the extensor expansions of ring and little finger. The stitching must be made under some tension, as there will be no helpful retraction as in case of complete sublimis removal.

Before doing the partial sublimis transfer we must make sure that there is sufficient power in the sublimis tendon. Failures are often due to powerless long finger sublimis, sometimes paralysed in violation of the rule that leprosy will damage only the small hand muscles and spare the forearm muscles.

Four finger disabilities can be operated in the same way: Long finger sublimis providing its ulnar half for index and ring finger, Index finger sublimis supplying ulnar half for long and little finger. Ring finger sublimis is spared for thumb reconstruction. Post-operative fixation is made in extreme flexion of the wrist joint, by special aluminium splints, avoiding plaster. For prevention of adhesions, early beginning of physiotherapy is essential. Failure has occurred, but was mainly due to powerless sublimis tendon or to insufficient tension in tying the sublimis tendon to the extensor expansion.

One year after the partial transfer of long finger sublimis.

A batch of 20 people have been operated on by the new method at the Sacred Heart Leprosy Hospital, Kumbakonam. Seventeen of them show satisfactory correction of their claw hand disability without a shade of over-correction. Contractures of the finger joints are always a strong contraindication for this type of transfer.

SUMMARY

A method of claw hand operation, using partial sublimis transfer, is described. The new procedure is especially convenient for reconstruction of isolated clawing of ring and little finger, very common in leprosy.

ACKNOWLEDGEMENTS

I am very grateful to Dr. N. Zwicky, M.D., to Mr. C. Pereira, as well as to the management of Sacred Heart Leprosy Hospital, for the assistance and encouragement in the production of this article.

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Lep. Rev. (1965) **38**, 1, 45-48

Gynaecomastia in Leprosy

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Gynaecomastia is one of the less frequent complications in leprosy. In a study it was found that only 11.8% of patients with lepromatous leprosy developed gynaecomastia[1]. The clinical features have already been described in a previous paper[2]. In this paper the histopathological appearance of the enlarged mammary gland is described in detail, and its significance is discussed.

MATERIAL AND METHODS

This study is based on the surgical specimens of gynaecomastia removed from 14 patients with lepromatous leprosy at the Schieffelin Leprosy Research Sanatorium at Karigiri. The tissues were fixed in 10% formalin and processed. Paraffin blocks were made and sections were cut at 6 μ thickness. Haematoxylin and eosin stain and acid fast stain for *M. leprae* were prepared from several blocks of tissue in each case.

RESULTS

Gross features

The enlarged mammary gland varied considerably in size from a small nodule of about 2 cm. in diameter to a large one of almost 10 cm. in diameter (Fig. 1). One of the largest specimens weighed 92 g. Clinically it had attained the size of the breast of a young woman (Fig. 2). Most of the specimens were of the larger variety because the patients with small lesions were not willing to undergo surgery.

The outer surface of the specimen was rounded, fairly smooth and clearly defined. There was no definite capsule. The consistency was mostly firm and it cut with considerable resistance. The cut section was uniformly greyish white. In patchy areas some yellowish fatty tissue was also present.

Microscopic findings

All the specimens showed marked proliferation of connective tissue (Fig. 3) and the enlargement of the gland was primarily due to this increase in the connective tissue. In most cases there was no definite arrangement of the connective tissue which surrounded the ducts. Even though all the specimens contained some fatty tissue it often formed only a small part of the mass.

There was also a significant proliferation of the ducts (Fig. 4) and a wide variation was seen in the extent of its proliferative activity. In some, small sized ducts widely spread in a large mass of connective tissue were seen and in others coiled, branched and distended ducts were seen. Occasionally mitoses were present. In every case there was marked increase in the number of layers of the cells lining the ducts (Fig. 5). Sprouting of lining epithelial cells and formation of locules were seen in 11 of the 14 patients examined. Intraductal papilla with connective tissue cores were present in 3 patients. In 1 patient the cellular arrangement resembled very much an intraductal papilloma (Fig 6). Pseudolobules were present, but true acini were not seen in any of the patients. In 1 patient there was cystic dilatation of the ducts.

Amorphus pink staining material was present inside the ducts in 10 patients (Fig. 7). Cells with basal vacuolation were seen in 8 patients. Shedding of epithelium was present in the ducts in all patients.

Periductal inflammation of varying intensity was present in every patient. The inflammatory cells were scanty in most specimens, but was very marked in 1 patient. The inflammatory cells consisted mostly of lymphocytes and plasma cells.

Total denudation of the wall of the duct was seen in 1 patient (Fig. 8). This was associated with marked inflammatory reaction. Denudation of the wall was followed by destruction of the epithelium and replacement of the duct with fibrous tissue. In 1 patient there were small foci of lepromatous granulomata consisting of lymphocytes and foamy macrophages (Fig. 9). The macrophages contained acid fast bacilli inside the cytoplasm.

COMMENTS

The hypertrophied male breast in leprosy consists largely of fibrous connective tissue. Adipose tissue forms only a small part of it. There is also proliferation of ducts which shows considerable variation. Many layered epithelial lining with budding and locule formation is a common feature. Secretion in the ducts is also evident in the majority of patients. However, no true acinar formation is noticed in any one of them. This picture is similar if not the same as described in gynaecomastia associated with conditions other than leprosy. In only 1 patient leprous granulomata are seen, but they are small foci, present in localised areas and are not obviously responsible for the enlargement of the breast. Therefore, it is reasonable to state that the development of gynaecomastia associated with leprosy is a process similar to those found in gynaecomastia due to other causes.

Karsner[3] while reviewing the literature on the aetiology of gynaecomastia quite justifiably states that the proliferation of connective tissue in the male breast can occur if oestrogenic substances are given for a considerable period of time and that in men oestrogens promote gynaecomastia. In most patients of lepromatous leprosy and in a few patients with borderline group of leprosy, the testis is infiltrated by leprous granuloma and there is atrophy of the seminiferous tubules. In some of the patients with testicular lesions the interstitial cells and Sertoli cells are spared and they stand out prominently. These cells are known to produce oestrogens. The presence of excess oestrogens may be an important etiological factor in the pathogenesis of hypertrophy of connective tissue in the breast of lepromatous leprosy patients.

Inflammatory cells are a common finding in the specimens studied. They consist of lymphocytes and plasma cells. They are few and scattered and are not part of leprous granuloma. Inflammatory cells are also present in gynaecomastia associated with non inflammatory diseases and there is no adequate explanation for their presence.

In all patients there is shedding of cells from the lining epithelium. In 8 patients the lining epithelium shows basal vacuolation. Pinkish secretion is present in the ducts of 11 patients. But it is not identified as colostrum or milk. There is no satisfactory evidence to prove that the enlarged mammary gland in the male secretes milk.

In one case there is marked cystic dilatation of the ducts resembling very much the changes seen in mammary dysplasia. However, this is present in a localised area and the lesion as a whole, is not similar to mammary dysplasia. Two other patients have a superficial resemblance to fibroadenoma. In these patients the fibroadenomatous proliferation is localised and the remainder of the enlarged gland shows a typical picture of gynaecomastia. Menville[4] has also reported similar changes in the patients he studied.

In one patient there is evidence of resolution with fibrous tissue replacing duct epithelium. These areas are small and are of no significance.

SUMMARY

The histopathological appearance of 14 patients of gynaecomastia in leprosy is described. Proliferation of connective tissue and duct epithelium are the typical features in all patients. This picture is identical with that described in gynaecomastia due to other causes. Two patients show small foci of lepromatous granuloma. It is

