Editorials

THE PEOPLE WE FAIL TO REACH

Leprosy is a disease which affects the body of the patient and the mind of the public. It carries a greater stigma than any other disease and the continued use of the word "leper" with its evil connotation is still commonly used in most societies. Can we truly blame the public when the majority of the medical profession continue to treat it as a disease apart from all others?

The age-old fear of leprosy was the result of the unsightly deformities and the fact that no cure was available. Today leprosy is curable, deformities can be prevented and if they should occur can be corrected by reconstructive surgery.

Nevertheless the age-old fear and stigma continues to persist and is probably the single most important factor which has prevented the control of leprosy, despite well planned national programmes based on effective drugs and modern scientific knowledge. Despite the expenditure of vast sums of money we realize that only a third of the estimated number of persons in the world suffering from leprosy are actually registered, and surveys demonstrate that of these less than 50% take regular if any treatment after diagnosis. At the end of 2 years probably another half drop out or become irregular. How can any disease be controlled, however effective the drugs, if the majority of patients do not take the treatment necessary for the cure? This is a problem common to many other chronic diseases like tuberculosis and filariasis.

Unfortunately these important social and psychological aspects of the disease receive scant attention in the planning of most major programmes, and the emphasis continues to be on "early detection and treatment". It has been demonstrated by the Belgian Centre at Polambakam that the addition of physiotherapy and surgery considerably improved regularity of attendance, for the patient felt something more was being done than mere distribution of pills. The experience of the Danish programme in Pogiri and Aksa was even more remarkable in that by education and ready availability of treatment, not only did the majority of patients come voluntarily for treatment but also that the regularity rate was much higher because the patient realized the importance of such treatment. It is also interesting to note that this programme had a minimal medical staff component.

These and other similar experiences have demonstrated that social and psychological factors are probably more important in leprosy control than the medical component of the programme. While it is not suggested that the medical aspect of the disease is unimportant, the medical profession who advise governments and plan most programmes have failed to realize the relative importance of the above factors which are hence generally given only token recognition, as is reflected in most budgets for leprosy control.

There are many booklets, posters, slides and other educational materials which

have been made available for leprosy in the last 2 decades. Public lectures are given, as well as radio talks and press publicity. Why is it then that the public attitude towards the disease has not shown any significant change? Unfortunately much of this educational effort, though well intentioned, is ill conceived and poorly executed. The appeal is often emotional and based on pathos rather than directed towards a more intellectual approach commensurate with modern scientific knowledge about this disease. Sometimes this is excused on the plea that only thus can funds be raised. Why is it that a grossly deformed victim is the usual picture rather than a cheerful young girl with a small skin patch? The latter is certainly more true to reality. The more factual presentations are usually restricted to small meetings, where the preacher preaches to an audience already converted, or through posters in leprosy institutions.

A change in public attitude can be achieved only by a sustained campaign of education using mass media of publicity. The radio, television and the press are potent but not the only available media. The schools, political platforms, and word of mouth are also important tools in the art of communication, education and persuasion. All these techniques are being used daily whether for the sale of soap or matches, for the sale of drugs by pharmaceutical firms or ideologies by politicians, and they reach the remotest village. That these methods can be employed in the field of health has been demonstrated by the campaigns for family planning and smallpox and poliomyelitis eradication.

In order to test this hypothesis 2 programmes were conducted in Bombay. One was an essay competition in about 50 schools, with teacher and student participation. About 100,000 students took part. Material on leprosy was provided for the teacher and after a suitable period the essays were evaluated and prizes distributed to the students, teachers and the schools at a public ceremony presided over by a popular dignitary, and hence well publicized in the press. This has been carried out over the past several years but since the programme was not varied the earlier enthusiasm has waned. The extent of knowledge of the disease was evaluated by a questionnaire filled by each student, and indicated a high level of awareness of the disease and its acceptance by a receptive group of the community.

The second experiment consisted of a weekly 10 minute radio broadcast in English by a well known former cricketer and radio commentator. This was continued over a period of about 2 years. At the end of the cricket anecdotes a couple of minutes were devoted to giving simple facts on leprosy. Though the English medium greatly restricted the audience, the response as measured by the mail was encouraging. The above 2 experiments conducted by a private organization in Bombay only indicate the possibility of the use of media for mass education. The result of such education is not easy to perceive in the short term, but methods of evaluation are available though expensive.

Our limited experience in leprosy and the vast experience of the effectiveness of mass media of communication in other fields indicates the need for the use of such an approach if we are to change public opinion and attitudes. Such education can be carried out most effectively by the respective governments as a part of their national leprosy control programme using the available expertise in this field, and with the technical guidance being provided by the medical profession.

A major handicap in the control of leprosy has been the unscientific attitude of the medical profession. This has resulted in the formation of a vertical programme

for leprosy. While vertical programmes may have certain advantages in the control of diseases like malaria and smallpox, they have proved a handicap when dealing with diseases like tuberculosis, venereal disease and leprosy. Such programmes perpetuate the stigma in the minds of the public and the medical profession. The latter is demonstrated by the failure to attract suitable personnel and the attachment of the stigma to those who join. If figures were available of the medical posts lying vacant in the national leprosy services as well as of the quality and turnover rate of those that are filled, they would reveal an important reason for the failure of our programmes. Fortunately the younger members of the medical profession do not suffer from the intense fear which prevailed among the older generation.

Our experience in the past 17 years in a large medical school has revealed that medical students, nurses and other personnel are willing to accept leprosy as any other disease if it is taught to them as part of the routine medical curriculum, and if they can see leprosy patients in the general outpatients and wards. Segregation and barrier nursing of infectious cases should be practised as in any other contagious disease. No patient has ever complained of leprosy cases being treated in our general ward.

It is my belief that the integration of leprosy in general medical education and hospital practice would probably prove a most potent factor in overcoming the stigma not only among the medical, nursing and paramedical workers but also among the lay public. A change in medical education is thus a prerequisite to integration and removal of stigma.

The recent emphasis on the delivery of health care to the rural and the poorer sections of the urban population by the training of paramedical workers from the community provides an opportunity to reach out to a large section of the population who are not adequately covered by the present leprosy services. The inclusion of simple facts about leprosy in the training of such workers will not only help in early detection but may also ensure improvement in regularity of treatment.

Lack of appreciation of the significance of social and psychological factors has resulted in the failure of otherwise well conceived programmes for the treatment and control of many diseases. Even where a "one shot" cure is available as in syphilis and gonorrhoea, control has not been achieved even in affluent countries. In a disease like leprosy where social stigma is even greater and where treatment has to be taken regularly over the years, programmes based chiefly on the medical concept are doomed to failure. It is time that detailed studies be undertaken by social scientists to delineate the factors responsible for the failure of our present control programmes. Based on the information from such studies a more realistic approach may be devised and the available budget be utilized to greater advantage.

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WHO EXPERT COMMITTEE ON LEPROSY, 5TH REPORT*

The Reports of the WHO Expert Committee on Leprosy have been of the utmost importance to leprosy workers everywhere, offering an international concensus of expert experience and guidance on matters of current concern and practice. The Report of the Fifth Expert Committee, held at Geneva, 19-25 October, 1976, is no exception. Coming at a time of very rapid development in leprology and high international concern, it distils into a relatively few pages a great deal of up-to-date information, corporate wisdom, and sound judgement.

The Report is divided into 4 main sections: Epidemiology, Strategy of Leprosy Control; the Formation and Management of a Leprosy Control Programme; and Research.

The section on Epidemiology emphasizes the scale both of the leprosy problem itself and social and economic effects of physical handicaps caused by leprosy. The new evidence on the transmission of leprosy is presented very clearly. The relevance and usefulness of information collected in Leprosy Control Programmes and prevalence and incidence rates leads to the conclusion that by present methods a significant impact can be made on the transmission of the disease.

Section 2 on the Strategy of Leprosy Control presents the latest views on this subject and many useful points are brought out. The increasing occurrence of dapsone resistance leads to other important suggestions for combined therapy. Problems in the treatment of reactions also receive attention, as do relapses, prophylaxis by BCG and chemoprophylaxis.

Section 3 deals with the practice of Leprosy Control, and in particular with aims, objectives, integration of medical services and evaluation.

Section 4 gives an impressive list of recommendations for future research priorities.

This Report needs to be in the hands of every professional member of Health Ministries and Voluntary Agencies concerned with leprosy, and will be a vital source of reference for several years to come.

Amid so much that is excellent, it is almost invidious to draw attention to one lack of emphasis in the Report. While there is reference to the need for Health Education in Urban Leprosy Schemes, the significance of leprosy as a social as much as a medical problem in general situations is not explored as explicitly as could be wished. Leprosy Control Schemes may be models of medical planning and practice, but they stand or fall on the response of patients and the public, and this is a social not a medical issue, but one of great importance.

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Dermal Microfilariasis and Leprosy

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In the course of studying over 13,000 biopsies referred to the Leprosy Study Centre in London between 1952 and 1976, it was found that approximately 26% showed no evidence of leprosy on histopathological examination. Some of these were normal and others showed minimal non-specific changes, but many revealed a wide range of dermatological and tropical conditions, amongst which the most important and frequently recurring was microfilariasis, due predominantly to *Onchocerca volvulus,* but also including infections with *Dipetalonema streptocerca.* Biopsies were submitted from Zaïre, Nigeria, Sierra Leone and Cameroon, mostly on account of a suspicion of leprosy, or in order to confirm a diagnosis of leprosy, in some cases after treatment had been started with dapsone.

A 12-year period (1964-1976) has been selected for detailed study and the histopathological findings are considered in close relation to the doctor's letter or clinical information supplied. It is apparent that in geographical areas where both leprosy and onchocerciasis or streptocerciasis are endemic, there is continuing confusion—even amongst experienced observers—which may lead to errors in the diagnosis, classification, assessment and follow-up of patients with leprosy.

Skin biopsies, with appropriate attention to (1) the body site selected, (2) laboratory technique, and (3) the careful examination of serial sections, may be invaluable in minimizing or eliminating these errors.

Introduction

In the case of both leprosy and onchocerciasis, it has not infrequently been stated that the diagnosis "should present no difficulty to the experienced observer". But in practice, patients suffering from these diseases may be handled by a succession of doctors or auxiliaries who have limited experience of the clinical appearances of the 2 conditions or of the laboratory procedures needed for accurate differentiation. In the case of leprosy, diagnostic confusion is particularly likely to arise in (1) the early stages of lepromatous disease, (2) the "doubtful macule", including those patients classified as "indeterminate", and (3) borderline (dimorphous) and tuberculoid cases after varying periods of treatment.

As a nucleus for teaching and a stimulus to research and histopathological

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diagnosis, the Leprosy Study Centre in London was conceived in the early 1950's by Dr R. G. Cochrane and by mid-1976 had handled over 13,000 biopsies from various parts of the world, often from doctors working in areas where leprosy is prevalent but who have no facilities for the processing and interpretation of biopsies.

In the present study we have concentrated on the 12 years from 1964 to 1976, since, during this period techniques of fixation, staining and interpretation were uniform and also because it contained a considerable number of skin biopsies in which microfilariae were present, either alone, or with evidence of leprosy. These have been examined in close relation to the doctor's letter or clinical information supplied. The present paper analyses the results with particular attention to the extent to which onchocerciasis or streptocerciasis may confuse the diagnosis and management of leprosy.

Patients and Methods

The patients came from the south west region of Cameroon, Nigeria, Sierra Leone and the north west and north east regions of Zaïre.
submitted to London because of a clinical suspicion of leprosy, or uncertainty in diagnosis, or to confirm the diagnosis of leprosy, in some instances in patients already under treatment with dapsone. One patient only was recorded as having recently had treatment with diethylcarbamazine (Banocide). With rare exceptions, fixation was in formol-Zenker, with transfer to 70% alcohol 15-24 h later, and staining was a combined trichrome with the Fite-Faraco modification of Ziehl-Neelsen; "TRIFF" (Wheeler, Hamilton and Harman, 1965). Tissues were mounted in paraffin and cut at 5 μm, at least 6, and often many more serial sections being examined, the TRIFF technique revealing bacilli, infiltrating cells and microfilariae (MF) with equal clarity (Figs 1-4). The criteria for the classification of leprosy in sections were essentially those of the 5-group system (Ridley and Jopling, 1966).

In this study, we have not attempted a complete differentiation between *Onchocerca volvulus* (OV) from *Dipetalonema streptocerca* (DS) except in a group of 69 patients from one area of Zaïre, in which DS was clearly identified, using the diagnostic criteria listed by WHO (Buck, 1974). Heads and tails were however, not invariably encountered in sections and more reliance was placed on the measurement of body width, using a screw-micrometer eyepiece and reference slide (1 mm-1000 μm).

Results

During the 12 years of this study, 8050 biopsies were submitted to the centre, of which 1156 were from tissues other than skin (mainly peripheral nerve), leaving a total of 6924 skin biopsies. From this total, 314 were positive for MF, 125 (39.8%) showing MF *only*, and the remaining 189 (60.2%) MF *with* leprosy.

(a) BIOPSIES SHOWING MF ONLY

Clinical findings

Lesions were variable in size and distribution but most often recorded on the trunk. They were all macular and most had vague or irregular edges though a few were described as distinct or sharp; many were coalescing. Two patients had

hyperpigmented lesions but the vast majority were hypopigmented, though occasionally with normal or even increased pigmentation in the centre. Referring letters noted some degree of anaesthesia in approximately 20% of all patients in this group. Itching was a virtually constant symptom.

Reasons for submission of biopsy

These may be summarized as follows:

	Number	%
1. ?Diagnosis*	12	9.6
2.	68	54.5
3.	14	11.2
4. Leprosy; for confirmation of diagnosis for classification	31	24.8
Total	125	

* Includes 3 patients: ?mycosis.

Histopathology

MF were found at various depths in the dermis, but most commonly high up, often close to the basal layer of epidermis and ascending into papillae between rete pegs. They were found only rarely within the epidermis and not recorded in surface keratin; intra-epidermal abscesses were not observed. They frequently lay between collagen fibres without exciting any cellular reaction, but were also seen with an infiltrate vhich was characteristically in the upper layers and mainly histiocytic, though with variable numbers of lymphocytes, mast cells and eosinophils. Plasma cells, however, were the dominant cell type in many sections, and their presence around compietely normal appendages (Fig. 1) was an indicator of microfilarial pathology in several instances. Many biopsies showed MF lying in the lumen of capillaries in transverse or longitudinal section.

Microfilarial species identification

As already stated, this was not attempted in all the biopsies available in this study. However, in 69 biopsies from one area of Zaïre, approximately 4 μm were recorded, and taken together with the available epidemiological, clinical and skin-snip data, these have been interpreted as indicative of DS. The vast majority, for similar reasons, and in whom a sample survey of biopsies gave average widths of 7 μm or more, have been interpreted as OV.

(b) BIOPSIES SHOWING MF WITH LEPROSY

Clinical findings

The clinical picture recorded was essentially that of the type of leprosy as classified on histopathological examination, viz.