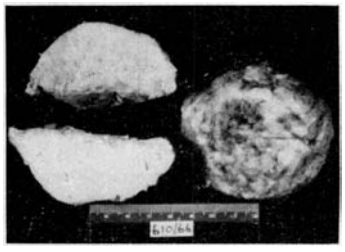

FIG. 1

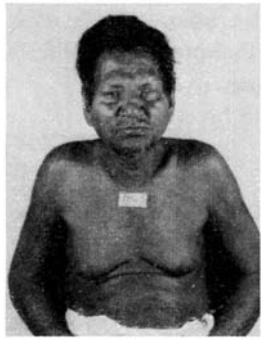

FIG. 2

FIG. 3

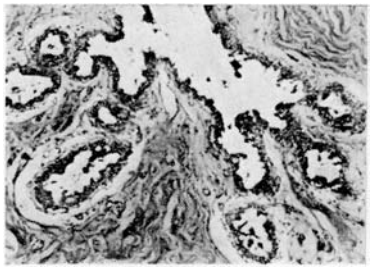

FIG.4

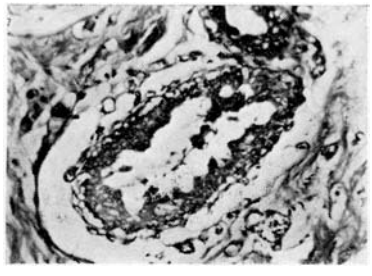

FIG. 5

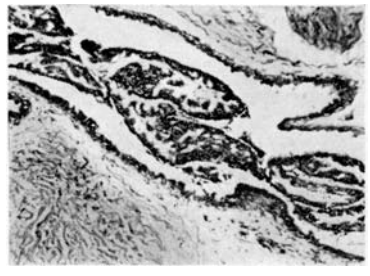

FIG. 6

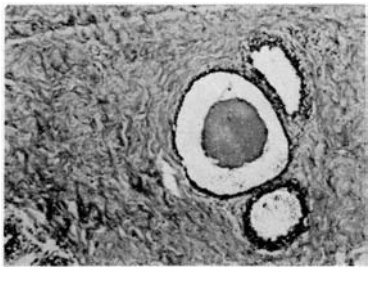

FIG. 7

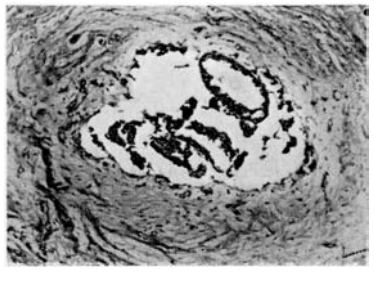

FIG. 8

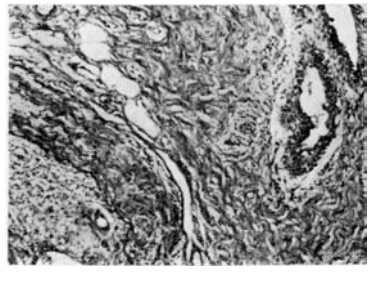

FIG. 9

Legend to figures

1. Specimen removed from a patient with bilateral gynaecomastia. Note the uniformly greyish cut surface and the fibrous nature of the tissue.
2. Photograph of a lepromatous leprosy patient with well developed gynaecomastia.
3. Photomicrograph showing branching ducts surrounded by dense connective tissue. Few small collections of fat cells are also seen (H & E × 35).
4. Photomicrograph showing the proliferation of the ducts (H & E × 125).
5. Note the many layered epithelium of the duct and the shedding of the epithelium into the lumen (H & E × 250).
6. The epithelium of the duct has proliferated considerably and the appearance is very similar to that of an intraductal papilloma (H & E × 125).
7. Note the dilated duct with secretion inside (H & E × 125).
8. Photomicrograph showing denudation of the wall of the duct. This is followed by inflammatory reaction and replacement of the epithelium with connective tissue (H & E × 125).
9. This picture shows lepromatous granulomata around a duct and a nerve bundle. Acid fast stain showed numerous bacilli in the granulomata in both the sites and inside nerve bundle (H & E × 125).

suggested that just as in gynaecomastia associated with other conditions hormonal imbalance and particularly an excess of oestrogens may be the cause of the enlargement of male breast in leprosy.

ACKNOWLEDGEMENTS

We acknowledge with gratitude the many helpful comments received from Dr. L. Chacko, M.B., PH.D., Professor of Anatomy, All India Institute of Medical Sciences, New Delhi. Our thanks are due to Mr. S. D. Sigamani and Mr. C. Dorairaj for the photographs, to Mr. S. Jesudass for technical help and Mr. George William for secretarial help.

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Lep. Rev. (1968) **38**, 1, 49-56

Some Genetic Aspects in the Epidemiology of Leprosy

(Study of Multiple case families)

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'No scientific investigation is final; it merely represents the most probable conclusion which can be drawn from the data at the disposal of the writer. A wider range of facts, or more refined analysis, experiment and observation will lead to new formulae and new theories. This is the essence of scientific progress.'
—PEARSON (1898).

INTRODUCTION

Leprosy is generally believed to be a disease of antiquity, with some historians claiming evidence of it in Egypt as far back as 4000 B.C. and in India and Japan probably earlier than 1500 B.C. Biblical references to the disease are legion, but there is considerable doubt today whether leprosy mentioned therein is the same disease that we now recognise. Though Hansen, a Norwegian physician, discovered the leprosy bacillus in 1872, until today all attempts at laboratory culture have been unsuccessful. Only limited success has been achieved in the field of animal inoculation. The exact means by which leprosy is transmitted—how the bacillus actually enters the body still remains a debatable point. However, it was generally believed that it is communicated only after prolonged and intimate contact with a patient, which is vague in itself. All those who now instinctively hold their breath when they pass a leprosy patient will be surprised to learn that it is classified only as a 'mildly communicable' disease. Indeed many medical men believe it is the least communicable of all communicable diseases. Although it is universally accepted that *M. leprae* is the causative organism of leprosy, it became apparent that the bacillus does not produce disease in all human beings with whom it comes in contact. A variety of factors has been invoked to explain this supposed variation in susceptibility and these include diet, climate, age, sex, incidence of other diseases and factors variously described as innate, inborn, constitutional, familial and hereditary.

Rotberg (1937), Aycock (1940, 1941, 1948, 1962), Steinigar (1941) suggested genetic factors in determining the susceptibility to leprosy. Kinnear Brown (1950, 1956, 1957, 1959) and Spickett (1962, 1963, 1964) have also supported the hypothesis that there is a genetic factor in determining the susceptibility to leprosy. Although several authorities have supported the concept that leprosy may only be manifest in those who are genetically susceptible to it, the hypothesis is not generally accepted.

Two different opinions

Leprologists all over the world are confronted with the problem of finding a clue regarding the aetiology of leprosy. There are two different opinions regarding how the disease is caused.

1. It is due to bacillary infection and the infection is caused by intimate and prolonged contact with a leprosy patient.
2. It is the genetic susceptibility in presence of bacilli and the intimate and prolonged contact that cause the disease.

If leprosy is an infectious disease, then all or at least the majority of the individuals who had

intimate and prolonged contact should have developed the disease.

Noordeen and Mohamed Ali (1964) studied 579 families each of which had more than 1 leprosy patient in the family. They found that occurrence of multiple victims in the same family was not strictly governed by the law of contagion. Particulars of these 579 multiple leprosy patient families are given below:

TABLE 1

Showing the population particulars of multiple leprosy patient families

Total No. of families	579
Total population	3382
Total No. of leprosy patients	1296
Average size of the family	5.84
Average No. of leprosy patients per family	2.24
Percentage of affected population	38.4

It is but natural that no other individual can have a more intimate and prolonged contact than between the members of the same family. If leprosy is an infectious disease and the infection is caused by intimate and prolonged contact with a patient, most, if not all those living in close contact should develop the disease. But it is seen that only 38.4% of the population contracted the disease. It is difficult to explain this apparent immunity of certain individuals to leprosy and this is taken to be due to the natural resistance the individual possessed. When it is the genetic susceptibility that is in operation he must inherit it from one or other of his parents. In such a patient it should be in accordance with the laws of inheritance. Let us analyse the various findings in the study of these multiple leprosy patient families and see if the occurrence of patients follows the laws of inheritance in any recognised manner.

Familial Aggregation

On looking into the family history of the different families, we find patients with varying degree of duration of the disease. The duration of the disease is the period between the age of onset of the disease and age of the individual at the time of survey. The individual having the longest duration of the disease in a family is taken as the source responsible for spreading the disease to the other members of his family and he is named the source patient.

In the population which provided the 579 multiple patient families we have thus 579 source patients as the source of infection. The total number of patients in these families was 1296; deducting source patients we have (1296—579)=717 patients who developed the disease by living with a source patient in intimate and prolonged contact and these 717 patients are termed secondary patients.

All the individuals who live with a patient in the same family are not affected. From this, one cannot escape postulating that infection alone cannot explain the incidence of the disease and may be that the individual susceptibility genetically governed has some say in the matter.

An analysis of the source and secondary patients arising from the source patient is given in Table 2:

It will be seen from the table that when parents are source patients, only sons and daughters (not all of them) were affected in spite of many other persons living with them in close contact. Secondly, when brothers and sisters are source patients, only their brothers and sisters were affected. When grandparents are source patients, only their grandchildren are affected and, lastly, when the paternal uncle was a source patient, his brother's children became affected. Thus whoever may be the source patient, only his blood relations were affected and not the others. Again when the husband was a source patient, some wives became affected. In the instance where spouses and in those when daughter-in-laws were affected, it was found that marriages generally took place among those families where there is a history of leprosy and among close relatives. All these things suggest that the disease is concentrated on family lines.

Genetic mechanism

At present there are different opinions regarding the role of genetic factors in determining the susceptibility to leprosy. They are:

TABLE 2

Showing the classification of source and secondary patients

Type of source patients

Secondary patient in relation to source patient	Source Patients	Head or Father	Mother	Son	Daughter	Brother	Sister	Wife	Grand-father	Grand-mother	Paternal Uncle	Others
Sons		161	73									
Daughters		67	38									
Wife		109										
Brother						66	14					
Sister						21	13					
Grandsons									9	9		
Granddaughters									2	5		
Brother's Son											6	
Brother's Daughter											3	
Mother				8	2							
Father				3								
Daughter-in-law		5	2									
Husband								10				
Son-in-law		1										
Others												90
Total		343	113	11	2	87	27	10	11	14	9	90

(1) based on a single dominant gene (Dominant inheritance);

(2) based on a single recessive gene (Recessive inheritance);

(3) based on a single irregularly dominant gene (Incomplete dominant inheritance);

(4) based on the influence of a number of genes (Polygenic inheritance).

Let us assume that a single gene A is responsible for susceptibility to leprosy. A gene is said to be dominant when it produces its effect if it is present on either one or both the pairs of chromosomes, and a gene is said to be recessive when it produces its effect only if it is present on both the chromosomes of the pair. In the case of dominant inheritance we expect the ratio between the affected and unaffected in the progeny to be 3 : 1 and in the case of recessive inheritance we expect the ratio to be 1 : 1. But our data do not conform to either of these categories.

Now let us assume incomplete dominance. Here the phrase 'incomplete dominance' needs some explanation. Incomplete dominance means a dominant gene which is not capable of fully penetrating as a heterozygote. In the case of incomplete dominance all the heterozygotes are not capable of producing the disease; only a few of them will penetrate and cause the disease.

We have from our data, 579 families, each family having a source patient who is considered as the source of infection to the other family members. All the 579 members who are source patients are suffering from leprosy, and therefore should possess the alleles either AA or Aa. (Here 'A' is the abnormal gene responsible for the susceptibility to leprosy and 'a' the normal gene.) We cannot rule out the possibility of some heterozygotes getting affected and this is in accordance with principle of incomplete dominance and their number may be small when compared to the homozygotes. Thus the source patients must be either homozygous to A or heterozygous to A and not homozygous to 'a' which indicates a normal person. In the course of life he or she (source patient) might have married an individual who is homozygous to A (AA) or heterozygous to A (Aa) or homozygous to a (aa) the normal. From this we can work out the expected type of progeny as a result of marriages between the above types of individuals.

Type of marriages	*Type of progeny*			
1. AA × AA	AA	AA	AA	AA
2. AA × Aa	AA	Aa	AA	Aa
3. AA × aa	Aa	Aa	Aa	Aa
4. Aa × AA	AA	AA	Aa	Aa
5. Aa × Aa	AA	Aa	Aa	aa
6. Aa × aa	Aa	Aa	aa	aa

These are the six possible types of marriage and as a result of such marriages we expect the progeny as:

AA : Aa : aa .. 9 : 12 : 3

or AA : Aa : aa .. 3 : 4 : 1

Now all the individuals possessing either AA or Aa are susceptible to leprosy, i.e., 87.5% of the progeny are susceptible to leprosy. But how many of them get the disease by living in contact with an open patient depends upon the rate of penetrance of the gene. Susceptibility and getting the disease are two different things. A heterozygous susceptible individual may not sometimes get the disease even by an intimate contact with a patient because of his having only 'Aa' and the necessary environmental factors. But we can certainly expect a homozygous person (AA) to get the disease earlier when compared to a heterozygous individual (Aa) because he is more prone to the disease by having 2 genes; probably this might be the reason for finding people getting affected with the disease at different ages though they are living with a patient in the same family under similar conditions. The susceptible individual getting the disease may also depend upon environmental conditions. As one of the studies conducted at the Central Leprosy Teaching and Research Institute (Dharmendra, 1961) showed that leprotic patches in children are often evanescent ones and therefore our findings in a survey might not have been the correct picture in the case of many children. Such cases may be heterozygous individuals who are susceptible to leprosy and by virtue of their susceptibility get a patch or two that disappear soon. Thus:

(1) All the heterozygous susceptible individuals may not contract the disease even by living with a patient. The same might be true with some homozygous susceptible individuals also by virtue of their having only a casual contact with a patient, but these may be small.

(2) Unless we know the penetrance rate in the population it is not possible to pronounce more precisely about how many heterozygotes will get affected.

Now let us see how far the observed things in our present study are in agreement with the projected hypothesis. For this, only those familes where parents were source patients and the secondary patients their children were considered. The total number of children in these families and the number affected in different cases are given in the following Table 3.

TABLE 3

Showing affected and not affected children with parents as source patients

Source Patients	Secondary Patients	Sons		Daughters		Sons and daughters	
		Total	Affected	Total	Affected	Total	Affected
Father	.. .. ..	479	161	287	67	620	228
Mother	.. .. ..	141	73	69	38	356	111
Total	.. .. ..	620	234	356	105	976	339

With the help of the above data an attempt has been made to test how far the proposed hypothesis is in agreement with the observed facts. From the available records we observed that the average age of the different secondary patients under consideration was 13.4 years. Since they were living in close contact with a patient for a considerable length of time we

expect many of the homozygous susceptible individuals to develop the disease during this period. To test this hypothesis the X^2 test has been applied and the results are shown below.

1. Sons and Daughters taken together (3 : 4 : 1) i.e. (3 : 5)

	Affected	*Not affected*	*Total*
Observed	339	637	976
Expected	366	610	976
Difference	—27	27	

$$X^2 = \Sigma \frac{(Obs—Exp)^2}{Exp}$$

$=3.01$

X^2 from tables at 5% level is 3.84.

X^2 on 1 d.f. is insignificant at 5% level.

2. Sons (3 : 4 : 1) i.e. (3 : 5)

	Affected	*Not affected*	*Total*
Observed	234	386	620
Expected	233	387	620
Difference	+1	—1	

$$X^2 = \Sigma \frac{(Obs—Exp)^2}{Exp} = \text{less than 1}$$

X^2 on 1 d.f. at 5% level is insignificant.

3. Daughters (3 : 4 : 1) i.e. (3 : 5)

	Affected	*Not affected*	*Total*
Observed	105	251	356
Expected	133	223	356
Difference	—28	28	

$$X^2 = \Sigma \frac{(Obs—Exp)^2}{Exp} = 9.4$$

The X^2 is significant at 5% level. The hypothesis that all the homozygous susceptible individuals will contract the disease when they are allowed to have an intimate contact with a leprosy patient is true in the case of (1) sons and daughters taken together (2) only sons and (3) in the case of daughters it was not true. In the case of these daughters our information is incomplete because generally daughters after marriage go to their husband's houses. Some of them must have developed the disease when they are living as wives. This may be the reason for finding a large number of wives as secondary patients, with the head of the family as the source patient. According to the theoretical ratio 3 : 4 : 1, we are having 87.5% of the progeny as genetically susceptible individuals (7 out of 8). These include homozygous as well as heterozygous individuals. Out of these genetically susceptible individuals only those who are homozygous to A got infected and showed the signs and symptoms of the disease and this is quite in agreement with the observed numbers as revealed by the tests of significance. The individuals who are homozygous to A will develop the disease earlier when compared to the individual who is heterozygous to A, under similar conditions of living. Because of greater susceptibility the majority of the homozygous individuals are sure to develop the disease when they are in contact with a leprosy patient and only a few may not develop the disease because of environmental factors. Some of the heterozygous individuals will also develop the disease and how many of them develop the disease depends upon the penetrance rate of the gene in the population. At present, in India, data are not available to work out the exact penetrance rate in the population. If we know this rate, in the population, then we can predict the number of individuals who are likely to develop the disease in future. In the absence of information on the penetrance rate in the population, the only way of finding the number of individuals who are likely to become infected in course of time is by keeping the family members under prolonged observation.

Penetrance Value

Penetrance value is the rate at which heterozygotes penetrate and develop the disease in the individual. Since the frequency of leprosy is high, the gene frequency also will be high and since the gene is not fully penetrant, the most satisfactory value of the penetrance rate may be obtained from a consideration of the

progeny, none of the parents of which had leprosy. The exact method of calculating the penetrance rate is to take the pedigrees of the affected families. But in the absence of such data, we will do the second best, viz., to consider the present generation in obtaining a value for the penetrance rate in the population.

In the study of conjugal leprosy (Mohamed Ali, 1965) conducted at the Central Leprosy Teaching and Research Institute information is available on the progeny where none of the parents had leprosy. We have information on 106 couples who were not affected with leprosy before marriage. After they got married they had children and some of the children developed the disease. The analysis of the progeny of these 106 couples gives us the following Table 4.

TABLE 4

Showing the distribution of children according to the size of the sibship

Size of sibships	*No. of sibships*	*Total No. of individuals*	*No. of affected*
0	5	0	0
1	22	22	5
3	21	42	8
3	26	78	17
4	12	48	4
5	11	55	11
6	5	30	1
7	4	28	2
	106	303	48

The observed proportion of affected individuals $= \frac{48}{303}$

The rate of penetrance is given by:

$$\frac{\text{Observed proportion}}{\text{Expected proportion}} \times 100$$

The expected proportion of affected individuals depends upon the type of mating. Here in our case we have 6 types of matings and we can calculate the expected proportion of heterozygotes in these 6 types of matings. The following Table 5 gives us the expected proportion of heterozygotes and the corresponding penetrance rates in the case of different types of matings.