Lepromatous 34 (18%)
Borderline (dimorphous) 137 (72.4%)
Tuberculoid 7 (3.6%)
Indeterminate 3 (1.6%)

In the remaining 8 biopsies (4.2%) there were tissue and cellular changes strongly suggestive or indicative of leprosy, but insufficient for exact classifica-

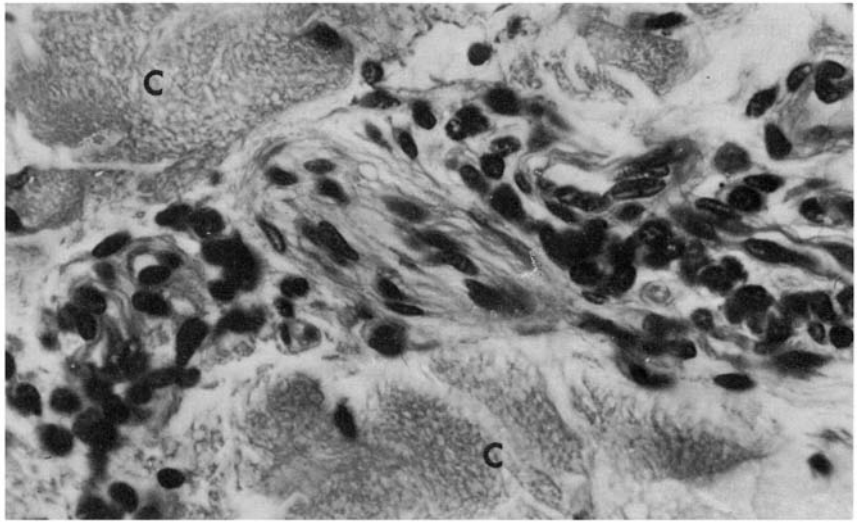

Fig. 1. Microfilariasis only. A completely normal nerve (centre) in the upper dermis is flanked by an infiltrate in which plasma cells are dominant. This is uncharacteristic of any form of leprosy and in fact MF were found in a closely adjacent field. C, collagen. TRIFF. Original magnification ×1250.

tion. Besides the classical features expected with the types of leprosy recorded above, one sign, namely the hypopigmented macule (or macules), and one symptom, namely itching, were recorded in well over half the cases.

Apart from the biopsies described in this study, a further group from areas where OV or DS are prevalent and which were originally regarded as indeterminate leprosy* are currently being re-examined and assessed in serial sections. The results to date show that in a considerable number the clinical and histopathological features originally suggesting leprosy were in fact due exclusively to changes consequent on the presence of MF.

Reasons for submission of biopsy

These may be summarized as follows:

	Number	%
1. ?Diagnosis*	2	1
2. ?Leprosy	33	17.5
3. ?Leprosy, ?filariasis	8	4.2
4. Leprosy; diagnosis or classification	146	77.2
Total	189	

* Includes 1 ?mycosis.

* WHO definition of Indeterminate leprosy:
bacteriologically pos ve, presenting flat skin lesions which may be hypopigmented or erythematous . . . the oup consists essentially of the 'simple macular cases' "
Leprosy Control, 19 .5).

Histopathology

MF lay as described in the cases above in which they were the only pathogen seen in sections, but were also frequently seen in or closely associated with the typical infiltrates of tuberculoid, borderline (dimorphous) (Figs 2 and 3) and lepromatous leprosy (Fig. 4). Even where numerous, there was no evidence to suggest that they had modified the patient's cellular response to the presence of the leprosy bacillus. Incontinence of pigment into the dermis or its presence in melanophores was common, but an examination of the basal layers of the epidermis gave no definite indication of depletion of melanoblasts or clear cells. As in the material showing MF only, this group also had numerous examples of MF lying in the lumen of capillaries. (More detailed histopathological findings of this dual pathology are to be described in a separate publication.)

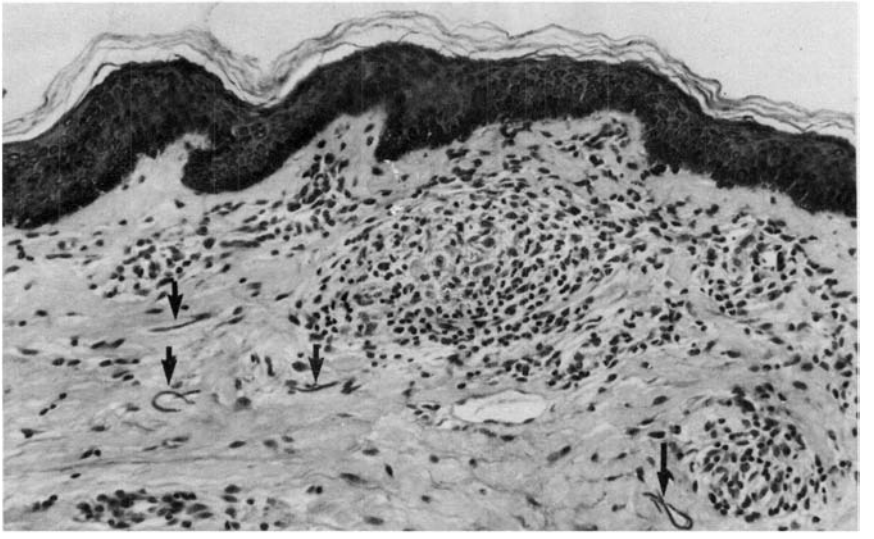

Fig.
surrounded by lymphocytes in the upper dermis and nerves lower down were similarly infiltrated. MF (arrowed) were numerous between these lesions. TRIFF. Original magnification ×500.

Discussion

It is important to emphasize that the figures revealed in this analysis are to some extent fortuitous, depending upon the enthusiasm and interest of doctors or leprosy workers who were in touch with the centre during the period of study and they certainly do not represent the prevalence of the 2 diseases in the areas concerned. Furthermore the clinical notes accompanying each biopsy were not uniformly adequate, partly because some doctors working in filarial regions had long since regarded the entire population as being infected at some time or other. Nevertheless, a careful reading of the clinical information has indicated the reason for submission of the biopsy in all cases, revealing an area of confusion—and even frank error—which mainly affects the diagnosis and management of leprosy.

It was originally thought that the finding of MF in sections where leprosy was

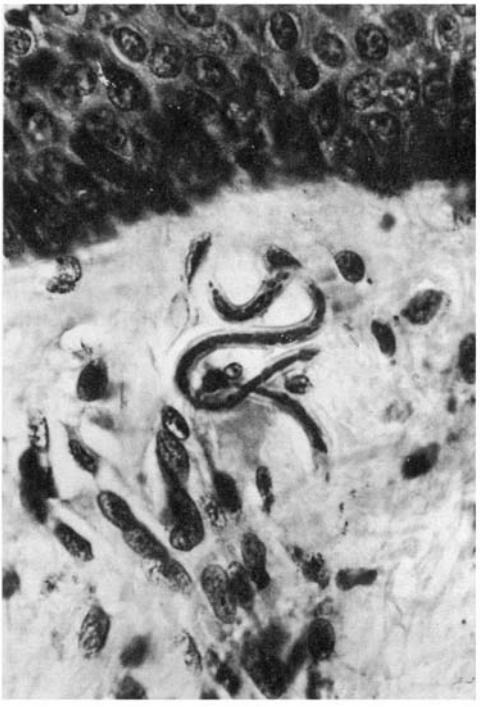

Fig.
and infiltrate. TRIFF. Original magnification ×1250.

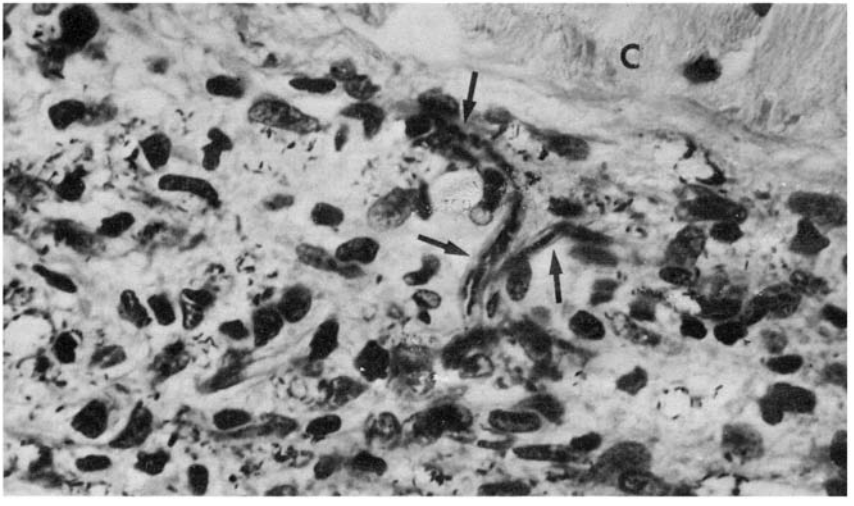

Fig.
lepromatous infiltrate consisting mainly of macrophages packed with *Mycobacterium leprae*. C, collagen.

also present might be incidental and of little significance. However, this conclusion became untenable after an examination of the clinical notes and of a number of cases in which several biopsies has been submitted over a period of years. These showed that onchocercal changes such as hypopigmentation, chronic dermatitis, erythema, secondary surface infections, etc., may create at least 2 practical difficulties in the mind of the doctor dealing with a patient already proven to have leprosy: (1) it becomes difficult to assess clinical progress and reactional changes; new MF lesions, or the spreading of established ones, may create the impression that the patient's leprosy is not being held by treatment, and (2) the selection of a profitable site for biopsy may be rendered difficult. As a symptom, itching is misleading, for in leprosy it is not characteristic but may however be present and can be confused in local tribal languages with words intended to mean (medically) paraesthesiae. As a sign, loss of sensation is of paramount importance in the diagnosis of leprosy in the field, but may be absent at certain stages of the disease and is liable to misinterpretation unless meticulously elicited. Perhaps even more misleadingly, as this study shows, it may be present in some patients who have MF but not leprosy, almost certainly due to the presence of chronic epidermal and dermal pathology, and to difficulties of interpretation.

The very real confusion encountered in the diagnosis of these diseases in the field is still more apparent from the 125 biopsies in which there was no evidence of leprosy of any kind, but in which MF were readily found. Some of these patients had been on dapsone for a year or more and the combined clinical and histopathological data of this study strongly suggest that leprosy had been incorrectly diagnosed. In others, however, the clinical information pointed to onchocerciasis or streptocerciasis as the correct (and only) diagnosis, but in reporting these "leprosy-negative" biopsies through the years, care has been taken to emphasize that the absence of any changes due to leprosy referred only to the biopsy submitted at that time. Indeed in some instances (where the clinical notes suggested leprosy but the biopsy was negative), a request for another biopsy from a more likely skin site has produced positive histopathology. Such cases confirm that oncho- or streptocerciasis can interfere with the selection of a profitable skin site for biopsy, but in practice confusion over the basic diagnosis of leprosy is commoner. Browne (1959, 1964, 1976) has drawn attention to the various ways in which onchocerciasis may mimic leprosy, or interfere with the diagnosis, and more recently Meyers *et al.* (1972) have described the close resemblance of hypopigmented skin lesions in streptocerciasis to those of leprosy in patients from Zaïre; these authors conclude that biopsy may be the only way to distinguish the 2 diseases, especially in children.

Running through the diagnostic difficulties of onchocerciasis, streptocerciasis, granuloma multiforme, leprosy and many other tropical dermatoses, is the factor of altered skin pigmentation. In the case of onchocerciasis, possible mechanisms have been reviewed in detail (Browne, 1954, 1960), though the definitive answer is still awaited, as it is also in streptocerciasis (Meyers *et al.*, 1972), where neither the degree of pigmentary incontinence nor the numbers of MF are definitely related to hypopigmentation. In leprosy, where changes in skin pigmentation may be early and extremely important diagnostically (and often in the absence of any sensory changes or diminution of sweating), the mechanism of hypopigmentation is similarly obscure, though the theory has been repeatedly advanced (Prabhakaran *et al.*, 1971, 1976) that dihydroxyphenylalanine (DOPA) may be an

essential metabolite for the growth and multiplication of the leprosy bacillus, thus interfering with normal pigment production by melanocytes.

These derangements of pigmentation, together with the possibility that biting arthropods (Narayanan *et al.*, 1972) or flies (Geater, 1975) may play a part in the transmission of leprosy suggest that there may be common ground of interest between leprosy and microfilariasis. This may be all the more worthy of investigation in view of the recent publication (Meyers and Connor, 1975) of a low frequency and reduced severity of Mazzotti reactions in patients with leprosy.

The value of slit-skin smears and skin-snips in the day-to-day handling of patients in the field cannot be over estimated and it is not our intention to belittle their importance. However, in further research on these 2 diseases, skin biopsies, properly taken and interpreted, may be invaluable. Furthermore, in the individual patient, skin biopsy may be the best—and at times the only—way of establishing the correct diagnosis and classification of leprosy.

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Note on Some Observations About the Post-lepromin Scar

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The post-lepromin scar was studied in 764 leprosy patients of the former (1964-1975) WHO Leprosy BCG Trial in Burma, Mandalay area. A bac./ml lepromin was used. Scar formation was analysed in its relation to the different forms of leprosy, its frequency to the size of the Mitsuda reaction, to BCG vaccination, to the tuberculin reaction, and, in some instances, in different age groups. 90.2% of the BCG vaccinated cases (336) showed post-lepromin scars whilst in the controls (410 cases) 80% had a scar. Five hundred and fifty-three (74%) of 746 cases had post-lepromin scars on first testing, and of the remaining 193 cases, 78 (40%) developed lepromin scars on subsequent lepromin testing. One hundred and fifteen patients (15%) remained scar negative throughout the period even after repeated lepromin testing (up to 6 tests). Ten of these constant scar-negative cases subsequently developed lepromatous and borderline forms; 38 were diagnosed as having indeterminate, 63 tuberculoid and 4 "Tr" leprosy.

It is tentatively suggested that the post-lepromin scar may be considered as an indicator for a stabilized immune situation, taking into account that 17-32% of the 2-5 mm late Mitsuda readings also leave post-lepromin scars.

Further studies with weaker lepromins (20 or 40 million bac./ml) in leprosy patients and in apparently non-leprosy affected groups of populations are suggested.

Introduction

Some reviews (Sato, 1967; Bechelli *et al.*, 1971) of the lepromin test list up to 270 references. However, the post-lepromin scar is the stepchild of the Mitsuda reaction. The Transactions of the VIIth International Congress of Leprology, Tokyo (1958, pp. 464-465), briefly refer to the lepromin scar by stating: ". . . the late lepromin reaction . . . later regresses, frequently leaving atrophy or a scar".

Post-lepromin scar formation in the different forms of leprosy, in different age groups, and its frequency in relation to the Mitsuda reaction, to BCG vaccination, and to the tuberculin reaction was studied in 746 leprosy patients of the former WHO Leprosy BCG Trial in the Mandalay area, Burma (1964-1975).

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The post-lepromin scar, which is hypopigmented, rarely more than 2-10 mm in diameter, and never of a keloid character, is best read at least 3-4 months after the late lepromin reaction and is perfectly visible after many years. The post-lepromin "scar" may follow either ulceration, or, less frequently, 3-5 mm (1+) and 6-10 mm (2+) reactions without necrosis or ulceration which leave, as a consequence of the inflammatory process, what French authors call "atrophie cicatricielle". For practical purposes scars and "atrophie cicatricielle" have been considered together under the title "scar".

Throughout the study a lepromin (H) preparation of 160 million bac./ml was used. The "standard" lepromin was kindly supplied by Dr Abe of the National Institute for Leprosy Research, Tokyo. For reasons of comparability, this provisional (Tokyo, 1958) standard remained unaltered, although ±10% of false reactions could not be excluded with certainty.

The frequency of scars in the trial (Bechelli *et al.*, 1970 is related to the size of the late lepromin reaction. Nodules of 10 mm and above following lepromin injection, and particularly ulcers, nearly always leave a scar. Scars are less frequently associated with smaller nodules (3-8 mm). For operational reasons, the size of the scar in this study was not related to the late Mitsuda reading.

Of the 794 cases, in the 2 (BCG vaccinated and control) trial groups diagnosed up to June, 1973, data on the lepromin scar is available for 746. During subsequent follow-up studies (1973-1975) the number of cases increased to 996. An analysis of these data, regarding scar formation, will be the subject of a further study with one exception, namely, the diagnosis of lepromatous and borderline cases during the years 1974-1975. As will be shown later, the inability of multibacillary (L and B) forms of leprosy to develop a lepromin scar is considered to be a constant feature.

Of the 746 cases that have been followed up, 336 belong to the BCG group, while 410 belong to the control group.

Results and Discussion

The data given in Table 1 suggest that BCG vaccination enhanced the lepromin-scar formation and confirm previously published data and findings which showed a comparable composition of the vaccinated and control group (Bechelli *et al.*, 1973-1974).

TABLE 1
Percentage of cases with scar on first or subsequent lepromin tests

	BCG group	Controls	Difference (BCG-controls) %
746	90.2	80.0	10.2*
T cases	93.6	86.2	7.4
Others† (I, Tr(B) and L)	76.5	60.6	15.9

* The difference is statistically significant.

† Of 81 indeterminate cases, the BCG group had 11 without scar while in the controls there remained 27 who even on repeated lepromin testing never developed a scar.

If, and this would be subject to confirmation, scar formation is an expression of a stable immune situation (corresponding to a strong lepromin reaction), a better prognosis of scar-positive cases is likely. The prognostic value of the Mitsuda reaction was extensively studied by de Souza and de Souza, who in 1948, published a 5-year follow-up observation, involving 216 I and 685 T cases. According to these authors, an initial 3+ Mitsuda reaction in the vast majority of cases indicated a favourable prognosis confirming Dharmendra (1967) and Rotberg and Bechelli (1950).

With regard to scar formation and the tuberculin test, the data showed that scar formation was enhanced by BCG vaccination among those cases with tuberculin reactions of less than 10 mm at intake. In subjects with a PPD reaction at intake of 10 mm or more, BCG vaccination apparently did not have a significant influence on scar formation.

Of the 746 leprosy cases followed up, 196 did not develop a scar on first lepromin testing. In a few instances there were as many as 6 lepromin retestings but in the majority only one subsequent testing was done. In both groups, BCG and controls, about 40% of these 196 non-scar forming subjects developed scars on subsequent lepromin testing. In the tuberculoid group, 50% showed scars on retesting compared to 26% subsequent scar formation in other cases (I, Tr, B and L). In general, those with weak Mitsuda reaction (3-5 mm) at first testing showed a lower conversion rate to scar positivity on subsequent testings compared to those with stronger Mitsuda reactions (6 mm and more in the first testing).

Concerning the relationship between the size of the Mitsuda reaction and the frequency of scar formation the data are as shown in Table 2.

TABLE 2

Mitsuda reaction and scar formation; first testing in leprosy patients

Mitsuda reaction (mm)	Number of cases	With scar	
		Number	Per cent
0-2 (– and ±)	24	2	8
3-5 (1+)	184	49	27
6-9 (2+)	118	82	69
> 10 + (u) (3+)	420	420	100
Total	746	553	74

It is evident that the greater the size of the Mitsuda reaction the higher the probability of scar formation. Seventy-four per cent of cases having a 2 to < 10 mm late lepromin reaction developed post-lepromin scars on first testing leaving 193 scar-negative cases.

On subsequent testing, 40% of 193 cases, who did not develop a scar in the first instance, eventually had scars leaving 115 cases scar negative throughout the time of observation (see Table 6).

TABLE 3
Mitsuda reaction and scar formation on subsequent lepromin testing in 193 non-scar forming cases on first testing

Mitsuda (mm)	Number of cases	With scar	
		Number	Per cent
0-2	22	6	27
3-5	135	54	40
6-9	36	18	50
> 10 + (u)	—	—	—
Total	193	78	40

When lepromin-scar development, after first and subsequent lepromin testing, is taken together, it appears from the data of the Burma trial that the percentage of cases developing scars in relation to the size of the lepromin reaction is as given in Table 4.

TABLE 4
First and subsequent testing

Mitsuda reaction (mm)	Percentage of patients with scar
0-2	17
3-5	32
6-9	64
> 10 + (u)	100

Although the 6-10 mm reactions including ulceration have the highest percentage of scar formation, as can be expected, a 17-32% scar formation, following the weaker (2-5 mm) reactions is also of interest.

Regarding classification, the distribution of 746 cases with data on scar formation on first and repeated lepromin testing was as shown in Table 5.

TABLE 5
Clinical classification

	T	I	TR	B	L	Total No.	Total %
No. of scar-positive cases:	524	96	11	0	0	631	85
No.	63	38	4	3	7	115	15
Total:	587	134	15	3	7	746	—
Percentage of scar-positive cases:	89	72	73	0	0		
Percentage of scar-negative cases:	11	28	27	100	100		

Of 746 repeated lepromin-tested cases not subdivided into BCG-vaccinated cases and controls, 84% were scar positive and 15% remained scar negative which included 10 B and L cases, 27% of Tr, 28% of I and 11% of T cases.

An analysis, by age and classification, of these 115 constant lepromin scar-negative cases is given in Table 6.

TABLE 6
Age and classification analysis

Age	T	I	Tr	B	L	Total
0-4	3	0	0	0	0	3
5-9	20	16	0	1	1	38
10-14	27	18	2	0	6	53
15-19	12	4	2	2	0	20
20 and over	1	0	0	0	0	1
Total	63	38	4	3	7	115
Bact. positive	1	1	4	3	7	16

When 10 B and L cases are deducted from the above, there still remain 105 cases, including 63 T cases, which remained scar negative. Ninety-four of these 105 cases had Mitsuda reactions between 4-9 mm. The number of Mitsuda doubtful cases in this group was 11. Information on the evolution of these 105 cases will only become available after further periods of observation, which are in progress.

An examination of lepromin-scar formation in household contacts of leprosy patients showed that the proportion with scars in non-household contacts was greater than among household contacts; however, the difference was not significant. No scar formation was observed in 10 histologically confirmed L, LL, BL and BB trial cases, as shown, in Table 7.

TABLE 7

Code	1st clinical diagnosis + lepromin			Evolution			Histological diagnosis
8-05	1969	I	3 mm	1973	L	1 mm	BB 1973
16-04	1971	"Tr"*	2 mm	1973	L	1 mm	BL 1974
83-07	1969	"Tr"	0 mm	1973	L	2 mm	Early L 1973
41-05	1974	B	0 mm	1975	B	2 mm	BL 1974
64-03	1967	"Tr"	6 mm	1975	L	1 mm	Pre-L 1973
76-09	1968	"Tr"	3 mm	1976	B	4 mm	Resid. B 1974
12-03	1969	"Tr"	2 mm	1974	L	neg.	Pre-L 1973
139-05	1969	"Tr"	5 mm	1973	L	1 mm	L 1973
140-03	1969	"Tr"	0 mm	1973	L	0 mm	BL 1974
155-03	1969	B	3 mm	—			BB 1976

* The use of tuberculoid in reaction (Tr) stems from the protocol of the trial (1964) and a certain number of Tr cases have evolved to B forms or perhaps some of them could have been nistologically classified as B cases when they were detected.

Five of these 10 L and B cases had late lepromin reactions at first diagnosis between 3 and 6 mm; however, all 10 were scar negative from the time of first clinical signs and remained so throughout the period of observation.

A small group of 15 adults were tested in 1974 in a double-blind study using a weaker lepromin (40 million bac./ml). Results are shown in Table 8.

TABLE 8

	First testing		Second testing	
	Mitsuda average (mm)	Scar average (mm)	Mitsuda average (mm)	Scar average (mm)
5 Cases TT	8.6	4.0	9.0	4.0
5 Cases LL	0.	0.	0.0	0.
5 Unaffected	6.0	3.4	7.4	4.0

As far as it is permissible to draw any conclusions from such a small group, there was good correlation between the lepromin test on first and second testing, sharing a constant average of scar sizes for TT cases and a slight increase in clinically non-leprosy affected subjects. LL cases all had, as expected, a negative Mitsuda and no scar formation.

Conclusions

From the above study it is tentatively concluded that:

(a) the post-lepromin scar, subject to further studies, might be regarded as a reliable indicator of a stabilized immune situation and could be a means of identifying high resistant individuals in the population; and
(b) its absence may help to recognize the false or doubtful lepromin-positive reactions in lepromatous and perhaps also in indeterminate cases, replacing, particularly under field conditions, histopathological examination of the lepromin nodule.

On the basis of the reported data, the interpretation of a certain proportion of lepromin reactions in the range between 3-5 mm may be raised. An exchange of experience and a repetition of the Burma study on the lepromin scar, even with smaller groups of patients but with the inclusion of clinically unaffected persons, using weaker antigen (20 or 40 million bac./ml) could help in clarifying the significance of the post-lepromin scar.

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Clofazimine and Eosinophilic Enteritis

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A case of eosinophilic enteritis associated with clofazimine (Lamprene) therapy is reported. A 29-year-old Samoan woman with leprosy developed abdominal pain after 3 years of clofazimine therapy at 600 mg daily. At laparotomy there was nodular thickening of the upper ileum with black-brown pigmentation of the ileal wall, mesentery and mesenteric lymph nodes. Ileal biopsy showed eosinophilic enteritis, and red crystals of clofazimine were present in unstained sections of the small bowel mucosa and submucosa, as well as in mesenteric lymph nodes. It seems that these histological changes and her peripheral eosinophilia represent a reaction to the drug. The potential hazards of long-term high dose clofazimine therapy are stated again.

Introduction

Jopling (1976) recently reviewed the side-effects of clofazimine in an Editorial in this journal. He stressed those affecting the gastro-intestinal tract. Abdominal pain, anorexia, vomiting, diarrhoea and weight loss have been most commonly documented. Diarrhoea has been seen in patients after only 3 weeks therapy (Imkamp, 1968). Abdominal pain seems to have developed only after more prolonged therapy and only in those receiving daily dosage. Some evidence suggests these effects may be dose related (Plock and Leiker, 1976).

Patients with abdominal symptoms have died soon after this drug has been stopped. In these patients, and in others taking the drug who have come to laparotomy for similar symptoms (Jagadeesan *et al.*, 1975), many tissues have been discoloured. Localized areas of thickening of the small bowel have been described (Karat, 1975). Clofazimine crystals have been demonstrated in gut-wall tissues and mesenteric nodes as well as in other extra-intestinal sites (Desikan *et al.*, 1975). An assessment of the total amounts of drug which can accumulate during treatment has recently been published (Desikan and Balakrishnan, 1976). Histological reaction to the crystals has generally been described as non-specific in type.

We describe here a patient with a predominantly eosinophilic and histiocytic reaction to the drug with peripheral eosinophilia.

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Clinical Details

A 23-year-old Samoan woman presented to the Infectious Disease Unit, Auckland Public Hospital, Auckland, New Zealand in 1970. When 13 and 14 years old, she had probably received dapsone for leprosy in Samoa. She had widespread skin nodules and a skin biopsy confirmed the diagnosis of leprosy (lepromatous end of spectrum).

She was initially treated with rifampicin alone. However because of frequent type II reactions, prednisone, and clofazimine at 600 mg/day, were begun in 1972. In view of her erratic drug taking no further rifampicin was prescribed after 1974, and she remained on this same dose of clofazimine until 1975.

In early 1975 she developed periumbilical post-prandial pain. There was no diarrhoea. She had a peripheral eosinophilia (maximum of $3600/mm^3$). Small bowel X-rays showed changes in the proximal jejunum which worsened distally. Dilatation of the lumen and coarsening of the mucosal pattern proximally became an irregular luminal calibre and a frankly cobblestone mucosa in the ileum. Tests for malabsorption were normal. No microfilarial or gut parasites were seen on repeated search and chest X-ray was normal. Rectal and peroral jejunal biopsies were done (see below).

With continuing increasing abdominal pain suggesting subacute bowel obstruction, she had a laparotomy in October, 1975, some 6 months after the onset of her symptoms. At laparotomy omentum, small bowel and mesentery were deeply pigmented brown. The jejunum and lower ileum appeared grossly normal but in the upper ileum there were about 20 nodular areas of thickening in the bowel wall. These areas were on both mesenteric and antimesenteric borders and involved only small segments of the total bowel circumference. There was slight inflammation of the overlying serosa. The mesentery contained lymph nodes measuring up to 2.5 cm across; they were almost black. An ileal "nodule" and a mesenteric node were biopsied and incidental appendicectomy performed. No acid-fast bacilli were subsequently cultured from these biopsies.

A diagnosis of eosinophilic enteritis was made histologically and post-operatively prednisone 60 mg/day was started. Symptoms and peripheral eosinophilia rapidly resolved and clofazimine and prednisone dosages subsequently decreased. Clofazimine was entirely withdrawn in April, 1976 and thiambutosine replaced it. As prednisone has been reduced she has had 2 further episodes of more severe abdominal pain in April and October, 1976. The second of these was again associated with peripheral eosinophilia. Small bowel X-rays in April, 1976 showed the same but less marked abnormalities as previously. Both episodes responded dramatically to increased prednisone dosage. Between these severe bouts of pain, she has had intermittently less defined abdominal pain controlled with simple analgesics.

Pathological Findings (Figs 1-3)

The initial peroral jejunal biopsy (4.9.75) (Fig. 1) showed an abnormal villous pattern with shortening and broadening of the villi and an increased inflammatory cell infiltrate in the lamina propria. In the submucosa there were prominent histiocytes; a few of these were multinucleated. Special stains for *M. leprae* were negative and there was no amyloid in the biopsy.

The full-thickness small bowel biopsy (Figs 2 and 3) taken at laparotomy

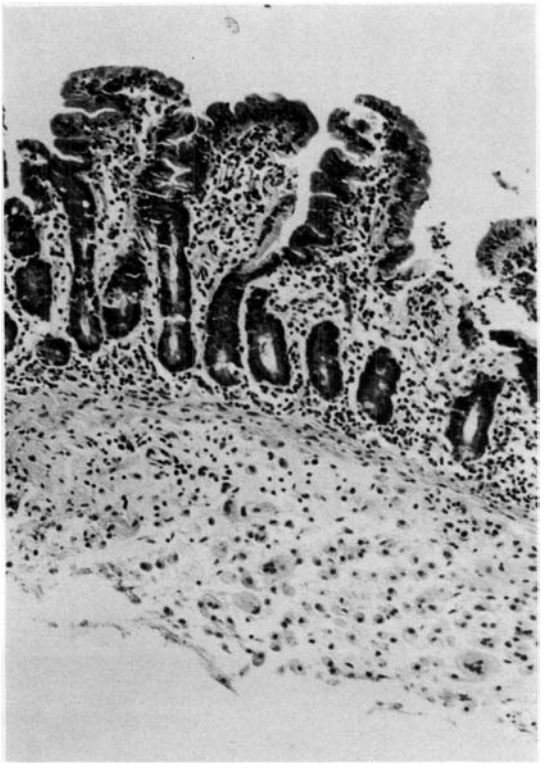

Fig. 1. Per-oral jejunal biopsy showing focal broadening of villi with prominent submucosal histiocytes.