It can be seen that the rate of penetrance changes with the type of mating and it takes the maximum value 31.7%. This happens in the case of matings between:

1. Homozygous vs Heterozygous individuals
2. Heterozygous vs Normal individuals

and it takes the minimum value in the case of mating between a homozygous vs normal individuals.

From this we observe that the maximum penetrance of heterozygotes is 31.7% and if they are allowed to live under similar conditions we expect 31.7% of the heterozygous individuals to become infected (in course of their average lifetime). In our problem we have 488 (4 out of 8) heterozygous individuals who are living with one or more patients and the number of in-

TABLE 5

Showing the penetrance rates in the different matings

Sl. No.	Type of mating	Proportion of heterozygotes	$\frac{\text{Observed proportion}}{\text{Expected proportion}}$	Penetrance rate
1	AA × AA	0	—	—
2	AA × Aa	$\frac{1}{2}$	$\frac{48}{303} / \frac{1}{2}$	31.7
3	AA × aa	1	$\frac{48}{303} / 1$	15.8
4	Aa × AA	$\frac{1}{2}$	$\frac{48}{303} / \frac{1}{2}$	31.7
5	Aa × Aa	$\frac{3}{4}$	$\frac{48}{303} / \frac{3}{4}$	21.1
6	Aa × aa	$\frac{1}{2}$	$\frac{48}{303} / \frac{1}{2}$	31.7

dividuals who are likely to become infected if they are allowed to live under similar conditions is given by:

$$\frac{488 \times 31.7}{100} = 155 \text{ (approximately)}$$

These are the total number of individuals whom we can expect altogether to get the disease in the course of their life. After knowing the number of individuals who are likely to get infection the next step is to know when they are likely to get the disease. From a contact survey conducted in the Institute (1963-66) we have got information on the attack rate in multiple patient families (Report in print). The attack rate per year during first contact survey period (22 months) is 1.60 and it is 2.19 during second contact survey period (12 months), the weighted average being 1.81 per year per 100. At this attack rate we expect

$$\frac{488 \times 1.81}{100} = 9 \text{ (approximately)}$$

9 heterozygous individuals to get infection in a time interval of 1 year. On this, we can say during the course of about 17 years from now $\left(\frac{155}{9} = 17\right)$ we expect all the heterozygous individuals are likely to develop the disease because of their genetic susceptibility provided we observe them under similar conditions of living. All these things are valid only if we disregard the effect of environment which may have some influence in the development of disease.

After working out the penetrance rate that is operating in the population and the expected number of heterozygous individuals to get affected every year, the next thing would be to see how far the observed things are in agreement with the calculated one. There are altogether 976 sons and daughters with father or mother as source patient. Out of this, 958 were examined at the time of the general survey. Assuming that the genetic ratio:

AA : Aa : aa .. 3 : 4 : 1

holds good in the population, the age distribution and the respective number of individuals in different classes are given in Table 6.

Though it is clear that the homozygous individuals will contract the disease earlier compared to the heterozygous individuals we cannot rule out the possibility of a few heterozygous individuals developing the disease. Also those homozygous individuals whose age is less than the probable incubation period of the disease may not develop the disease. Thus the 339 individuals who were affected at the time of the general survey include heterozygous individuals also but their number will be much smaller compared to the homozygous individuals. Many of the studies so far done on the incubation period shows that the period varies from 3 to 15 years. The long incubation

TABLE 6

Showing the age distribution of the sons and daughters with parents as source patients

Age	Son	Daughter	Total	AA	Aa	aa
0—4	78	72	150	56	75	19
5—9	137	86	223	84	112	27
10—14	124	117	241	90	120	31
15—19	74	51	125	47	63	15
20—24	92	14	106	40	53	13
25—29	42	11	53	20	27	6
30—34	25	4	29	11	15	3
35—39	13	5	18	7	9	2
40—44	6	2	8	3	4	1
45—49	1	1	2	1	1	0
50—54	3	0	3	1	2	0
Total	595	363	958	360	481	117
Average Age			13.4	13.4	13.5	

period in certain individuals may be due to heterozygosity of the individual. It will be seen from the table that the average age of the homozygous individuals is 13.4 years and that of the heterozygous individuals is 13.5 years. Taking the average maximum incubation period as 9 years it is clear that most of the homozygous individuals will have developed the disease. In the case of heterozygous individuals the disease takes a long time to develop the signs and symptoms, generally more than 9 years. The average age of heterozygous individuals being 13.5 years we cannot expect an appreciable number of heterozygous individuals to get affected. From this we can presume that almost all the affected individuals are homozygous individuals.

During the first 2 contact survey periods, i.e., during an interval of 3 years, we observed 49 patients among these sons and daughters. From the table, it will be seen that there are 360 homozygous individuals in the population, out of whom 339 were already affected. There are 21 homozygous individuals left unaffected at the time of the general survey. According to the calculated penetrance rate which is operating in the population, we expect 9 heterozygous individuals to get affected in a period of 1 year, thus giving 27 during a period of 3 years. All the homozygous individuals who were living with patients and not affected at the time of the survey may get affected during this interval and thus the total expected number of individuals who are likely to get infected during this interval of 3 years is $21+27=48$, and the actual number observed is 49. It is indeed a very striking coincidence of the observed with the expected.

CONCLUSIONS

(i) The data relating to the multiple patient families supports the theory that the disease leprosy may be determined genetically.

(ii) A genetic ratio exists between the affected and non-affected progeny under the assumption of incomplete dominance.

(iii) Penetrance rate has been calculated for the population under study with the help of which we can predict something about the prevalence of the disease in future.

It is clearly worthwhile to plan a genetic study in this population which enables us to pronounce more definitely about the factors operating in the spread of the disease.

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ACKNOWLEDGEMENT

We wish to express our thanks to Major-General P. N. Bardhan, Director, Central Leprosy Teacihng and Research Institute, for scrutiny and permitting us to publish this paper, and to Mr. P. Sirumban, Statistical Assistant, for his help in the compilation of data.

Lep. Rev. (1966) **38**, 1, 57-61

The Role of Ayurvedic "Samshodhan-Karm"* in Treatment of Leprosy

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INTRODUCTION

Various texts[1 9 10] of the ancient Indian system of medicine have indicated 'Samshodhan-Karm' (purificatory measures) with great stress in the treatment of 'Kushthas'[6] (skin diseases including leprosy). These measures have been prescribed not only before the administration of specific drugs, but also to be repeated several times in between the actual drug therapy. This particular procedure consists of several processes. Those meant for the treatment of leprosy are 'Snehana' (oleation), 'Vamana' (emesis), 'Virechana' (purgation) and 'Raktamokshana' (blood-letting). However, as the majority of leprosy patients already suffer from anaemia it was not desirable to impoverish further the blood of such patients by blood-letting and, therefore, this procedure was not adopted in this study.

Leprosy is a chronic disease and a number of remedies have been tried from time to time without finding an ideal one. The first and foremost drug used in the treatment of this disease was the oil of 'Tubarak' (Hydnocarpus or Chaulmoogra oil). This remedy was extensively used all over the world and was the mainstay in the treatment of leprosy till it was replaced by sulphones about 20 years ago. At present DDS in small doses is almost universally used and is the drug of choice in the chemotherapy of leprosy. No other drug has been found better, whether given singly or in combination with other drugs. The aim behind planning the present study was to investigate the role of purificatory measures of the ancient Indian system of medicine in comparison with the general standard treatment of leprosy by using DDS.

MATERIALS AND METHODS

Twenty male patients of untreated, advanced, infiltrated and nodular forms of lepromatous leprosy were the subject of study. When selecting the patients care was taken to choose pairs of identical patients. They were grouped into pairs by keeping 1 person of each pair to 1 group and the other person in the other group at random. In this way, 2 groups of 10 patients each were made, 1 for the trial and the other for control.

Group 1 received purificatory measures of the ancient Indian system of medicine followed by DDS.

Group 2 received DDS alone.

The duration of disease in these patients was 3 to 5 years, and the age range was 18 to 48 years. Purificatory measures of the ancient Indian system of medicine were carried out in the case of each patient in Group 1 before starting the administration of the specific DDS therapy and each procedure was repeated twice during the whole period of study of one year. 'Snehana' (oleation) was carried out by two standard methods: 1. Inunction of 'Tubarak Taila' (Hydnocarpus oil) mixed with equal parts of 'Nimb Taila' (*Azadirachta indica* oil), and 2. Oral administration of medicated and

* Purificatory measures of the ancient Indian system of medicine.

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processed 'Mahatikta-Ghrita'" (a compound preparation of herbal drugs and ghee, i.e., clarified butter) in a gradually increasing dose. A total of 56 oz. of 'Mahatikta-Ghrita' was administered starting from 2 oz. on the first day and increasing by 2 oz. every successive day and thus completing the total amount within 7 days. Inunction and oral administration of 'Mahatikta-Ghrita' were carried out concurrently.