(21.10.75) showed the villous architecture to be normal, although there was some broadening of a few villi. Within the deeper part of the lamina propria and the superficial submucosa there was a dense cellular infiltrate of eosinophils and histiocytes. A sparse infiltrate of eosinophils was also present in the muscle layers. The mesenteric lymph node showed retention of the basic follicular architecture, but within the node there were focal abscesses confined to the paracortical zone and medulla. These abscesses had centres packed almost exclusively with eosinophils; many of them were degenerate. They were surrounded by a zone of histiocytes with occasional eosinophils but no giant cells were present. The sinuses and medullary cords also contained numerous eosinophils.

The histological appearances of the small bowel biopsy fitted well into the described pattern of eosinophilic enteritis. The eosinophilic lesions in the lymph nodes were unusual and their presence suggested the possibility of a more widespread process.

Sections of both the small bowel biopsy and mesenteric lymph node were sent to Dr D. J. Harman of the Leprosy Study Centre, London, and he drew our attention to the presence of clofazimine crystals within both biopsies in the unstained sections.

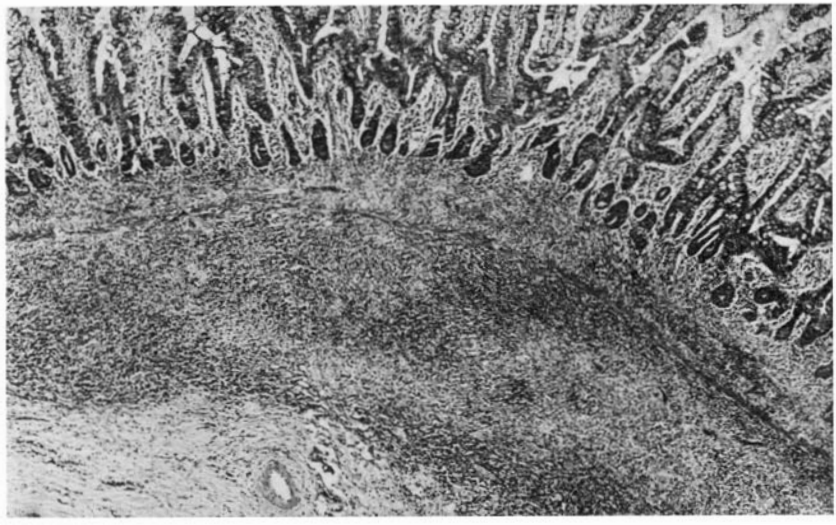

Fig. 2. Full-thickness ileal biopsy showing marked submucosal infiltrate of eosinophils and histiocytes. H. and E. ×28.

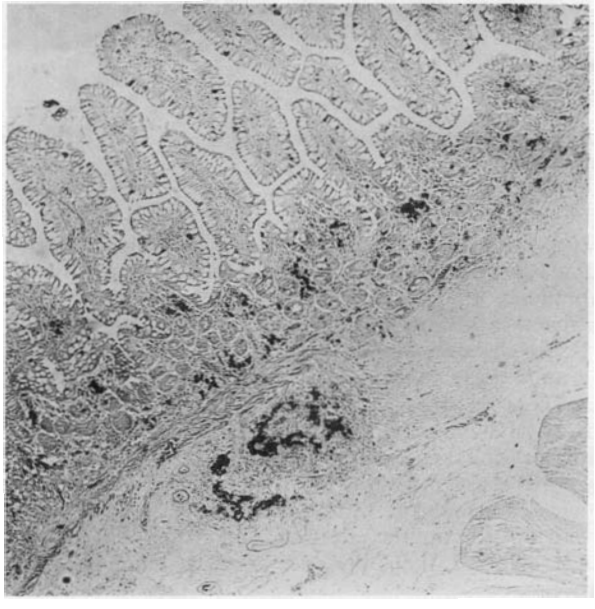

Fig. 3. Full-thickness ileal biopsy showing mucosal surface with black crystal deposition in the deeper lamina propria and superficial submucosa. Picric acid. ×32.

Clofazimine is alcohol soluble and is thus removed by alcohol used in both processing tissue and in staining the slides. Surprisingly however, enough had remained within the laparotomy biopsies (presumably a reflection of the size of the tissue blocks), to be seen in unstained sections. This red crystalline material present in the deeper lamina propria and superficial submucosa was related anatomically to the heavy eosinophilic and histiocytic infiltrate present in the small bowel biopsy and accounted for the pigmentation seen grossly. Similar crystals were concentrated in the mesenteric lymph nodes at the sites of the focal abscesses described.

The original per-oral jejunal biopsy was re-examined but no crystals were found. This was probably because the crystals dissolved during the processing of this small biopsy. We have assumed that the submucosal histiocytic response was related to crystal deposition. The appendix and the previous rectal biopsies were examined for crystals but none were found. The appendix and the rectal biopsies did however show melanosis coli, and ceroid pigment deposition has been noted before in association with clofazimine treatment (Ridley, quoted by Jopling, 1976). Ceroid pigment was not prominent in the small bowel biopsies. We carried out spectrophotometric examination of an alcoholic extract of clofazimine and of a similar extract of the jejunal biopsy. Similar absorption peaks at about 220, 285 and 450 nm for both samples confirmed the presence of clofazimine in the biopsy.

Discussion

Eosinophilic infiltration of the small intestine is uncommon and can be separated into 3 main entities (Morson and Dawson, 1972). They are eosinophilic enteritis, eosinophilic granulomatous polyp (inflammatory fibroid polyp) and allergic gastro-enteropathy. The latter has been described recently in children and is thought to represent an allergy to milk.

Patients with eosinophilic enteritis have shown either single or multiple thickenings of the pyloric end of the stomach and short or longer segments of the small intestine, producing variable degrees of acute or subacute obstruction. There is usually peripheral eosinophilia, and occasional patients have had concomitant malabsorption or protein losing enteropathy. Suggested causes range from food sensitivities e.g. onions and chocolate, to parasite ingestion and infestation.

Only one other patient taking clofazimine has had eosinophilic infiltration of the gut noted on histological examination (Jagadeesan *et al.*, 1975) and peripheral eosinophilia has not previously been reported. Eosinophils were not found in animal tissues in early studies of the drug (Conalty, quoted by McDougall, 1976). Nevertheless the apparent anatomical relationship of the drug to the tissue eosinophils and the exclusion as far as possible of other causes of intestinal eosinophils and peripheral eosinophilia make the causal association in this case quite strong.

Fourteen months after initial reduction in dosage to 100 mg 3 times per week, and 6 months after completely stopping clofazimine this patient still has abdominal symptoms suggesting continuing reaction to it. Clofazimine crystals have been found present in lymph nodes almost 4 years after the drug was stopped (Jopling, 1976). The use of this agent at high dosage for lengthy periods is thus clearly contra-indicated if potentially toxic tissue accumulation is to be avoided. Life-threatening toxic effects have not been described in patients who

have taken only the low clofazimine dosage which is recommended for its anti-leprotic effect. Those who would use it for its "anti-reactional" properties must be aware of this potential long term toxic effect if used excessively—as, in retrospect, it was in this case.

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Anabolic Steroid as an Adjuvant in the Treatment of Chronic Lepra Reaction and ENL Under Corticosteroid Therapy

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Fourteen lepromatous patients in the various stages of reaction with ENL episodes were put on Methandienone in addition to steroid therapy. Methandienone, an anabolic steroid, was found to be useful as an adjuvant and helped both in reducing the dosage of steroid needed, and in making possible the institution of DDS in about 60% of cases.

Introduction

Various anabolic steroids are known to be good adjuvants in the treatment of a number of chronic protracted diseases which give rise to an excessive catabolic process. In pulmonary tuberculosis these agents have been found useful as an adjuvant in addition to anti-tuberculous therapy (Nandi *et al.*, 1962; Frank, 1963; Miczoch, 1962). Miczoch (1962) laid more stress on the use of anabolic steroids to combat excessive catabolic processes occurring in pulmonary tuberculosis, a chronic inflammatory disorder. He further observed the usefulness of anabolic steroids in patients receiving corticosteroids for a long time, as the latter exert an additional catabolic effect. Similar observations were reported by a number of workers (Aepli, 1964; Editorial, 1968; Roy, 1964; Mitra, 1964; Bhatia and Roy, 1966) who advocated the usefulness of anabolic steroids in the treatment of chronic protracted diseases, together with specific therapy or in combination of specific therapy and corticosteroids.

Chronic lepra reaction and chronic ENL are well known enigmas, especially in respect to their therapeutic management, and these chronic inflammatory processes are mostly steroid dependent (Moldawar, 1968; Editorial, 1970). The inflammatory disorders, i.e. lepra reaction and ENL, produce a catabolic process resulting in loss of weight, reduced muscle tone, osteoporosis, muscular wasting and pain all over the body, and presumed reversal of serum albumin-globulin ratio with hypoalbuminaemia (Kapoor *et al.*, 1971; Balkrishnan, 1965; Deluma, 1967; Mukherjee and Ghosh, 1972; Tarabini, 1958; Paras, 1950).

These are further aggravated by the addition of steroid therapy. Nandi *et al.* (1962) observed prevention of protein catabolism and considerable improvement

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in the blood biochemistry as regards serum protein and albumin globulin ratio with anabolic steroids used as an adjuvant in addition to specific therapy.

Tarabini (1958) was of the opinion that serious symptoms of leprosy are caused by 3 factors, of which changes in the blood serum protein, i.e. diminution of albumin, increase of globulin and deposition of paraprotein (amyloidosis) in the viscera are most dangerous. Paras (1950) reported that lowering of serum calcium in lepra reaction is not due to disturbed calcium metabolism but is a consequence of reduction of albumin concentration in the serum.

Considering all the above observations it was thought worthwhile to study the place of anabolic steroid as an adjuvant in the management of chronic lepra reaction and ENL in patients receiving steroids for a long period.

Material and Methods

Fourteen lepromatous cases in the various stages of reaction with ENL episodes at frequent intervals were selected for the study. All the patients had been taking steroids regularly in a dose varying from 20-30 mg daily for a prolonged period ranging from 6 months to 2 years for the control of their chronic reaction and ENL episodes. Any attempt to induce specific chemotherapy with sulphone, long-acting sulphonamides and other drugs was faced with utter failure.

Routine investigations included proper recording of clinical findings, blood counts, urine examination, and periodical serum protein estimation. Bacteriological examinations were repeated at intervals. All of the patients were put under Methandienone 25 mg intramuscular injection twice weekly for 2 weeks, followed by 25 mg once a week for 12 weeks. Along with Methandienone, the dosage of steroids was reduced by 5 mg every 2 weeks and sulphone was administered in a dosage of 10 mg once a week to every patient for 4 weeks, followed by 10 mg twice weekly.

Results

All the patients reponded clinically by gain in weight, marked reduction in oedema of the extremities and return of appetite with a sense of well being. In 6 cases no episodes of lepra reaction or ENL were observed during this period, the dosage of steroid was reduced to zero, and all these 6 cases were able to tolerate sulphone 10 mg twice weekly without showing any tendency to reactional episodes. In another 4 cases reactional episodes continued but revealed manifestations of milder nature with lesser frequency. In all these 4 cases, the dosage of steroid was reduced to one-fourth of the initial dose and sulphone was introduced 10 mg twice a week with good tolerability. The remaining 4 cases though improved, showing increased tolerance to sulphone and reduction of dosage of steroids, could not be followed up regularly because of their absence from the clinic. Bacteriological improvement was without significance. Other investigations revealed no abnormality. Assessment of serum protein estimation (vide Table 1) showed increase in total protein in 6 cases, increase of albumin in 6, and increase of globulin in 3 cases as compared to the initial findings. On further scanning it has been found that a slight increase of globulin fraction occurred in 3 cases in spite of moderate clinical improvement with Methandienone.

TABLE 1
Estimation of serum proteins

No.	Name	Initial			After 3 months		
		T.P. (g)	Alb. (g)	Globulin (g)	T.P. (g)	Alb. (g)	Globulin (g)
1.	K.M.	7.6	3.6	4.1	8.1	4.8	3.3
2.	B.D.	7.8	3.9	3.9	6.9	3.8	3.1
3.	J.S.	6.9	3.2	3.7	7.4	4.2	4.2
4.	G.R.	8.2	3.6	4.6	8.9	4.6	4.3
5.	R.B.	7.4	4.4	3.0	7.1	3.8	3.3
6.	S.D.	7.9	4.4	3.5	8.0	4.6	3.4
7.	B.S.	7.1	4.8	2.3	8	4.7	3.3
8.	M.S.	9.1	3.8	5.3	7.6	4.1	3.5
9.	A.G.	8.6	4.6	4	7.9	4.4	3.5
10.	P.K.	7.2	4.0	3.2	8.0	4.9	3.1

Discussion

The beneficial effects of anabolic steroid in chronic wasting diseases, and particularly in patients who are on prolonged steroid therapy are reported by many (Nandi *et al.,* 1962; Frank, 1963; Miczoch, 1962; Aepli, 1964; Editorial, 1968; Roy, 1964; Mitra, 1964; Bhatira and Roy, 1966). A review of the literature gave scanty information regarding the efficacy of Methandienone in the management of lepra reaction and other reactional episodes. Usefulness of anabolic steroids in chronic wasting disease receiving steroids for a prolonged period is not empirical as this has been substantiated by the results of observation with anabolic steroids. Similar good results have been achieved with anabolic steroids in chronic lepra reaction and chronic ENL as evident by marked clinical improvement with lesser or no occurrence of reactional episodes, appreciable reduction in the requirement of steroids sometimes leading to stoppage of steroid. Further, it has been observed that sulphone could be well established in those cases without precipitating reactional episodes, with almost normalization of albumin-globulin ratio in the 60% cases of our series, and reduction of globulin in 70% cases.

It appears that Methandienone has some role as an adjuvant in the management of chronic lepra reaction and chronic ENL, especially with regard to dose schedule of steroids and institution of DDS in about 60% of cases.

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A Review of Drop-foot Corrective Surgery

GILLIAN HALL

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The late results of 65 tendon-transfer operations for drop-foot are reviewed, especially in relation to the various surgical techniques employed. It is concluded that from the patient's point of view range of movement was more important than gait. For young patients with good pre-operative mobility, single-tendon transfers were preferable, but for patients with inverted, deformed or stiff feet, where range of movement was less important than stability, the two-tendon Carayon techniques could be preferable.

Introduction

In this report 65 tendon transfer operations, which were performed on 54 patients to correct drop-feet due to leprosy, have been reviewed. All the operations were performed at the All Africa Leprosy and Rehabilitation Training Centre (ALERT) in Ethiopia between 1968 and 1976. The cases have been divided into 5 groups according to the date of surgery, the procedure used and the surgeon who performed the operation.

Most cases had been assessed prior to surgery in the physiotherapy department and had been taught isolation exercises for the tendon or tendons to be transferred. They attended the department again after surgery and were taught isolation and co-ordination of the transferred tendon in its new site and were trained to use it when walking.

Patients were usually asked to return to the department for review of the surgery after 6 months, but this did not always happen. Most cases were reviewed by the surgeon or physiotherapist or both when they happened to return to the hospital for some other reason.

Measurements

These were taken using a foot protractor with the patient sitting with his knee bent. The angle between the posterior aspect of the lower leg and the sole of the foot was measured taking the neutral position between dorsiflexion and plantarflexion as 90°. Thus decreasing figures indicate increased dorsiflexion and increasing figures increased plantarflexion.

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Gait

Where this is recorded it has been assessed as follows:

Good. The patient walks naturally. There is no difference in gait between the operated foot and a normal foot the other side.
Fair. The patient walks well. However, there is an obvious difference between the operated foot and a normal foot the other side. He may use the transfer quite well when he thinks about it, but tends to drag his foot when observed unnoticed.
Poor. The patient still tends to drag his foot, although there is some improvement in the position of the foot.
Bad. The operation has not improved the patients' gait or the position of the foot at all.

Group A

This small group consisted of 3 patients one of whom had had bilateral transfers. The operations were performed between 1969-1971 by one surgeon. He used Tibialis Posterior which he transferred anteriorly through the interosseous membrane and sutured to the tendon of Extensor Hallucis Longus and ligaments of the intercuneiform joints on the dorsum of the foot. The patients were seen for review between 5 and 7 years after surgery. Measurements taken at discharged and review averaged as follows:

	Discharge	Review 5-7 years
Active dorsiflexion	82.5	87.5
Resting position	91.2	100
Active plantarflexion	100.7	108.7
Range of active dorsiflexion from the resting position (designated range A)	8.7	12.5
Range of active dorsiflexion from active plantarflexion (designated range B)	18.2	21.2

OBSERVATIONS

Three of the feet (2 patients) had a good gait with straight stable feet and no ulcers. In the other case the gait was bad because the transfer had stretched out 20° since discharge to a resting angle of 110°.

Group B

Of this group of 10 patients, 2 had had bilateral transfers. One was performed in 1968 and reviewed 6 years later, the rest were done in 1972 and 1973 and reviewed between 3-4 years later. The 3 surgeons concerned used Tibialis Posterior which they transferred anteriorly around the tibia and divided into 2 slips which were inserted into the tendons of Extensor Hallucis Longus and Extensor Digitorum Longus at the level of the tarsus. In some notes it was also recorded that a stitch was made between the transferred tendon and the Extensor Retinaculum. Measurements taken at discharge and at review averaged as follows:

	Discharge	Review 3-6 years
Active dorsiflexion	74.5	85.9
Resting position	84.3	94.8
Active plantarflexion	94	103.3
Active range A	9.7	8.9
Active range B	19.5	17.4

OBSERVATIONS

1. *Gait*

This was assessed as described above. The resting angles and range of movement A of each group were between the figures indicated.

Gait	Resting angles	Range A
Good 7 cases	85- 95	5-26
Fair 4 cases	100-102	2-8
Poor 1 case	110	8

2. *Recovery*

In 2 cases there was recovery of Tibilais Anterior. One of these cases had a weak muscle preoperatively. At review he had a very high range of dorsiflexion but no ulcers. In the other case the recovered Tibialis Anterior caused inversion during the active phase of gait but no ulcers.

3. *Stability*

One other case had inversion causing an unstable foot postoperatively but the foot was mobile and there were no ulcers.

4. *Ulcers*

Two cases had toe-tip ulcers despite an apparently good gait. One case had severe multiple ulcers but was an unco-operative patient who would not wear prescribed shoes.

Group C

This was a group of 20 patients of whom 3 had had bilateral transfers. They were performed during 1974 and 1975 by 2 surgeons. The operation was a Tibialis Posterior transfer using the same technique as described above for group B. In cases with an inadequate passive range of dorsiflexion the tendo achilles was lengthened usually by a simple percutaneous approach. Of these 23 operations, 16 were reviewed between 3-12 months after surgery and 18 between 1-2$\frac{1}{2}$ years after surgery. Nine cases were reviewed during both periods. Measurements recorded at discharge and review were as follows:

	Discharge	Review 3-12 months	Review 1-2$\frac{1}{2}$ yr
Active dorsiflexion	83	88.5	87.2
Resting position	92.3	96.9	98.3
Active plantarflexion	98.5	104.2	107.2
Active range A	9.3	8.4	11.1
Active range B	15.5	15.7	20

OBSERVATIONS

1. *Gait*

Gait was assessed and the corresponding angles were as follows:

Gait	Resting angles	Range A
Good 3 cases	83-90	4-13
Fair 12 cases	90-110	5-20
Poor 7 cases	95-110	5-17
Bad 3 cases	105-115	5-9

2. *Stability*

Of these 23 feet, 15 had complete nerve lesions, 2 had weak peronei, one had an active extensor hallucis and the rest had incomplete records. Postoperatively there were 6 cases of feet inverting, 5 of the complete lesions plus the one with an active extensor hallucis. In at least 3 of these cases inversion was present preoperatively but records were inadequate in the other 3 cases. Two of these cases had lateral border ulcers and stiffness, one had a lateral heel ulcer and stiffness. Two had no ulcers but the feet were very unstable in walking; the last caused no real problem. The inversion was noticed immediately after operation and in 4 cases an attempt was made to correct it by reoperating to tighten the lateral slip. It was not successful. In another case an attempt at correction was made later by transferring the Flexor Digitorum Longus tendon through the interosseous membrane and suturing it laterally into the tendon of extensor digitorum longus. This did not significantly improve the deformity either.

3. *Ulcers*

Twenty-two of the feet had evidence of preoperative tibial nerve damage with records of anaesthesia, dryness, cracks or ulcers. Only one case definitely had good sensation preoperatively. Fourteen of the cases had had ulcers preoperatively and of these 8 recurred after surgery. Four others had developed ulcers after surgery which were not recorded beforehand.

Group D

Between April and July, 1975 a series of operations were performed using a "Modified Carayon" technique. Of these 6 patients were seen for review between 4-12 months after surgery. One patient had had a bilateral transfer. The surgeon used 2 tendons. Tibialis Posterior was transferred circumtibially to the dorsum of the foot where it was sutured into the tendon of Tibialis Anterior. Flexor Digitorum Longus was transferred through the interosseous membrane and sutured to both the tendons of Extensor Hallucic Longus and Extensor Digitorum Longus in the lower leg. Measurements recorded at discharge and review were as follows:

	Discharge	Review 4-12 months
Active dorsiflexion	83.9	86.1
Resting position	88.9	95.1
Active plantarflexion	91.7	98.3
Active range A	5	9
Active range B	7.9	12.2

Gait was assessed and the corresponding angles were as follows:

Gait	Resting angles	Range A
Good 1 case	92	11
Fair 4 cases	90-95	4-13
Poor 2 cases	100-104	5-15

Group E

From April, 1975 until May, 1976, 41 operations were performed using Professor Carayon's two-tendon technique. Tibialis Posterior and Flexor Digitorum Communis were both brought anterior through the interosseous membrane. They were sutured to the tendons of Tibialis Anterior and Extensor Hallucis Longus plus Extensor Digitorum Longus in the lower leg. Lengthening of the tendo achilles was also done in cases with an inadequate range of passive dorsiflexion. When done an open division was performed. In some cases a release of the tibial nerve was performed, at the same time to try to improve the circulation through the tibial artery and thus to the sole of the foot. Of these cases 15 patients, 4 of whom had had bilateral transfers, were seen for review between 3 and 11 months after surgery. Measurements recorded at discharge and review were as follows:

	Discharge	Review 3-11 months
Active dorsiflexion	84.9	86.6
Resting position	87.6	92.4
Active plantarflexion	91	98
Active range A	2.7	5.8
Active range B	6.1	11

OBSERVATIONS

1. *Gait*

This was assessed and the corresponding resting angle and range of movement A were as follows:

	Resting angles	Ranges of movement
Good 6 cases	75-95	0-19
Fair 7 cases	80-98	0-9
Poor 4 cases	95-114	2-10
Bad 2 cases	94-105	0-2

2. *Range of movement*

At discharge the range of movement was very limited. Of these 19 feet, 9 had no active range from rest at discharge and one had no active range from full plantarflexion. After a few months the resting angle dropped and the plantarflexion increased thus the active range of dorsiflexion increased. At review 3 still had no active dorsiflexion from rest, but all cases had some active range from plantarflexion. The gait of the patients was often assessed as good or fair even though the patient had very little active range of movement. However the patients were much happier with the operation if they had a greater range.

3. *Stability*

Preoperatively 17 of these feet had complete nerve lesions and 2 had weak peronei. Postoperatively some had slight inversion but in none had it caused any problems such as instability in gait or ulcers.

4. *Ulcers*

Preoperatively there was evidence of tibial nerve damage in 17 feet. In 2 cases good sensation was recorded. Ten patients had ulcers before surgery and 5 had recurrence of ulcers postoperatively.

5. *Recovery*

One patient had recovery of Tibialis Anterior. His records showed that he had had a complete lesion preoperatively.

Summary

GROUP A. TPT INTEROSSEOUS ROUTE 1969-71

The range of movement was good and had increased at review. The average resting position had dropped 9° in the 5 years. The results seemed encouraging but too few cases were seen to make any judgement.

GROUP B. TPT CIRCUMTIBIAL ROUTE 1968-1972/73

There was a good range of active dorsiflexion both from rest and from full plantarflexion. This range did not alter much between discharge and review. The angles of maximum dorsiflexion and the resting angles had dropped by about 10° at review. However this did not afford the overall good results as assessed by gait. Only one case was inverting.

GROUP C. TPT CIRCUMTIBIAL 1973-75

There was a good active range of dorsiflexion which increased slightly after $2\frac{1}{2}$ years. Active dorsiflexion dropped by 5° during the first year but then remained constant. The resting position dropped 4° during the first year and another 2° in the next year.

Of these cases, 6 had bad inversion postoperatively. An attempt to correct this by tightening the lateral slip was not successful.

GROUP D. MODIFIED CARAYON TECHNIQUE 1975

The range of movement was not as great as in the above 3 groups. During the first 6 months the resting position dropped by about 5° and the range of movement increased about 4°. No cases were recorded with inversion.

GROUP E. CARAYON TECHNIQUE 1975/76

The range of active dorsiflexion was very poor at discharge. It increased during the first 6 months. The maximal dorsiflexion position was on the whole maintained and the resting position had dropped 5°. In none of the cases were there problems with inversion.

Further study at a later stage needs to be done for the Carayon Technique to provide a fair comparison with the other methods.

A comparative summary of angles at discharge and review

		Dorsiflex.	Rest.	Plantarflex.	Active range	
Group A	Discharge	82.5	91.2	100.7	8.7	18.2
	Review 6 yr	87.5	100	108.7	12.5	21.2
Group B	Discharge	74.5	84.3	94	9.7	19.5
	Review 4 yr	85.9	94.8	103.3	8.9	17.4
Group C	Discharge	83	92.3	98.5	9.3	15.5
	Review 6 mth	88.5	96.9	104.2	8.4	15.7
	Review 2 yr	87.2	98.3	107.2	11.1	20
Group D	Discharge	83.9	88.9	91.7	5	7.9
	Review 6 mth	86.1	95.1	98.3	9	12.2
Group E	Discharge	84.9	87.6	91	2.7	6.1
	Review 6 mth	86.6	92.4	98	5.8	11

Conclusions

1. The gait of the patient did bear a relationship to the angles measured, but angles alone were not sufficient to predict the result of surgery. The gait might be good if the patient had a poor range of movement provided the resting angle of the foot was fairly high. It could also be good with a lower resting angle but a better range of movement.

2. The resting angle did not seem to be significantly better in any one technique. It dropped to varying degrees in all techniques.

3. Patients were happier if the operation gave them a good range of movement. They were not so happy with a foot they could not move even if their gait was apparently good. This could be due to other factors such as difficulty climbing hills or walking on rough ground and further investigations need to be done in this respect.

4. The active range of dorsiflexion was greatest with the single tendon techniques. It was less at least initially in the Carayon two-tendon techniques.

5. There were more cases with inversion problems in the circumtibial single-tendon technique. Some of these cases had a definite tendency to inversion preoperatively. It would seem sensible then to avoid this technique where there is a tendency to inversion preoperatively. Results did not however prove that the technique would cause inversion in a foot which preoperatively was straight and mobile.

6. Records were not sufficient to show whether the operations really helped to prevent any further foot damage and ulceration. There were certainly a large proportion of patients with postoperative as well as preoperative ulcers. This might have been because such patients were more likely to return to the hospital and be seen for review whereas those with no further problems might not have bothered to come.

7. My impression from the study was that for young patients with a good mobile straight foot preoperatively, the single tendon transfers were preferable as they gave a better range of movement. However for any patients with a tendency to inversion or for those with badly deformed or stiff feet where range of

movement was less important than stability the two-tendon Carayon techniques might be preferable.

Acknowledgement

I would like to thank the doctors of ALERT and my head of department Miss Jean Watson for their help and encouragement whilst undertaking this follow-up study.

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Leprosy and the Community

MASSIVE ATTACK ON LEPROSY: WHO PRESS RELEASE WHA/12 OF 14 MAY, 1977

A massive attack on leprosy under WHO's special programmes for Research and Training in Tropical Diseases (TDR) was reported today to one of the main committees of the Thirtieth World Health Assembly meeting in Geneva.

A report presented to the Assembly said leprosy remained in many countries an important public health problem. The total number of cases in the world is conservatively estimated to be between 10 and 11 million. A rough breakdown by regions gives the following figures: Asia, 6.5 million; Africa, 3.5 million; the Americas, 350,000. In 1970, there were 2,877,481 registered patients in the world.

A chronic ailment caused by a bacillus, *Mycobacterium leprae,* leprosy produces lesions in the skin tissues and the peripheral nerves. It affects people at all ages and of all races. There are 2 main forms: the tuberculoid form, in which the body's strong defences prevent the bacillus from reproducing, and the highly contagious lepromatous form, in which the bacillus grows unchecked.

Under the special TDR programme, priority is being given to 2 main lines of research: immunology and chemotherapy. Research in immunology concentrates on development of a safe and effective vaccine and on finding a simple diagnostic test for subclinical infections. Progress made over the past 3 years strengthens the hope that a vaccine against leprosy can be developed. However, a vaccine for large-scale application cannot be expected in the immediate future.

One of the major research problems is the resistance of the leprosy bacillus to the sulphone drug, dapsone, the most widely used drug to treat the disease. Some other drugs, such as clofazimine, rifampicin and thiacetazone, have been shown to be active against leprosy but they are much more expensive or else more toxic than dapsone. Another challenge to research is the persistence of bacilli in the body of the treated patient that could lead to a relapse later.

These research programmes and other research activities (in epidemiology operational research and in *Mycobacterium leprae* cultivation) are being developed with maximum involvment of investigators from leprosy endemic countries. In this connection, a regional plan for research in leprosy was adopted by the Regional Advisory Committee on Medical Research for the South-East Asia Region during its last session.