'Vamana' (emesis) was introduced after 24 hours of completion of 'Snehana' process. A powder made of equal parts of 'Patola Patra' (*Trichosanthes diocias* leaves), 'Pippalee' (*Piper longum*) and 'Nimba' (*Azadirachta indica*) bark with 'Madanphala' (*Randia dumetorum*) was administered orally for 'vamana' in the early morning only for a day. In each individual the dose differed but ranged between 10 to 20 g. for the full process. A complete morning intake was weighed and measured prior to the start of the process and at the end the total output was weighed. Only when the output was found to be more than input was the process considered complete and perfect otherwise 'vamana' (emesis) was repeated the same day. After this the patients were kept in bed for complete rest without any medication for one week, following which the 'Snehana' process was repeated and the patients were not given anything on the succeeding 3 days. On the fourth morning the 'Virechana' (purgation) process was commenced by oral administration of a powder made of 'Trivrit' (*Operculina turpethum*). Here also the dose differed in individual patients but ranged from 10 to 15 g. If the number of stools passed was at least 15, the process was considered complete and perfect, otherwise it was repeated. Following 'Virechana' the patients were advised complete bed rest of 1 week but without giving any medication. Thus the 'Samshodhan-Karma' was completed in 34 days. In the case of Group 1 the standard treatment of DDS was given by following a pattern of gradual increasing dose, starting from 10 mg. once a day and increasing by 10 mg. every week, till the dosage of 100 mg. daily was reached. In this dosage the drug was given for 6 days in a week[8].

Patients in Group 2 were put on DDS from the very beginning following the same pattern.

Records and Laboratory Investigations

The history and clinical condition of the patients were recorded on history sheets. The clinical picture of the patients was depicted with the help of notations given in 'Notes on Leprosy'.[3] Weight records were maintained. Bacterial Index (B. I.) was calculated in each case by taking smears from 6 sites and adding the degrees of positivity of all the smears and dividing the total by the number of smears examined.[3] Haematological examinations including the erythrocyte sedimentation rate by Weatergren method were done. Urine and stool examinations were carried out.

All the above-mentioned records and laboratory investigations were done before starting the therapy and at 3 monthly intervals.

Criteria for Assessment

The criteria for the assessment of improvement were denoted as 'Stationary', 'Improved' and 'Deteriorated'[5 7]. These categories are defined in Table 1.

RESULTS

There were 10 patients in each group, some of whom discontinued the treatments after some time. In Table 2, statistical analysis of B. I. is reproduced. It will be seen from the Table 2 'A' that the mean B. I's before treatment, after 6 months and after 12 months of treatment in the 2 groups remain more or less the same. When the decrease in B. I. after 6 months and 12 months of therapy was tested for significance it was found that the 2 groups did not indicate any difference. Thus there is no evidence of difference in action between the 2 groups.

In Table 2 'B' analysis of only those patients who remained throughout the therapy is included, which shows again no significant difference between the 2 groups.

In Table 3 the findings of this study are tabulated. It will be seen that the majority of the patients in both the groups improved.

TABLE 1

Criteria for the assessment of patients under treatment

Clinical condition	Stationary	Improved	Deteriorated
Nodular and Infiltrative	No change	Nodules and thickened areas flattening or flattened, with wrinkling. Freedom from reaction, relief of nerve pain and eye symptoms and nasal obstruction. Bacteriologically still positive.	Increase in thickening and/or number of patches and nodules, ulceration of nodules, occurrence of repeated reaction. Onset of complications in nerves (nerve pain), eye (iritis), nose (nasal obstruction). Bacteriologically more highly positive.
Diffuse and Macular	No change	Almost complete subsidence of erythema, shininess and thickening in the skin, maybe with some wrinkling of the skin. Freedom from reaction, relief of nerve pain and eye symptoms and nasal obstruction. Bacteriologically still positive.	Increase in thickening, number or size of patches, appearance of nodules, occurrence of repeated reactions. Onset of complications in nerves (nerve pain and tenderness), eye (iritis) and nose (nasal obstruction). Bacteriologically more highly positive.

Statistical analysis for bacterial index (B. I.)

TABLE 2 'A'

Group	No. of cases	Before treatment	After 6 months of treatment		After 12 months of treatment	
		Mean B.I.	Mean B.I.	Mean of difference (with initial) ±S.E.	Mean B.I.	Mean of difference (with initial) ±S.E.
Group 1	10	3.24	2.98	—0.262±0.08	2.70	—0.541±0.09
Group 2	10	3.15	2.89	—0.265±0.06	2.71	—0.435±0.09
't'				<1		<1
				>0.05		>0.05

TABLE 2 'B'

Group	No. of cases	Before treatment	After 6 months of treatment		After 12 months of treatment	
		Mean B.I.	Mean B.I.	Mean of difference (with initial) ±S.E.	Mean B.I.	Mean of difference (with initial) ±S.E.
Group 1	6	3.17	2.97	—0.186±0.13	2.58	—0.580±0.30
Group 2	8	3.25	2.95	—0.302±0.13	2.79	—0.456±0.19
't'				<1		<1
P				>0.05		>0.05

TABLE 3

Summary of results after 12 months' treatment

Groups	Total No. of cases	Age range in years	Duration of disease in years	CLINICAL			DDS		
				Stationary	Improved	Deteriorated	No. of cases who had reaction	Continued (No. of cases)	Discontinued (No. of cases)
Group 1	10	18—48	3—5	x	6	4	4	6	4
Group 2	10	20—46	3—5	x	8	2	2	8	2

All the patients withstood well the measures adopted, but some patients had to be withdrawn from the trial as they developed reactions. They indicated good absorption of the drug used during the 'Snehana' (oleation) measure, both externally and internally. In the patients of both the groups in which the clinical and bacteriological progress was noted, they were almost similar. Both the groups showed considerable improvement: the size of the nodules of the lepromata became markedly less, some of the smaller lenticulate nodules on cheeks and ears almost disappeared, infiltration decreased; repigmentation of lepromatous macular lesions also took place. No patient in any group remained stationary either clinically or bacteriologically, barring those who had had reactions. Out of 10 patients in Group 1, 2 improved and 4 deteriorated, while out of 10 patients in Group 2, 8 improved and 2 deteriorated (Table 3). The DDS was stopped in all the deteriorated patients in whom lepra reactions occurred. Reduction in the Bacterial Index and degenerative changes in *M. leprae* ran parallel with clinical improvement in both the groups. The weight and haemoglobin gradually increased in both the groups during the first 6 months, but during the next 6 months of the treatment it gradually decreased.

Toxicity and Complications

No signs of toxicity developed during the treatment except reactions in some patients.

DISCUSSION

The classics of the ancient Indian system of medicine reveal that 'Samshodhan-Karm' therapy is the main measure in the approach to the treatment and prevention of diseases and maintenance of health. Yet while the physicians of the northern part of this country do not practise this therapy, their colleagues in South India are well known for the successful use of these measures. In view of these facts the present scientific inquiry was pursued on different measures (which are indicated in the treatment of leprosy) of this therapy. The combined administration of DDS and Ayurvedic 'Samshodhan-Karm' has not shown any significant beneficial effect either clinically and/or bacteriologically in comparison with the administration of DDS alone. The rate of improvement does not seem to have been accelerated by adding Ayurvedic 'Samshodhan-Karm' in any way.

Reaction was encountered but could not be definitely attributed to the Ayurvedic 'Samdhodhan-Karm' as very little is known about its direct cause, but reaction is most commonly associated with chemotherapy and the administration of sulphones.[4] This view is supported by the fact found in the present study as whenever during reaction the drug DDS was temporarily suspended it resulted in the disappearance of the inflammatory signs. However, it is felt that this particular procedure of the ancient Indian system of medicine should be given further trial by planned methods in a longer series of lepromatous patients before rejecting finally the aforesaid procedure.

SUMMARY

Some preliminary preparation of the patient for 'Samshodhan-Karm' (purificatory measures) is an essential pre-requisite for the Indian system of adoption of any specific therapy of leprosy in Ancient Medicine. This particular procedure has been evaluated under this study. The DDS given alone was taken as the control drug against which the results obtained with Ayurvedic 'Samshodhan-Karm' with DDS were compared after 6 months and 12 months of treatment. The assessment made at various intervals after treatment has not shown any appreciable improvement (clinical and/or bacteriological) in any of the patients. At the same time there was no untoward effect encountered which could be definitely attributed to the Ayurvedic 'Samshodhan-Karm'.

ACKNOWLEDGEMENT

The help in statistical analysis from Mr. E. G. Phadia, Statistician, P.G.I.I.M., Banaras Hindu University, Varanasi, is acknowledged with thanks.

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Reports

1. Report of the Tenth World Congress of the International Society for the Rehabilitation of the Disabled, 1966, by Dr. N. D. Fraser, M.B., CH.B., D.T.M. & H.