A scientific working group met in Geneva last April to finalize a standard protocol for chemotherapy trials, making it possible to determine fairly

rapidly the most appropriate drug regimen for leprosy control services. Plans have also been made for drug development, including the identification of active principles in plants. The working group will also study proposals for further research into dapsone resistance, better animal models, development of better and safer drugs and proposals for training young investigators from leprosy endemic countries. The ethical aspects of drug trials as well as the question of co-operation with pharmaceutical firms will also be studied.

The report to the Assembly pointed out that, if the treatments available so far are not perfect, the progress that has been made is far from negligible. In some countries where it has been possible to mount well-organized programmes against leprosy, it has proved possible to reduce the total number of cases by as much as 75% after 15 years of effort. The slow evolution of leprosy, which is preceded by a long incubation period (3-9 years or more), and the equally long periods needed for treatment and follow-up of leprosy patients and their household contacts, single out leprosy control as an activity particularly well suited for inclusion within community health care systems.

ILEP: GUIDELINES FOR THE CAMPAIGN AGAINST LEPROSY

ILEP (then ELEP) published in 1970 a booklet summarizing the common grounds on which its member Societies and Associations approached leprosy control. This booklet now appears in a new Edition, updated by the Medical Commission of ILEP to July, 1976. Adopted by the General Assembly of ILEP, the largest world agency actually operating in the field of leprosy control, this is a policy document of great importance and interest to leprosy workers everywhere, a companion booklet to the Memorandum on Leprosy Control, written by Dr Browne and issued jointly by OXFAM, Lepra and The Leprosy Mission.

The ILEP Guidelines appear to be addressed as much to supporting agencies and supporters as to actual field workers. While presenting up-to-date scientific information regarding leprosy and the approach to its control, the booklet also aims to correct out-dated attitudes and prejudices, and includes a Section by Dr Brand on the Economics of Leprosy Control. There is an interesting Section on the Technique of "Barrier Nursing" in Contagious Leprosy, which, accepting the thesis that leprosy patients needing hospital treatment can and should be nursed in general hospitals, offers guidance to nursing staff. There are uncompromising Sections on the segregation of patients with lepromatous leprosy and the segregation of the children of leprosy patients.

A great deal of reliable information and trustworthy judgment is condensed in this valuable booklet. One aspect included at some length in its British counterpart receives only scant mention here, namely the education of the public regarding leprosy. There is now a mass of evidence that it is not sufficient to include leprosy in programmes of health education without giving leprosy special emphasis. Nothing but sustained and specific carefully planned emphasis seems capable of defeating the stubborn prejudice so widely associated with leprosy, and this is true not only at the receiving end of the leprosy control programme, but at the supporting end as well.

T. F. Davey

CHRISTIAN KUSHT NIRMULAN YOJNA

This is a new leprosy control project in North India, commendable for its location in an area of unusual deprivation. This first summary report not only reveals an unsuspected degree of leprosy activity, but illustrates both the problems and the approach appropriate to such situations.

Christian Leprosy Eradication Project, Seorahi, Dist. Deoria, U.P. India 274406

BRIEF SKETCH OF ACTIVITIES FOR THE YEAR 1976

The Project was started in June, 1975 under the auspices of the Fellowship of Free Baptist Churches in N. India. It covers an area of 100 sq. miles with a population of 120,000, and is situated on the U.P.-Bihar border in an area ravaged by floods year after year during the months of July to September.

The area is noted for its economic backwardness and abject poverty and the resultant malnutrition. A great majority of the people are illiterate, and live in make-shift congested huts, sleeping huddled together, especially during the cold season.

The goal of the Project is the eradication of leprosy from this area within the next 10 years.

Five trained paramedical workers are working under the direction of a Medical Officer, doing systematic house to house survey in their respective zones. Patients detected during the survey are referred to any of the 5 clinics situated in vantage points for confirmation and treatment. Twenty villages with a total population of 20,156 have been surveyed. The overall incidence of leprosy is 1.6%. But there are pockets where the incidence is alarmingly high. In a village hamlet with a population of 256, 27 persons have been found to have leprosy, and in another hamlet, 33 persons were diagnosed to be suffering from leprosy out of a total population of 323. Even in affluent homes, a number of leprosy sufferers were found where domestic servants with the infectious type of leprosy and congested living conditions were contributing factors for the infection.

A 20-bedded hospital with all amenities has been built to accommodate those of the patients who may need hospitalization. Dr V. P. Das, Secretary for S. Asia, the Leprosy Mission, declared the hospital open on 15 August, 1976.

Public response and co-operation were abundantly forthcoming in the initial stages, but received a set-back when ignorant village people who are set against the Family Planning Campaign of the Government mistook us for the Campaigners and refused to co-operate with our Paramedical workers in their survey work. We had to explain our position and do much persuasion before they gave their co-operation once again. We have 2 anti-leprosy films which have very good reception and have high education value. A good number of early leprosy cases come to us voluntarily for diagnosis and treatment, because of the films. We display anti-leprosy posters in schools and other public places and distribute literature on leprosy to teachers and students, who are helpful in our outreach work in the villages.

The whole Project is administered by the Project Officer, who is responsible for its proper day to day functioning.

P. Ratnaswamy
(Project Officer)

POONA URBAN DISTRICT LEPROSY CONTROL PROGRAMME

The progressive outlook on leprosy control in Maharashtra State, India, is reflected in the vigorous urban leprosy control programme now in progress in the city of Poona, Dr J. M. Mehta, Honorary President of the Poona District Leprosy Committee has sent the following summary report on the first 21 months of the programme.

Pune Urban Leprosy Investigation Centre Conducted by Poona District Leprosy Committee and Supported by Deutsches Aussatzigen-Hilfswerk E.V. of West Germany

A summary of the work done for the period 1 April, 1975 to 31 December, 1976 is given below:

During the period under report work was being done in 7 different areas (called sectors) of the city of Poona.

Sector no.	Sector name	Total population (approx.)	Slum population (approx.)	School population (approx.)
1.	Bhavani Peth	125,000	35,000	25,000
2.	Mangalwar Peth	125,000	15,000	20,000
3.	Wadarwadi	100,000	20,000	20,000
4.	Tadiwala Road	75,000	15,000	10,000
5.	Parvati	125,000	20,000	20,000
6.	Hadapsar	100,000	20,000	10,000
7.	Yerawada	100,000	25,000	10,000
	Total	750,000	150,000	115,000

(1) SURVEY WORK

Type of population	No. of families/ schools covered	Population enumerated	Population examined	No. of cases detected	Suspicious cases k under observation
Slum dwellers	17,340	81,923	58,866 (71.9%)	374 (6.4/1000)	2
School children	234	142,328	119,796 (84.2%)	203 (1.7/1000)	36
Voluntary	—	—	—	347	—
Total	17,340/234	224,251	178,662 (79.7%)	924 (5.17/1000)	88

(2) CASES THROUGH SURVEY

Type of population	Children			Adults			Total
	L	N	Total	L	N	Total	
Slum dwellers	2	69	71	79	224	303	374
School children	–	180	180	–	23	23	203
Total	2	249	241	79	247	326	577

(3) CASES THROUGH VOLUNTARY REPORTING

Type of population	Children			Adults			Total
	L	N	Total	L	N	Total	
Slum dwellers	3	26	29	48	81	129	158
School children	–	6	6	–	–	–	6
Dapodi Colony	–	9	9	58	98	156	165
Miscellaneous	–	1	1	3	14	17	18
Total	3	42	45	109	193	302	347

(4) TREATMENT OF CASES

Area	No. of clinics	Total no. of patients detected		Total no. of patients under treatment	
		Slum dwellers	School children	Slum dwellers	School children
Bhawani Peth	2	152	84	98	60
Mangalwar Peth	3	196	49	168	35
Wadarwadi	1	24	52	20	30
Dapodi Colony	2	165	–	165	–
Tadiwala Road	1	35	–	35	–
Parvati	2	106	24	97	21
Hadapsar	1	–	11	–	11
Yerawada	1	26	–	20	–
Total	13	704	220	603	157

(5) PATIENTS HAVING DISABILITY*

Sector	Children			Adults			Total
	L	N	Total	L	N	Total	
Bhavani Peth	–	4	4	16	31	47	51
Mangalwar Peth	2	2	4	45	29	74	78
Wadarwadi	–	2	2	1	5	6	8
Dapodi Colony	–	–	–	55	93	148	148
Tadiwala Road	–	–	–	3	8	11	11
Parvati	–	–	–	5	14	19	19
Yerawada	–	–	–	1	4	5	5
Total	2	8	10	126	184	310	320

* Patients having only sensory loss of hands and feet are also included.

(6) SPECIAL TREATMENT

(a) *Temporary hospitalization*

During this year 41 patients were referred to Dr Bandorawalla Leprosy Hospital for treatment of ulcers, reconstructive surgery, reaction, other complaints and special investigations.

(b) *Other services*

Patients were provided with protective footwear, eyeglasses and other services as needed.

(c) *Dapodi colony*

The treatment centre for beggar leprosy patients is well attended and as a result the ulcers of these beggars are getting healed.

(7) HEALTH EDUCATION PROGRAMME

This programme is given due importance. Intensive health education is carried out with the help of audio-visual aids such as slide shows, photographs, film shows etc. The following table shows the abstract of health education work done so far:

Type of group	No. of programmes conducted	No. of persons attended
Teachers	128	1894
Students	44	3503
Others	177	9060
Total	349	14 457

(8) TRAINING COURSE AND OTHER ACTIVITIES

(a) A short training course was arranged for 26 leprosy technicians from Pune Zilla Parishad. This training included school survey, slum survey, lectures and a film show. The paramedical workers of the Pune Zilla Parishad worked with our workers and saw the way in which school surveys are conducted and how the patients are detected and treated.

(b) Dr P. Kapoor, Joint Director of Health Services (Leprosy) paid several visits to our surveys and clinics and demonstrated to our paramedical workers the correct method of examination and diagnosis of early cases. His visits were very valuable to the programme.

(c) A refresher's course was arranged by the centre for general medical practitioners. A large number of doctors participated in it. A film show accompanied by slide show and a lecture was arranged for this purpose. The discussions that followed were very fruitful.

J. M. Mehta (President Poona Dist. Leprosy Committee)

REPORTS RECEIVED

All India Leprosy Workers Conference Silver Jubilee & Centenary of Hansen's Bacillus Discovery, Sevagram, 12 to 16 October, 1973

This was an important Conference, covering all major aspects of leprology, and reflecting the emphases which have given such importance to the contributions of leprologists in India to our understanding of leprosy, its control and rehabilita-

tion. The Report is published by the Hind Kusht Nivaran Sangh, New Delhi. It is a pity that it has been so long delayed.

Sacred Heart Hospital, Kumbakonam, S. India, Diamond Jubilee

Founded in 1916, this hospital has rendered distinguished service to the cause of leprosy control in South India. Prior to modern chemotherapy the hospital cared for nearly 1000 patients, mostly neglected and abandoned people, but in more recent years, with the help of EMMAUS-SUISSE the hospital was able to develop into a modern leprosy control centre with outreach covering 4 Taluks and a population of 100,000, and a full range of specialist services at the centre. Research is actively encouraged. LEPRA and ILEP have also assisted the control project undertaken by this forward looking hospital, and we add our congratulations on its 60th anniversary.

Lepr. Rev. (1977) **48**, 200–201

Field Workers' Forum

GUIDELINES TO FIELD STAFF ON EARLY DETECTION OF NERVE INVOLVEMENT

The Southern Asia Conference of the Leprosy Mission at Nagpur in January, 1977 appointed an expert Committee to establish guidelines for field staff on the early detection of nerve involvement in leprosy. The Committee consisted of Drs R. H. Thangaraj, E. P. Fritschi, C. K. Job, A. J. Salvapandian, Phyllis Taylor and Ramprasad. Their findings are as follows.

Introduction

The onset of paralysis in a nerve can be averted in a proportion of cases if the muscle weakness or sensory loss can be detected at a very early stage and the patient immediately transferred to the referral centre for full investigation and treatment.

It is of the utmost importance therefore that cases of neuritis be recognized and transferred by the field staff at a very early stage.

Neuritis is here defined as "an inflammation of a nerve which may give rise to sensory or motor deficit".

Persons to be Examined

All early cases in the field who do not have paralysis.
All cases showing exacerbated skin lesions.

Frequency

Examination should be done at every clinic, i.e. every 4 weeks. All cases should have a full sensory charting of both hands and feet at every annual re-assessment.

Method of Examination

Motor deficit

Facial nerve. Blink reflex is noted when the examiner waves his hand before the eyes.

Ulnar, median, and radial nerves. The patient is asked to approximate the tip of the thumb to the tip of the *straight* little finger with the hand outstretched in the pronated position.

Lateral popliteal nerve. Patient is asked to dorsiflex the great toe against resistance.

Posterior tibial nerve. The patient is asked to spread the toes.

Sensory

(a) Ulnar border of both hands felt for softness and sweating (b) Radial border of both hands felt for softness and sweating. (c) Sole of the foot felt for softness and sweating.

Pain and tenderness

The examiner gently palpates both ulnars, both medians, both lateral popliteal, both posterior tibials and watches for wincing.

Lepr. Rev. (1977) **48**, 202–203

News and Notes

1981—UNITED NATIONS YEAR FOR DISABLED PERSONS

At its last General Assembly the United Nations proclaimed 1981 as the International Year for Disabled Persons, with the intention during that year of focussing attention throughout the world on the social and economic needs of those who have the misfortune to be disabled. Among the objectives set for that year are (a) to help disabled persons in their adjustment to society; (b) to promote efforts to provide assistance, care, training and guidance, to make suitable work available and ensure social integration; (c) to encourage study and research projects on subjects such as access and transportation; (d) to educate the public regarding the rights of disabled persons to participate in and contribute to the economic, social and political life of their communities. As detailed programmes are to be studied at the 1977 General Assembly, it is to be hoped that the needs of leprosy sufferers will figure prominently in the measures to be considered.

NEW LEPROSY MISSION FILM "THE NET"

"THE NET" is a 16-mm colour sound film which tells how the modern domiciliary approach to leprosy control operates in practice. Located in and around Salur, India, it shows teams of workers in action in the villages, surveying, treating, checking and caring, supported by the central hospital, with its laboratory facilities maintaining a check on progress and its specialist medical and surgical services for patients in special need. This excellent film runs for 25 min and enquiries should be addressed to the nearest Leprosy Mission representative or to 50 Portland Place, London W1N 3DG.

INTEGRATION IN PAPUA/NEW GUINEA

With the coming of independence, basic leprosy control policy in Papua/New Guinea will be one of integration into the general medical programme. The Government leprosaria, beginning with the large one on Gemo Island, near Port Moresby are being closed, and special wards in general hospitals will look after those in need of extra care. The existing Leprosy Mission programme in the Southern Highlands provided the basis of experience on which future policy is being built. The Mission's 12-bed hospital at Tari will close and become an out-patient clinic, with the local general hospital taking leprosy patients. At Mendi integration has already taken place; Leprosy Mission staff care for leprosy patients in the general hospital, and the Mission's representative, Alex Packett, is the Government Leprosy Officer for the District. Considerable development is planned in the Southern Highlands. Papua/New Guinea is thus setting a pattern for enlightened leprosy care.