The Tenth World Congress of the International Society for the Rehabilitation of the Disabled met in Wiesbaden, Germany, between Sept. 11 and 17, 1966, under Pastor Werner Dicke, President. Some 2,000 representatives and delegates from 80 countries attended the meetings, at which all aspects of the problems connected with the rehabilitation of the disabled from whatever cause were fully discussed. Business firms, Societies and Missions occupied 3,000 sq. m. exhibiting their activities, and the many aids available from the simplest grip for fork or spoon to electrically controlled artificial limbs and wheel-chairs. Eighty films submitted in a competition for Honorary Mention presented the Film Committee with a difficult problem.

The Section on 'Planning Rehabilitation Programmes for Leprosy Patients' met under Dr. N. D. Fraser as Chairman and Dr. K. F. Schaller as Vice-Chairman to hear addresses from:

Dr. S. G. Browne on 'Leprosy—the Prime Disabler.'

Dr. O. W. Hasselblad on 'Prevention of Social Dislocation of the Leprosy Patient.'

Dr. N. H. Antia on 'Prevention of Deformities in Rehabilitation by Non-surgical Methods.' (Illustrated with colour slides.)

Dr. A. J. Selvapandian on 'Problems of Rehabilitation of Leprosy Patients in India.' (Illustrated with colour slides.)

It was interesting to note that though 3 out of the 4 speakers were surgeons, the emphasis of all the speakers was on the importance of prevention.

In the section discussing the Basic Requirements for the Supply of Prosthetics in the Emerging Countries, Mr. J. Steensma presented a paper on the 'Special Problems of Shoes and Braces for Leprosy Patients'; and Mr. J. A. E. Gleave's paper on 'Training of Orthopaedic and Prosthetic Appliance Technicians in Emerging Countries' was read for him as he was unable to be present.

In a plenary session on 'Regional Differences in the Acceptance of Disability and Desire for Rehabilitation', Dr. R. V. Wardekar's paper on the problem affecting leprosy patients in India was read for him.

The Film Committee awarded one of the first prizes to The Leprosy Mission's Film 'Day of Good Tidings'.

The Leprosy Mission and American Leprosy Missions combined in an Exhibition Stall illustrating activities in many parts of the world, and offering literature for the use of those who wished to know more about the problems of the treatment and rehabilitation of victims of the disease.

The following resolutions were approved by the Section on 'Planning Rehabilitation Programmes for Leprosy Patients' and submitted to the Resolutions Committee for presentation to the Congress. The Section

1. Deprecates the appalling fact that 4 out of every 5 of the 15 million of leprosy patients in the world are still without any treatment.
2. In view of the fact that deformity in leprosy is largely preventable, given early diagnosis and adequate treatment, urges that real efforts should be made to deal with the problem of leprosy in every country where the disease is endemic by means of surveys, education and treatment so that existing knowledge is applied.
3. Urges that steps be taken to bring before all concerned awareness of the threat that leprosy poses to the welfare of the community. The medical profession itself must change its attitude towards this disease and

there must be a similar change of attitude at all levels of society.

4. EMPHASISES that the ultimate solution of the leprosy problem depends on leprosy becoming part of the public health service of every country; and that rehabilitation facilities available to patients suffering from other diseases should be extended to leprosy patients. Every doctor and medical auxiliary should be trained in leprosy and its rehabilitation wherever the problem is endemic.

5. REITERATES that many of the deformities of leprosy can now be corrected by surgical means and that facilities for such reconstructive surgery should be made available wherever possible in general hospitals. A surgical programme is of great value in any anti-leprosy campaign encouraging patients with early disease to present themselves for treatment.

2. Report of the East African Leprosy Research Centre (John Lowe Memorial), Alupe, Kenya, 1964-65.

The report of the East African Leprosy Research Centre by Dr. Otsyula, Director, gives a record of the progress of the work started by the late Dr. C. M. Ross. The excellent suggestion is made that Dr. Otsyula should go for further study in medical research.

3. Report on Visit of General Secretary to Malawi—October, 1966, by Air Vice-Marshall W. J. Crisham, C.B., C.B.E.

The General Secretary visited Malawi in October, 1966, primarily to represent the Association at the ceremony of laying the Foundation Stone of the Project centre building in Blantyre by the President of Malawi, Dr. H. Kamuzu Banda, at 10.00 hrs. on October 20. The visit also provided a timely opportunity of seeing the Project in operation and for discussions with Dr. Molesworth, the Project Director, and his staff.

The Foundation Stone Ceremony

The President arrived for the ceremony exactly on time (10 a.m.) with everything in order. The seated audience, including everybody of consequence in the country (excepting the British High Commissioner who was indisposed—his wife was there)—Ambassadors, Ministers, Bishops, Chiefs and other distinguished people. These numbered about 1,000, with perhaps a further 1,000 standing around including a large contingent of dancing women who apparently attend such functions when the President is present. Dr. Molesworth noticed that one of the dancers had leprosy.

There was strong press representation, also television. 'Vis News', which is under contract to the B.B.C., filmed and recorded the whole proceedings, and said that this would be available in London a day or two later.

The introductory address was given by the Minister for Health, who then introduced the General Secretary; the latter made a short address, ending with an invitation to the President to unveil the Foundation Stone.

The President, who was very relaxed and cheerful, then spoke for some 40 minutes in very effective terms about the Project, ending with a strong appeal (amounting almost to a directive) to all those in positions of power and influence to co-operate with the Director of the Project and his staff. He then unveiled an inscribed Foundation Stone which had been set in a side wall of the building. The latter was already up to roof level and should be completed early next year.

Field activities of the Project

The General Secretary spent 2 days in the field with the Mobile (Landrover) teams, visiting villages and local clinics on pre-arranged circuits.

On the first occasion he went as a member of an otherwise all Malawi team—Medical Assistant (in charge), Clinic Attendant, and Driver/Writer on a North-East (Monday) Treatment circuit. These circuits are carried out to a pre-arranged timed programme so that patients know precisely where and on what day and time they

can receive treatment each week. Regularity and punctuality was essential for the good attendance of patients. There was only one patient absentee. The Medical Assistant examines the patients and dispenses drugs; the Driver/Writer records observations on the special record card for each patient; the Clinic Assistant is dispatched on his bicycle into villages/hamlets where the Landrover cannot go, and rejoins the vehicle later. These mobile operations call for a good deal of experience, discipline and dedication, and of course need regular supervision. At present a total of 15 treatment circuits are carried out each week (Monday to Friday) by the 3 Landrover treatment teams. It is now necessary to provide a fourth such team in order to cover the Project area fully. This will raise the number of treatment clinics to 20 each week.

On the second occasion the General Secretary joined Mr. Drake's Survey/Case-Finding team (there is only one such team at present) visiting a large village in the south-west area, to examine contacts with known leprosy sufferers; to record any new cases found; and to give BCG injections to contacts up to 20 years of age.

The detailed examination of contacts, young and old, was carried out by Mr. Drake and the Medical Assistant, Mr. Mwakusula. The females were examined by Mr. Drake in a hut, and the males at the Landrover by Mr. Mwakusula, who also gave the BCG injections. The patients'/contacts' cards were written up by the Writer, Mr. Kayeaera. The whole proceedings took several hours since there were some 200 contacts to be examined. These had been collected together by the village Headman. The villagers showed great interest and gave fullest co-operation. In all, only 3 new cases were found among those examined, and these were registered for regular treatment.

Work of this kind calls for a high degree of responsibility and dedication, and can be very tiring. The General Secretary was much impressed by the work of Mr. Drake and his team.

At present there is only one survey/case-finding team, and it is thought that this will meet the needs of the Project until the end of 1967, when the Director expects to be able to assess the needs of the Project with greater accuracy. Depending on progress in the meantime, it seems likely that a second case-finding team may be needed in 1968.

General

The starting date for the Project has been officially recorded as 25 May, 1965. In fact, only small scale activities in the field were practicable until the middle of the present year, when the current programme of treatment and survey circuits was set up. Good general progress is now being made. Increasing numbers of new patients are being found and brought under treatment as the mobile teams extend their activities into new districts and villages. However, it is likely that the retention of trained and efficient local staff will be a problem, also there is a danger that patients will tire of coming regularly for treatment as their condition improves.

The General Secretary is confident, however, that the Director and his team, firmly supported by the Malawi Government, will overcome this, and the many other practical problems that are bound to arise in a project of such complexity.

Abstracts

1. **Isoniazid plus Thioacetazone compared with Two Regimens of Ioniazid plus PAS in the Domiciliary Treatment of Pulmonary Tuberculosis in South Indian Patients,** by TUBERCULOSIS CHEMOTHERAPY CENTRE, MADRAS. *Bull. Wld. Hlth. Org.*, 1966, **34**, 4, 483-515.

Two hundred and forty South Indian patients with advanced pulmonary tuberculosis and with similar clinical, radiographic and bacteriological conditions were allocated at random to treatment for one year with one of 3 regimens of daily oral chemotherapy. They were treated on an out-patient basis and required to administer the drugs themselves at home. The 3 regimens and the daily dosages for a patient weighing 100 lb. (45.4 kg.) were:—

PH : Isoniazid 200 mg. plus sodium PAS 10 g. in 2 divided doses.

TH : Isoniazid 300 mg. plus thioacetazone 150 mg. in one dose.

P_6H/H : Isoniazid 200 mg. plus sodium PAS 6 g. in one dose for the first 6 months, followed by isoniazid 300 mg. in one dose for the second 6 months.

This study has shown that the regimen of isoniazid plus thioacetazone (TH) was as effective as the standard regimen of isoniazid plus PAS (PH) in the treatment for one year of patients with advanced pulmonary tuberculosis. However, the thioacetazone regimen had a higher incidence of side-effects. A 2-phased regimen of isoniazid plus 6 g. of PAS for the first 6 months followed by isoniazid alone for the second 6 months (P_6H/H) was less effective.

2. **A Controlled Study of the Influence of Segregation of Tuberculous Patients for one year on the Attack Rate of Tuberculosis in a 5-year Period in Close Family Contacts in South India,** by S. R. KAMAT *et al. Bull. Wld. Hlth. Org.*, 1966, **34**, 4, 517-32.

The authors undertook a controlled survey in South Indian families to assess the value of domiciliary treatment of pulmonary tuberculosis for one year as compared with sanatorium treatment. There were 693 close family contacts and the majority of the families came from lower income groups with poor living conditions and dietary standards. The findings in this report together with those published previously for patients demonstrate that ambulatory treatment of patients with pulmonary tuberculosis is practicable and effective and safe for the close family contacts.

3. **A 5-year Study of Patients with Pulmonary Tuberculosis in a Concurrent Comparison of Home and Sanatorium Treatment for One Year with Isoniazid plus PAS,** by J. J. Y. DAWSON *et al. Bull. Wld. Hlth. Org.*, 1966, **34**, 4, 533-51.

A total of 193 patients was admitted to a controlled comparison of home and sanatorium treatment of pulmonary tuberculosis, all patients receiving a standard regimen of isoniazid plus PAS for one year. The present report deals with the progress of all these patients (96 home, 97 sanatorium) during the 2nd, 3rd, 4th and 5th years. Of the total of 193 patients 8 died from non-tuberculous causes during the 5-year period. Of the remaining 185, 90% had bacteriologically quiescent disease at 5 years, 4% had active disease and 6% had died of pulmonary tuberculosis. The proportion of patients who had quiescent disease at 5 years was very similar for the home and the sanatorium series, being 90% and 89% respectively.

4. **The Diet, Physical Activity and Accommodation of Patients with Quiescent Pulmonary Tuberculosis in a Poor South Indian Community,** by C. V. RAMAKRISHNAN *et al. Bull. Wld. Hlth. Org.*, 1966, **34**, 4, 553-71.

A study was undertaken of the diet, physical activity, occupation and living accommodation of 127 South Indian patients with pulmonary tuberculosis whose disease had attained bacteriological quiescence after one year of treatment with isoniazid plus PAS. Despite adverse environmental conditions bacteriological quiescence has proved to be stable over 4 years in the great majority of patients. This study does not provide information on the influence of environmental factors on the susceptibility of the individual to tuberculosis, on the spread of the disease in the community or on the progression of the disease in untreated or inadequately treatedpatients.

5. **Comparative Value of Sputum Smear Examination and Culture Examination in Assessing the Progress of Tuberculosis Patients receiving Chemotherapy,** by S. DEVADATTA *et al. Bull. Wld. Hlth. Org.*, 1966, **34**, 4, 573-87.

This paper compares the value of smear examination for tubercle bacilli of overnight specimens of sputum, month by month, with that of culture examination and isoniazid-sensitivity tests in assessing the progress of patients treated with isoniazid, either alone or with sodium PAS, in 3 chemotherapy studies. The comparisons are based on the ability of these bacteriological methods to predict during treatment, the response at the end of 12 months, which was classified as favourable or unfavourable, mainly on the basis of culture results at 10, 11 and 12 months. Reliable conclusions could be drawn regarding the therapeutic efficacies of regimens by considering the results of smear examination, since the 2 types of assessment (smear and culture) yielded on the average identical classifications in 95% of the patients. However, smear examination was slightly less sensitive than culture examination in detecting differences in the therapeutic efficacies of various antituberculosis regimens. This disadvantage can usually be offset by admitting about 20% more patients.

An Epidemiologist's View of Leprosy, by K. W. Newell. *Bull. Wld. Hlth. Org.*, 1966, **34**, 6, 827-57.

The author from the point of view of an epidemiologist gives a critical review of some recent publications on leprosy. Leprosy appears to be an infectious disease resulting from an infection with *M. leprae*. The method of spread and point of entry of the bacillus are unknown but it is probably airborne and may enter a susceptible person through either the skin or the nasopharynx. In a proportion of persons infected the disease shows a clinical form, lepromatous leprosy, with an unfavourable prognosis, greater infectivity and different symptomatology. The number of patients of this type in a community may be a major influence upon the continuation of the disease and its prevalence in a given area. At present, potential patients with lepromatous leprosy cannot be identified beforehand although they are probably included in that part of the population which is Mitsuda-negative. The infected individual without symptoms cannot be identified at present although the incubation period of leprosy may be several years. It is probable that symptomless infections frequently occur. Immunity is said to vary because of inherent differences in susceptibility. No known disease (including tuberculosis and BCG vaccination) has been adequately demonstrated to be related to infection with *M. leprae* or to alter the course of a leprous illness occurring subsequently. Leprosy has had an almost world-wide distribution but it is now largely restricted to the tropics and subtropics and within endemic areas its distribution is uneven. No non-human reservoir of *M. leprae* is known or postulated. The lepromin test (Mitsuda reaction) is the first objective test related to prognosis but at present it is unstandardised in both its nature and its interpretation. Reactivity has been demonstrated in many uninfected population groups in endemic and non-endemic areas but few major variations have been shown. Such an unusual disease that apparently has such difficulty in survival and that cannot be identified outside the human body must surely be controllable. The problems connected with its prevention appear soluble if reasonable effort and objectivity and existing scientific methods of approach are directed towards it.

7. **The Histopathological Appearance of Leprous Rhinits and Pathogenesis of Septal Perforation in Leprosy,** by C. K. Job, A. B. A. Karat and S. Karat. *J. Laryng. & Otol.*, 1966, **80**, 7, July, 718-32.

Forty-eight biopsies from the noses of 38 patients—2 tuberculous, 3 indeterminate and 33 lepromatous—were studied. The histopathological appearance of leprous lesions in the nose is described. In the tuberculoid and borderline patients there is infiltration of the nasal mucosa with lymphocytes, epithelioid cells and giant cells but no obvious destruction of the nasal cartilage or bone is seen. In lepromatous leprosy the septal cartilage is surrounded by vascular granulation tissue which may promote the absorption of cartilage cells but the chief cause of the destruction of the cartilaginous septum is the gradual invasion of the cartilage by lepromatous granulation tissue. In addition there is atrophy of the nasal mucosal lining followed by ulceration. The ulcers invariably are secondarily infected and the acute inflammatory granulation tissue formed may invade the nasal cartilage and destroy it. Part of whole of the nasal septum and the tissue around it are replaced by fibrous tissue and the nose which has lost its main support is subject to the pull of the contracting fibrous tissue as well, and the end result is a retracted, collapsed and deformed nose.

8. **Rehabilitation in Leprosy,** by V. K. Sharma. *J. Ind. Med. Ass.*, 1966 **47**, 8, 408-409.

This paper is of great practical value and should be studied intimately in the original.

9. **The Management of Dry Skin in Leprosy Patients,** by J. R. Harris and S. G. Browne. *Lancet*, 1966, May 7, 1011-13.

The authors discuss, with 4 case-reports, the frequent and serious complication of dry skin in patients with leprosy. The low water content of the skin is associated with diminished sweating and the occurrence of peripheral neuropathy, and aggravated by low atmospheric humidity. The condition may be relieved, and fissuring prevented, by daily soaking of the affected part in water, followed by an application of soft paraffin. This simple and valuable practical hint is welcomed.

(From abstract by J. R. Innes in *Trop. Dis. Bull.*, 1966, **63**, 9, 984.)

10. **Nimbadi-Lepa in the Treatment of Leprosy. A Preliminary Report,** by D. Ojha. *Indian J. Med. Sci.*, 1966, **20**, 3, Mar., 217-21.

The Ayurvedic or ancient Indian system of medicine makes available several varieties of 'lepas' or inunctions in the treatment of leprosy and the author, encouraged by the reported success of Etisul or ditophal in the treatment of leprosy by inunction, chose Nimbadi-Lepa for trial on 6 patients with lepromatous leprosy selected from out-patients. The results were compared with those of DDS given to another group of 6 patients with leprosy. The results were encouraging and the drug was without toxic effect during the whole period of treatment of 6 months. Further studies are desirable.