"MEMORIES AND REFLECTIONS OF DR G. A. HANSEN"

Following the recent review of this book (*Leprosy Review* Vol. 48 No. 1, p. 53), Herr Kober, Senior Executive of the German Leprosy Relief Association has written to say that copies of the book are still available and may be obtained from the Association at the following address: 87 Wurzburg 1/West Germany, Dominikanerplatz 4, Postfach 348.

BACK ISSUES OF *LEPROSY REVIEW*

Dr Felton Ross has written to say that the Library of American Leprosy Missions, Inc., is short of copies of the following back Issues of *Leprosy Review:*

1. Vol. XVI No. 3
2. Vol. XVI No. 4
3. Vol. XVII No. 4
4. Vol. XVIII No. 2
5. Vol. XVIII No. 4
6. Vol. XXI No. 2
7. Vol. XXI No. 3
8. Vol. XXI No. 4

Stocks of these Issues are exhausted at the publishers, and it would be very much appreciated if anyone able to help would communicate with Dr Felton Ross, American Leprosy Missions, Inc., 1262 Broad Street, Bloomfield, N.J. 07003, U.S.A.

Lepr. Rev. (1977) **48**, 205–206

Letter to the Editor

Enzyme Activity of Hyaluronic Acid

We reported earlier, in the *Leprosy Review* (Prabhakaran, 1974; Prabhakaran *et al.*, 1977) a rapid identification test for *Mycobacterium leprae,* based on the oxidation of D-DOPA by the bacillus. In the *International Journal of Leprosy* (1976) (which appeared in April, 1977), Kato *et al.* published a paper claiming that a polysaccharide, hyaluronic acid, contains DOPA oxidase activity. In an earlier report in *Leprosy in India* (Prabhakaran, 1976), we had shown that hyaluronic acid contains no phenoloxidase. Any one with a basic understanding of biochemistry would recall that all enzymes are proteins. Other substances like polysaccharides do not contain any enzyme activity. No nonprotein enzymes exist. These facts were established early in the century by giants in the field like Sumner and Northrop. In fact, a Nobel Prize was awarded for crystallizing and proving that enzymes are proteins. It is an anachronism to say now that a polysaccharide contains the phenoloxidase enzyme. I am making the following specific comments about this claim, because silence might be misconstrued.

(1) The DOPA oxidation they report is not enzymatic; heated hyaluronic acid also would give similar results. Excessive amounts of tissue extracts like hyaluronic acid containing metal ions would stimulate the auto-oxidation of DOPA. In the experiments reported by Kato *et al.*, they have used no controls using heat-inactivated preparations. In the studies we reported (*Leprosy in India* **48**, 268-271) we used 2 types of hyaluronic acid, prepared from umbilical cord and from vitreaous humor. We measured not only quinone formation but also oxygen uptake. Both types of hyaluronic acid showed no enzymatic oxidation of DOPA. Unheated preparations gave the same results as heated samples. In the report of Kato *et al.* itself, it may be noted that 10 μg of an enzyme like mushroom tyrosinase gives an absorbance of 0.250-0.350 in 5 min; whereas hyaluronic acid is used in 1-4 mg concentrations. No purified preparation with enzyme activity has to be used at such high concentrations. What they measure with hyaluronic acid is not enzymatic activity. When using other tissue extracts and bacterial preparations as well, Kato *et al.* do not have heated controls. The readings have to be corrected for those given by the heated samples. It should be recognized that DOPA is an unstable amino acid. Without proper controls, the results obtained are not valid.

(2) The *M. leprae* preparation they used probably had no enzymatic activity to start with. If the *M. leprae* preparations are not made from fresh material or from tissues transported at 0°C or below, the bacilli would have no phenoloxidase activity. Kato *et al.* do not state in what condition, the tissues were transported from Dakar. If this was done (as on previous occasions) at ambient temperatures in acetic acid, the enzyme would be inactivated. They also do not mention the amount of bacilli used in their reactions. Kato *et al.* state that we demonstrated

DOPA oxidation by *M. leprae* in crude preparations. We have treated our bacterial preparations with NaOH, trypsin and also acetone and ether, without loss of enzyme activity. The activity was lost on heating, indicating that the phenoloxidase is an enzymatic process. We have also separated the enzyme from the bacterial pa[illegible] shown it to be a copper-containing protein. Recently we tested 2 cultures of mycobacteria, claimed to oxidize DOPA. When the organisms were thoroughly washed free of the culture media, the bacilli had no DOPA oxidase activity.

When DOPA undergoes auto-oxidation or enzymatic oxidation, there is a general increase in absorbance in the spectrum. Therefore, at whatever wavelength of the spectrum) the absorbance is measured, there would be an increase. Taking g at 2 wavelengths (as Kato *et al.* have done) is not enough to prove that a ar pigment is formed in the reaction. To prove that, the whole spectrum be measured and the absorbance peak characteristic of the pigment has to monstrated. Kato *et al.* have not done so.

K. PRABHAKARAN

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Book Review

A Laboratory Manual for Rural Tropical Hospitals, by Monica Cheesborough a. McArthur. C... Livingstone, Edinburgh, London and New York, 1976. Price in the £2.50.

This very important book is described as a basis for Training Courses, but it is more than that. In the field of leprosy there are hundreds of laboratory technicians working in rural centres, either on their own or in small groups, and called upon to undertake a range of laboratory work including large numbers of procedures directly relative to leprosy. Here is a highly up-to-date and comprehensive manual for such workers, clearly written, and giving precise instructions, and published at a very reasonable price, which includes the innovation of a set of transparencies and folding viewer conveniently contained in a pocket in the back cover.

The range of laboratory procedures demanded nowadays of the technician is enormous, and the whole book, in covering this, is necessarily concise and sometimes brief.

The worker in leprosy will find his needs very well covered, but pressure for space has prevented some elaboration of details which one has found in practice do need emphasis.

One of these relates to the staining tank method for staining leprosy smears in bulk. This method deserves mention, with the caution that staining solutions need frequent renewal. Indeed, written for the worker in the tropics, the effects of evaporation on the concentration of staining and other laboratory fluids needs frequent emphasis.

Some elaboration on the technique of nasal smears would also have benefitted the leprosy worker, with added emphasis on nasal discharge as a useful and extremely simple source of examination material provided that smears are made from purulent or slightly sanguineous areas. The internal examination of the nose really calls for specialist training, as the inferior turbinate is often a richer source of bacilli than the septum, especially in early lepromatous leprosy.

Some expansion of the chapter on fungal infections would also be invaluable.

Any laboratory at a leprosy centre would be enriched by having this book available for reference.

T. F. DAVEY

Lepr. Rev. (1977) **48**, 208–215

Abstracts

1. MICROBIOLOGY

69. FIELDSTEEL, A. H. & LEVY, L. **Neonatally thymectomized Lewis rats infected with *Mycobacterium leprae:* response to primary infection, secondary challenge, and large inocula.** *Infection & Immunity,* 1976, v. 14, No. 3, 736-741.

Several experiments were carried out to measure the ability of neonatally thymectomized Lewis rats (NTLR) to limit multiplication of *Mycobacterium leprae.* NTLR inoculated in one hind foot-pad with 10^7 viable *M. leprae* and challenged in the other hind foot-pad with 5×10^3 organisms simultaneously or 120 or 180 days later permitted multiplication in both sites. By contrast, immunologically intact rats similarly inoculated did not permit multiplication from either inoculum. NTLR and immunologically normal BALB/c mice were equally susceptible to infection with *M. leprae,* in that multiplication occurred regularly in the foot-pads of both species when inoculated with a bacterial suspension diluted to provide 5 organisms per foot-pad. Finally, multiplication occurred when 5 viable *M. leprae* diluted with 10^7 heat-killed organisms were inoculated into the foot-pads of NTLR. Although there was some evidence that NTLR are not completely immunosuppressed, NTLR appear to be capable of detecting much smaller proportions of viable *M. leprae* than can be detected by immunologically normal mice.

70. BEIGUELMAN, B. & PISANI, R. C. B. **Chromosomal aberrations in leukocyte metaphases of leprosy patients under dapsone therapy.** *Hansenologia Int.,* 1976, v. 1, No. 1, 53-60.

. . . Chromosome analyses were made on leukocyte metaphases of 18 leprosy patients who were ingesting daily doses of 50 mg or 100 mg of DDS and of 40 healthy individuals used for control.

These analyses have shown that the proportion of numerical chromosomal aberrations in the leukocyte metaphases of the leprosy patients did not differ significantly from that observed in the cells of the controls. In contrast, the frequency of cells with chromatid or chromosome breaks and gaps was significantly increased in the leukocytes of leprosy patients.

Multiple regression analysis applied to the data recorded has shown that the increase of breaks and gaps in the chromosomes of leprosy patients cannot be attributed to age, years under sulphone-therapy or to concentration of DDS in blood.

71. DESIKAN, K. V. **Correlation of morphology with viability of *Mycobacterium leprae.*** *Lepr. India,* 1976, v. 48, No. 4, 391-397.

A concept has been developed in the recent years that the evenly stained "solid" bacilli are living and the "non-solid" forms are degenerate and dead. This communication presents the findings in experimental mice inoculated with material containing 1-10% solid evenly stained *M. leprae* and also with material containing 0% solid organisms. There was multiplication of the bacilli in both the groups. Quantitatively, the yield also was not significantly different. These findings do not support the belief that the non-solid bacilli are necessarily dead. The non-solid bacilli were further classified on the basis of their morphology to the following forms: (a) short

but evenly stained, (b) indented, (c) beaded, (d) dumb-bell shaped, (e) coccoid, and (f) fragmented. Material without solid bacilli, but containing different proportions of the above types of bacilli also gave similar results, making it difficult to say which types of morphological forms are non-living. It appears, therefore, that the recognition of the living status of *M. leprae* by its morphology is highly equivocal and subject to error.

72. CHATTERJEE, B. R. **A non-acid-fast coccoid precursor—possible cultivable phase of *Mycobacterium leprae*.** *Lepr. India,* 1976, v. 48, No. 4, 398-405.

A non-acid-fast coccoid organism isolated from human leproma, and skin and nasal smears of leprosy patients shows tendency to revert to an acid-fast mycobacterial form during test-tube passages. One of these coccoid isolates gave strong DOPA oxidase activity. There is also preliminary evidence of mycobacterial conversion from these coccoids in intraperitoneally inoculated mice. The possibility that these non-acid-fast coccoids could be a cultivable precursor phase of *M. leprae* has been raised and discussed.

2. BIOCHEMISTRY, PATHOLOGY, IMMUNOLOGY

73. ABE, M., IZUMI, S., SAITO, T. & MATHUR, S. K. **Early serodiagnosis of leprosy by indirect immunofluorescence.** *Lepr. India,* 1976, v. 48, No. 3, 272-76.

A fluorescent antibody absorption test for leprosy was found to be highly sensitive. Leprosy bacilli were extracted from a histoid leprosy lesion for use as antigen in the indirect immunofluorescent test using sera which had been absorbed with cardiolipin, lecithin and the polysaccharide of tubercle bacilli (to remove cross-reacting antibodies), and bovine albumin. The screening dilution was 1 in 40.

The test gave the highest titres with sera from lepromatous leprosy patients but, even so, positive results were obtained in 82% of tuberculoid cases, 2 out of 4 indeterminate cases and 3 out of 4 contacts. This compares with a "previous finding" that none of 50 sera from non-contacts was positive. It is acknowledged that further work is needed to establish the specificity of the test. The same technique could be used for the quantitative staining of *Mycobacterium leprae,* and possibly for its identification.

D. S. Ridley

74. SAHA, K., MITTAL, M. M. & MAHESHWARI, H. B. **Passive transfer of immunity into leprosy patients by transfusion of lymphocytes and by transfusion of Lawrence's transfer factor.** *J. Clin. Microbiol.,* 1975, v. 1, No. 3, 279-288.

About 1200 million viable lymphocytes from normal but lepromin- and tuberculin-positive human beings were transfused in 4 patients with lepromatous and one with tuberculoid leprosy 3 times at monthly intervals. Three lepromatous patients suffered from erythema nodosum leprosum (ENL) whereas the other 2 developed severe reaction whenever put on the smallest doses of dapsone. In one lepromatous patient minimal or no improvement was observed. In the other 4 patients clinical, bacteriological and histological improvement occurred, and 2 patients started to tolerate dapsone. The authors consider that immunotherapy might have a definite role in the management of the disease, especially in cases with ENL.

The repeated transfusion (3 times) of Lawrence's factor into 4 patients intolerant of leprosy drugs produced no discernible improvement.

T. F. Davey

75. MITTAL, M. M., SAHA, K. & MAHESWARI, H. B. **Passive transfer of immunity in lepromatous leprosy patients by Lawrence's transfer factor.** *J. Indian Med. Ass.,* 1976, v. 66, No. 9, 197-199.

Lawrence's transfer factor prepared from leucocytes from healthy donors who were tuberculin and lepromin (Mitsuda) positive was transfused into 4 patients with lepromatous leprosy, each patient receiving transfer factor prepared from 250 ml blood on 3 occasions at monthly intervals. All 4 patients were intolerant to anti-leprosy drugs. After each transfusion reactive symptoms were exaggerated for 3-5 days. Seven and a half months after the first transfusion, while appreciable improvement had occurred in the immunological status of the patients, there was no considerable improvement in clinical histological or bacteriological status. [See also *Trop. Dis. Bull.,* 1977, v. 74, abstr. 357.]

T. F. Davey

76. DE VRIES, R. R. P., FAT, R. F. M. L. A., NIJENHUIS, L. E. & VAN ROOD, J. J. **HLA-linked genetic control of host response to *Mycobacterium leprae*.** *Lancet,* 1976, Dec. 18, 1328-1330.

Non-random parental HLA-haplotype segregation is demonstrated in siblings with leprosy. A method is described for the statistical analysis of non-random segregation among sibships of different sizes. Sibs with the same type of leprosy show a significant excess of identical HLA haplotypes. This is also true for families in which only tuberculoid leprosy is found, which is by far the commonest type in the population studied. However, sibs affected with different types of leprosy share a haplotype less often than expected. This indicates that both susceptibility to and type of leprosy are controlled by at least 2 HLA-linked genes. Our findings suggest that the equivocal results of previous population studies are due to differences of linkage disequilibrium between HLA-linked genes controlling the host response to *Mycobacterium leprae* and alleles of HLA A and B loci in various populations.

77. BJORVATN, B., BARNETSON, R. S., KRONVALL, G., ZUBLER, R. H. & LAMBERT, P. H. **Immune complexes and complement hypercatabolism in patients with leprosy.** *Clin. Exp. Immunol.,* 1976, v. 26, No. 3, 388-396.

The occurrence of immune complexes in the serum and the level of the C3 breakdown product C3d in the plasma from patients with leprosy were studied by quantitative methods and the results were compared in various forms of the disease. These studies were performed on 62 samples from 26 patients. The serum ^{125}I-C1q binding activity was found to be increased by more than 2 s.d., as compared to the normal values, in most of the sera from patients with erythema nodosum leprosum (ENL) (80%) and uncomplicated lepromatous leprosy (82%), but also in the sera from patients with tuberculoid leprosy (58%). *In vitro* studies suggested that immune complexes involving mycobacterial antigens were present in leprosy sera. An increased C3d level (>2 s.d.) was also found in most of the plasma from patients with ENL (70%), but rarely in the plasma from patients with uncomplicated lepromatous leprosy (18%) and never in tuberculoid leprosy patients' plasma. The absence of a significant correlation between the ^{125}I-C1q binding activity and the C3d level in leprosy patients may suggest that extravascular immune complexes are involved in the complement activation occurring in ENL. The quantitation of C3d in plasma may be of some practical interest in the early diagnosis of ENL complications of leprosy.

78. BJUNE, G. & BARNETSON, R. ST C. **Plasma factors in delayed-type hypersensitivity. Augmentation of lymphocyte responses in borderline leprosy reactions.** *Clin. Exp. Immunol.,* 1976, v. 26, No. 3, 397-402.

The phytohaemagglutinin-induced response of lymphocytes were found to be inhibited by plasma from patients with leprosy when compared with their responses in pooled serum from healthy donors. When patients developed reversal reactions, the initial inhibitory effect of their plasma was replaced by an augmentary effect on the responses to phytohaemagglutinin. The period of augmentation coincided with that of the reversal reaction in patients with borderline tuberculoid leprosy, but was delayed in patients with borderline lepromatous leprosy. The plasma from each leprosy patient was also observed to have the same effect on lymphocytes from unrelated individuals, showing that the inhibition and augmentation were due to factors in the plasma and not to a change in lymphocyte receptors.

It is possible that the normal stable state of leprosy results from the presence of factors in plasma which act as a control mechanism, and that delayed hypersensitivity reactions may be caused by a breakdown of this control.

79. BALAKRISHNAN, S. **Biochemical aspects of reaction states in leprosy.** *Lepr. India,* 1976, v. 48, No. 4, 406-412

Sequential biochemical investigations conducted in cases of leproma cutis in the reactive as well as subsided phases indicated elevated serum levels of mucoprotein and uric acid and skin levels of hydroxy-proline and hexosamine in the reactive phase of leproma cutis. Elevation of the urinary excretion of hydroxy-proline and certain other amino acids was noticed during "lepra reaction". Enhancement of serum levels of aldolase, CPK, LDH and transaminases was observed in the reactive phase of lepromatous leprosy. These findings taken as a whole suggest a generalized tissue breakdown in lepra reaction.

80. PADMA, M. N., PREMANATH, M. & DESIKAN, K. V. **Bacillaemia in reactive states of leprosy.** *Lepr. India,* 1976, v. 48, No. 4, 413-418.

Thirty-five cases of lepromatous and near-lepromatous cases of leprosy in reaction have been investigated for the presence of acid-fast bacilli in blood at the height of the reaction as well as at its subsidence. Only 3 cases exhibited bacillaemia during reaction. It is therefore unlikely that dissemination of the disease is accentuated during reaction as commonly believed. Further, the immune complexes demonstrated to be circulating during reaction are possibly formed by bacillary products and not by whole or fragmented bacilli.

81. SHEPARD, C. C., VAN LANDRINGHAM, R. & WALKER, L. L. **Immunity to *Mycobacterium leprae* infections in mice stimulated by *M. leprae,* BCG and graft-*versus*-host reactions.** *Infection & Immunity,* 1976, v. 14, No. 4, 919-928.

Infections of mice with *Mycobacterium leprae* in one rear foot-pad immunized them against a second infection in the other rear foot-pad. Purified bacilli harvested from the first infection also produced immunity when injected into the foot-pads of previously uninfected mice. Injections of BCG afforded similar protection, but had no adjuvant effect on *M. leprae. M. duvali,* a cultivable mycobacterium that is reported to be more closely related antigenically to *M. leprae* than BCG is, provided much less protection against *M. leprae* challenge than BCG did. Moreover, when *M. duvali* was mixed with BCG, it was not any more effective than BCG alone. Graft-*versus*-host reactions, induced by injections of parental spleen cells into F1 hybrids, provided no protection against *M. tuberculosis* and *M. marinum* challenge. They gave moderate protection against *M. leprae* in one experiment but not in another with a different

schedule. Allogenic spleen cells had a protective effect when injected locally into the infected foot-pad. The effect produced by these injections of spleen cells was a delay in the appearance of bacterial growth; however, there was no decrease in the rate of logarithmic growth when it did appear and no reduction in the eventual plateau level.

3. CLINICAL ASPECTS

82. GANAPATI, R., DESHPANDE, D. H. & CHULAWALA, R. G. **Calcification of cutaneous nerves in leprosy—a case report.** *Lepr. India,* 1976, v. 48, No. 3, 309-310.

A boy aged 13 years, attending a leprosy clinic in Bombay, had an anaesthetic tuberculoid lesion on the front of the right forearm. There was thickening of the ulnar nerve and also of the cutaneous nerves in relation to the lesion. Firm nodular swellings along the course of the cutaneous nerves showed evidence of calcification on X-ray (the radiograph is reproduced). Calcification was also demonstrated histologically. The authors comment on the rarity of reports of nerve calcification in leprosy but suggest that if more radiological and histological studies were undertaken more such cases would be revealed.

F. I. C. Apted

83. ISHIHARA, S. [**A case report on leproma in the tongue.**] *Lepro,* 1975, v. 44, No. 4, 199-201. [In Japanese.]

The English summary appended to the paper is as follows:

"A male patient aged 75 had complained of the paresthesia on the both soles about 10 years ago. He noticed the nodules on bilateral earlobes, and swelling of the face in 1970. He had been not registered as leprosy, and had been treated as a heart disease until October, 1973.

"On that time he had been diagnosed as lepromatous leprosy and admitted to National Suruga Leprosarium. The patient had remarkable lepromatous lesions in the oral cavity, uvula, soft and hard palate and tongue together with skin lesions.

"One of the lepromas of the tongue, sized 3 mm x 4 mm, was taken off surgically and it was observed histopathologically. The mucous membrane is thinner than usual without rate pegs. Submucous tissue is occupied by masses of leprous infiltration, without 'free zone'. And the leprous infiltration invade into the muscle tissue of the tongue. Many acid-fast bacilli are detected in the leproma.

"Since he had been treated over 1 year with DDS, lepromas of the tongue clinically disappeared, and also the sense of taste has gradually recovered."

[The appearances of the tongue before and after treatment, and the histological changes, are illustrated in photographs.]

84. FLEURY, R. N., OPROMOLLA, D. V. A., TOLENTINO, M. M. & TONELLO, C. J. S. Hanseniase virchoviana do couro cabeludo. [**The scalp in lepromatous leprosy.**] *Hansenologia Int.,* 1976, v. 1, No. 1, 25-32.

The English summary appended to the paper is as follows:

"A study was made of the scalp involvement in 30 males suffering from active Virchowian hanseniasis (lepromatous leprosy). Clinical evaluations were made before and after the patients' heads were shaved and 4 'punch' biopsies were performed in standardized locations. The results showed that shaving increased the possibility of detection of clinical lesions, which are present in the large majority of the patients. These lesions were principally of the macular form. The results also showed the existence of alopecia related to the specific process. Histopathologically,

all patients showed signs of specific involvement either by the presence of infiltration or by the presence of bacilli in the core of infiltrated mononuclears. In spite of this involvement, it could not be compared with that observed in the rest of the skin. The infiltrated areas were always discretely regressive. Bacilli were always few and granular. This finding demonstrates the anatomical peculiarities of the scalp, which is not a suitable locus for the development of bacilli."

4. THERAPY

85. BULL. WLD HLTH ORG., 1976, v. 53, No. 4, 425-433. **Experimental chemotherapy in leprosy.**

The Memorandum reviews the considerable progress that has been made in research on the chemotherapy of leprosy during the last 10-15 years, as a result of which it is now possible to study the same topics in leprosy as are studied in other bacterial diseases. Thus drugs have been screened in mice for their activity against *Mycobacterium leprae.* Those that have been found to have the greatest activity against *M. leprae* at acceptable dosages—dapsone, rifampicin, and clofazimine—have been characterized in terms of the minimal effective dosage and rate of bacterial kill. Similarly, their pharmacokinetics in man and in certain animals have been defined. The theoretical basis for drug trials in leprosy patients is discussed in terms of the number of viable and the number of dead *M. leprae* that remain at various stages of therapy.

[There are 59 references.]

86. GANAPATI, R., NAIK, S. S., SHAH, M. H., SHIRSAT, L. S. & GAITONDE, B. B. **Clinical trial of DADDS in lepromatous leprosy.** *Lepr. India,* 1976, v. 48, No. 3, 238-243.

Injection of 225 mg acedapsone (DADDS) every 70 days to 23 patients with lepromatous leprosy produced clinical regression noticeable shortly after the second injection. Three to 7 injections led to a fall in the morphological index from 5.0-0.6. Erythema nodosum leprosum was encountered in 7 patients and it is thought advisable to discontinue dapsone when this complication occurs. Dapsone levels in the blood were found to be more than 10 ng/ml before each fresh administration of acedapsone. The trial extended to 7 injections.

T. F. Davey

87. BARNETSON, R. ST C., PEARSON, J. M. H. & REES, R. J. W. **Evidence for prevention of borderline leprosy reactions by dapsone.** *Lancet,* 1976, Nov. 27, 1171-1172.

Sixty-eight patients were included in a prospective study of the treatment of borderline leprosy. Thirty-four were treated with dapsone 5 mg daily, and 34 with 50 mg daily. Reversal reactions developed in 11 of those on 5 mg daily and in 3 of those on 50 mg daily. The statistically significant difference between the 2 treatment groups indicates that, contrary to previous teaching, dapsone given in higher dosage does not predispose patients to reversal reactions and indeed may prevent them.

88. CARAYON, A. Limites actuelles de la chimiothérapie antihansénienne sur la névrite et danger de ses effets secondaires immunologiques. **[Current limitations of anti-leprotic chemotherapy for neuritis and danger of secondary immunological effects.]** *Méd. Afr. Noire,* 1976, v. 23, No. 10, 567-577.

From his long and wide field experience in Africa, the author gives timely warnings against generalizations in the treatment of leprosy. Since the pathology of nerve damage is complex

and multifactorial, treatment that is successful in controlling the disease may have little effect, or an adverse effect, on the appearance or worsening of damage to peripheral nerves. The action of anti-leprotics on leprosy bacilli present within the nerves depends on such factors as diffusion of the drug and its relative solubility in lipids, and on such side-effects as rupture of the bacilli and of tissue cells. Another factor that has some bearing on the limitations of drug therapy is the apparent induction of suprarenal insufficiency through some little understood mechanism.

The author reviews the wide range of drugs now available for the treatment of leprosy and attempts to assess their place in the prevention and control of damage to the peripheral nerves. He favours clofazimine in the general treatment of multibacillary leprosy and suggests that, despite the fact that it does not enter the nerves themselves, it appears to exert its bacteriostatic effect by intracellular concentration in the neighbourhood of engulfed and multiplying bacilli.

The apparent effect of the various drugs on cellular immunity in relation to progressive nerve damage is briefly assessed and the indications for the use of rifampicin, clofazimine and the sulphonamides are reviewed, together with the action of the various anti-inflammatory products now available. He gives a warning against the use of drugs in borderline leprosy that might provoke dangerous degrees of cellular reaction, with resulting irreversible damage to peripheral nerve fibres.

This paper should be consulted in the original for its summary of wide-ranging work.

S. G. Browne

5. SURGERY

89. MILLER, S. H. & WOOD, A. M. **Surgical treatment of facial nerve involvement caused by leprosy**. *Am. J. Trop. Med. Hyg.,* 1976, v. 25, No. 3, 445-448.

Following a discussion of nerve damage underlying facial paralysis in leprosy, muscle transfer procedures are described: temporalis transfer to the eyelid, and masseter transfer to the mouth and nasolabial fold. These were found successful in small minimally equipped hospitals in

T. F. D[illegible]

90. NAMASIVAYAM, P. R. **A spiral splint for claw fingers**. *Lepr. India,* 1976, v. 48, No. 3, 258-260.

A simple spiral splint made from galvanized iron wire is described for use in early paralysis of the small muscles of the fingers and in claw fingers. This splint will prevent stretching of the weak or paralysed muscles by keeping the metacarpophalangeal joints of the fingers in slight flexion. It will also help to prevent flexion contractures of the interphalangeal joints by encouraging active extension of these joints.

91. ANTIA, N. H., VANKANI, B. & PANDYA, N. J. **Surgical decompression of the ulnar nerve in leprous neuritis**. *Lepr. India,* 1976, v. 48, No. 4, 362-370.

[illegible]ed extraneural and intraneural decompression without jeopardizing the vascular supply, in [illegible]e early cases gave satisfactory results in 41 ulnar nerve decompressions undertaken in this study.

Sensory as well as motor recovery was obtained. However, sensory recovery was more significant in all and also in each patient with motor recovery.

The recovery was better in patients seeking treatment within 6 months of the onset of the symptoms.

The patients with tuberculoid type responded better to the nerve release.

A funicular biopsy is a feasible and practical method not only to confirm the diagnosis but also to histologically classify the disease and provides a guide to the type of damage to the nerve.

6. EPIDEMIOLOGY AND CONTROL

92. NOORDEEN, S. K. **Leprosy in Lakshadweep Islands.** *Lepr. India,* 1976, v. 48, No. 3, 244-257.

This territory, under the administration of India, was surveyed for leprosy in 1961 and again in 1965-67, when a prevalence rate of 24.4 per 1000 was found, its features consistent with an active epidemic situation. A fresh epidemiological survey in 1974 by a very experienced leprologist is reported and indicates a continuing serious situation with a prevalence rate at 25.1 per 1000, and with incidence among non-contacts similar to that among contacts. There are encouraging features, such as very few open cases and most new patients having only minimal disease potentially unlikely to produce deformities.

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93. WKLY EPIDEM, REC., 1976, v. 51, No. 51, 389. **Leprosy control.** [In English and French.]

In 1971 a Leprosy Control Unit was established in Trinidad and Tobago, with the emphasis on an out-patient approach and on case-finding and case-holding. The intensification of case-finding efforts raised the average number of newly diagnosed cases from 46 per year for the period 1961-70 to 92 per year in 1971-75. At the end of December 1975 a total of 914 patients were on the registry. The prevalence is 0.86 per 1000 population. There are 10 clinics throughout the country. The disability rate fell from 70% in 1968 to 11% for the period 1971-75. This is attributed to the maintenance of regular chemotherapy and to the prompt treatment of reactional episodes. Sixty per cent of the cases diagnosed in the past 5 years are of the lepromatous type.

F. I. C. A.

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Immunology in Medicine

edited by E. J. Holborow and W. G. Reeves

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The aim of this book is to provide a succinct and practical guide to clinical immunology throughout the whole range of medicine. Its thirty-three expert contributors are all leading practitioners in the clinical fields of which they speak, and strike an intelligent balance between the academic and the clinical aspects of immunology which will be of vital interest to the busy practising physician, surgeon or pathologist. The range is wide, and enough basic information is provided to remove the need for prior knowledge of the subject. It should prove to be an invaluable and comprehensive reference work for all workers in the field of medicine.

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