The inunction of Ayurvedic origin contained 13 ingredients as follows:—(1) the bark of *Azadirachta indica*, (2) the rhizome of *Curcumalonga*, (3) the wood of *Berberis aristata* and other species, (4) the leaves and flowering top of *Ocimum sanctum*, (5) the leaves of *Trichosanthes dioica*, (6) the root of *Saussurea lappa*, (7) the root of *Withania ashwagandha*, (8) the wood of *Cedrus deodara*, (9) the bark of *Moringa oleifera*, (10) the seeds of *Brassica nigra*, (11) the fruits of *Coriandrum sativum*, (12) the fruits of *Zanthoxylum alatum*, (13) the plant of *Angelica glauca*.

It was found that Nimbadi-Lepa speedily reduced the external signs of leprosy, decreasing the size of nodules and skin lesions. It promoted pigmentation and caused marked reduction of the bacterial index and this reacted favourably on the general psychological state.

It can be used with other anti-leprotic drugs such as DDS. Nimbadi-Lepa gives quick and encouraging results, but a longer time of study is needed for full assessment as to the time of treatment required and study of drug resistance and relapses.

(From abstract by J. R. Innes in *Trop. Dis. Bull.*, 1966, **63**, 9, 985.)

11. **La situation de l'endémie lépreuse en Guyane Française en 1965** (Leprosy in French Guiana in 1965), by H. Floch and M. Duchassin. *Bull. Soc. Path. Exot.*, 1965, **58**, 3, May-June, 401-9.

The senior author refers to his intimate knowledge of the leprosy situation in French Guiana since 1938. With Duchassin, he now reviews the present state of leprosy control in the territory.

Since mid-1964, a town leprosy clinic has catered for certain categories of patients: those suffering from recently-diagnosed lepromatous leprosy, or from the more serious kinds of borderline leprosy; those with bacillary-positive tuberculoid lesions passing through reactional episodes; leprosy patients suffering from acute intercurrent illnesses; and those requiring surgical treatment for residual paralysis or neuropathic ulceration. The standard treatment is dapsone, either by the mouth or by intramuscular injection. A long-acting sulphonamide has proved to be slower in action than dapsone and shows no superiority over dapsone in the incidence of acute exacerbation.

The anti-leprosy campaign has halved the prevalence of leprosy (to 2.3% in a population of 36,670) since 1949. The authors are satisfied with the system of survey and diagnosis of leprosy among school children, in whom indeterminate and tuberculoid leprosy is diagnosed at an early stage, and in whom cases of serious lepromatous disease are not seen. It would appear that adequate treatment of patients in the early stages of leprosy will prevent the development of bacilliferous forms. They give a warning, however, against premature optimism, especially in view of the fact that adults with unsuspected and untreated advanced lepromatous leprosy are now being discovered. They plead for a restoration of legal powers (such as insistence on a certificate of non-infectivity for food-handlers and others brought into contact with the public) both at the national and at the communal levels, and express some regret that the excellent methods of survey and control which were a feature of the French colonial system have been abandoned.

(From abstract by S. G. Browne in *Trop. Dis. Bull.*, 1966, **63**, 10, 1094-5.)

12. **Les classifications de la lèpre. Pour une classification immunologique** (Classification of Leprosy. Towards an Immunological Classification) by J. Languillon. *Méd. Trop.*, Marseilles, 1966, **26**, 2, Mar.-Apr., 115-23.

After a brief historical review of the main pronouncements on the classification of leprosy by international conferences (Manila, 1933; Cairo, 1938; Madrid, 1953) and of the systems proposed by the South American and the Indian leprologists, the author stresses the importance of the immunological basis for classification. While unimportant differences of opinion exist regarding the lepromatous and tuberculoid 'polar' types, controversy continues in respect of the precise nomenclature to be used for patients exhibiting lesions in the broad unstable intermediate zone. The author considers that the indeterminate stage is essentially transient, and that persistently achromic and inactive macules (sometimes referred to as 'indeterminate') should be regarded as scars indicating healed lesions. (This attitude will commend itself to most leprologists.)

Patients who have had adequate and regular treatment for 'polar' tuberculoid leprosy may safely be placed 'on observation without treatment'; but treatment for life is advocated both for those with lepromatous leprosy who have, necessarily, a persistently negative Mitsuda reaction, and for those with the type of borderline leprosy the authors refer to as 'interpolar' unstable leprosy.

(From abstract by S. G. Browne in *Trop. Dis. Bull.*, 1966, **63**, 10, 1095-6.)

13. **Critères de blanchiment et de guérison pour les lépreux** (Criteria of Arrest and Cure of Leprosy), by M. Labusquiere. *Méd. Trop.*, Marseilles, 1966, **26**, 2, Mar.-Apr., 130-33.

During the first Technical Conference of OCCGEAC (*Organisation de Coordination et de Coopération pour la Lutte contre les Grandes Endémies en Afrique Centrae*) held at Yaoundé in December, 1965, the crieteria of arrest and cure of leprosy as laid down by successive conferences and meetings of experts of WHO were reviewed.

It was agreed that since these criteria could not be—and have not been—applied to mass campaigns in the French-speaking countries of West Africa represented at Yaoundé, the statistics of patients who are still regarded as being under treatment for leprosy were inflated and misleading. It is therefore recommended that bacterioscopic examination of the skin and nasal mucosa in a patient who has had adequate treatment for tuberculoid leprosy—being both unnecessary and impracticable—should not be required before discharge. Clinical criteria of 'arrest' and 'cure' are laid down.

For 'malign' leprosy, which includes bacilliferous borderline leprosy as well as lepromatous leprosy, bacterioscopic examination in addition to clinical evidence is necessary to establish inactivity. While such patients may be declared 'arrested' (*blanchis*), a patient who has had lepromatous leprosy may never be said to be cured. (This forthright statement is open to criticism; it certainly errs on the side of caution.)

(From abstract by S. G. Browne in *Trop. Dis. Bull.*, 1966, **63**, 10, 1096.)

14. **Limited Multiplication of *Mycobacterium lepraemurium* in Parabiotic Culture, as influenced by Osmolarity of an Alkaline-Galactomannan Medium,** by L. Kato and B. Gozsy. *J. Bacteriology*, 1966, **91**, 5, May, 1859-62.

During a study of the factors affecting the multiplication of *Mycobacterium lepraemurium in vitro* it was found that limited multiplication could be obtained in a medium containing a muco-polysaccharide, galactomannan, at *p*H 8.4. This substance was not metabolized but appeared to be necessary for the high viscosity which it produced and upon which growth depended. The necessity for the high alkalinity has not been explained. The physical properties of the medium appeared to be as important as its chemical constitution. The optimum concentration of sodium chloride in the medium was 2.0%; and growth was further enhanced when *Torula minuta* was added to the medium, although In the presence of 2.0% Na Cl the torula cells were lysed. Organisms were inoculated into rats after 4 and 8 weeks culture and produced lesions typical of murine leprosy.

(From abstract by D. S. Ridley in *Trop. Dis. Bull.*, 1966, **63**, 10, 1097.)

15. **Vole Bacillus Vaccine as an Immunising Agent in Leprosy,** by S. Ghosh and R. Bose. *Bull. Calcutta School Trop. Med.*, 1965, **13**, 4, Oct., 134-5.

The demonstration that an extract of vole bacillus gave skin reactions similar to those given by lepromin (this *Bulletin*, 1965, v. 62, 1004) suggested that vole bacillus might be used as a vaccine in leprosy. Accordingly 10 guinea-pigs were vaccinated to see if the vole bacillus caused conversion of their lepromin reactions; all the animals were lepromin and tuberculin negative before vaccination. One month after vaccination they were retested. Nine animals had become lepromin, but not tuberculin, positive (the 10th animal died). After a 2nd vaccination they gave strong lepromin reactions. Four unvaccinated control animals remained lepromin negative after repeated testing.

The conclusion is drawn that vole vaccine might be a useful immunizing agent in leprosy.

(From abstract by D. S. Ridley in *Trop. Dis. Bull.*, 1966, **63**, 10, 1098.)

Book Review

Ten Fingers for God by Dorothy Clarke Wilson, 247 pages, 16 illustrations, published by Hodder & Stoughton Ltd., Warwick Lane, London, E.C.4, 21s. net (in U.K.). Copies may be obtained from Friends of Vellore, Vellore House, Claverley Villas, London, N.3.

This is a most valuable and absorbing book of 247 pages and is recommended for general perusal as well as for leprologists. Dorothy Clarke Wilson gives ample examples of the human details and her work will be received with gratitude. This is the story of Paul Brand's quest to end the ravages of leprosy. As Professor of Orthopaedic Surgery at the Christian Medical College and Hospital, Vellore, he first developed the operation which has restored usefulness and movement to hands hopelessly crippled by leprosy, and as Director of Surgery and Rehabilitation for the Leprosy Mission he has combined the teaching of orthopaedic surgery with an intense programme of research and training in leprosy rehabilitation. This work, which began at Vellore and the Schieffelin Leprosy Research Sanatorium, Karigiri, has spread throughout the world and thousands of sufferers from deformity are today finding new life and hope. The end papers give excellent maps of Vellore and in the text are 16 illustrations. This is a truly fascinating book and is highly recommended to all.

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